1984

The carbene/carbenoid chemistry of lithium and tin cyclopropylidenoids

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The carbene/carbenoid chemistry of lithium and tin cyclopropylidenoids

by

Robert D. Herold

Volume 1 of 2

A Dissertation Submitted to the

Graduate Faculty in Partial Fulfillment of the

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Ames, Iowa
1984

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DEDICATION

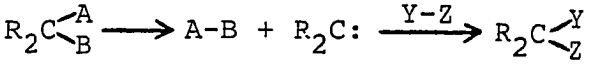
To my loving wife,

LuLu

INTRODUCTION

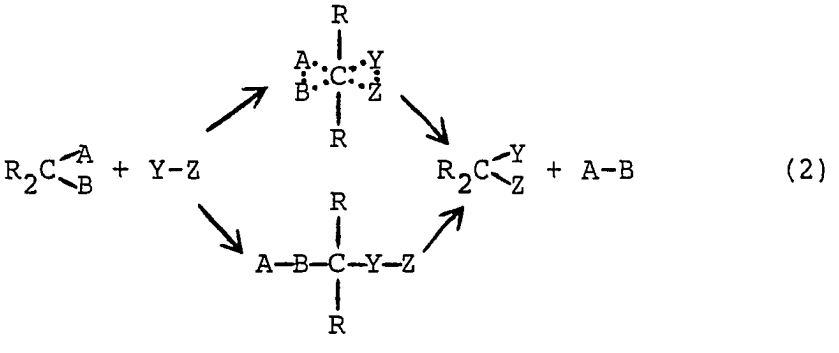
This introduction will begin with a general discussion of carbene vs. carbenoid reaction mechanisms, paraphrased from the discussion provided by Kirmse.[1]

The simplest way to visualize a methylene transfer reaction is the unimolecular mechanism shown in equation (1) below. It involves two steps: a) dissociation of the methylene donor (R_2CAB) to A-B plus a carbene, and b) reaction of the carbene with a methylene acceptor (Y-Z).



(1)

The other mechanistic extreme, shown in equation (2) below, is a bimolecular reaction between the methylene donor and the methylene acceptor, which leads to a concerted, or successive displacement of A and B by the groups Y and Z.



(2)

Very weak bonding of A and B to the carbon in the transition state of the bimolecular reaction minimizes the

difference between the unimolecular and bimolecular mechanisms shown in equations (1) and (2), respectively. The term "carbenoid" has been coined to classify such borderline cases of methylene transfer. (A similar gradation of mechanisms can exist between S_N1 and S_N2 reactions in solvolysis studies. In both fields of study, however, the first approximation provided by the unimolecular and bimolecular mechanisms can be quite useful.) A "carbenoid" is an intermediate which exhibits reactions qualitatively similar to those of carbenes, without actually being a free carbene, i.e. a free divalent carbon species. Although a carbene is structurally well defined, a carbenoid usually is not.

In the literature, "carbenoid" sometimes refers to a reactive intermediate which undergoes reactions typical of a carbene, but whose precise structure is not certain. In this dissertation, however, "carbenoid" will refer to such an intermediate which is not a free carbene.

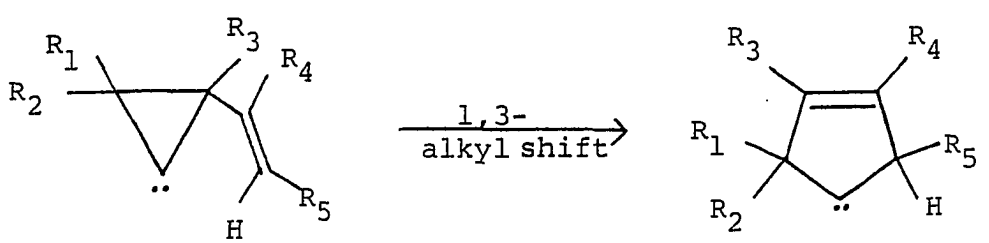
Chapter I of this dissertation will deal with the 1,3-rearrangement of 1-bromo-1-lithio-2-vinylcyclopropanes, in so far as it relates to the 1,3-rearrangement of 2-vinylcyclopropylidenes (the so-called "Skattebol rearrangement"[2,3]). Chapter II will concern itself with the conditions required in order for 7-bromo-7-lithiobicyclo[4.1.0]heptane to generate the corresponding cyclopropylidene. This study

relates directly to that conducted in Chapter I in the sense that it explores the question of whether it is reasonable to postulate free carbene intermediates for the rearrangement reactions of 1-bromo-1-lithio-2-vinylcyclopropanes. Chapter III will investigate the suitability of 7-bromo-7-trimethylstannylbicyclo [4.1.0] hept-2-ene for a study of the 1,3-rearrangement of bicyclo [4.1.0] hept-2-en-7-ylidene. Finally, Chapter IV will reinvestigate the pyrolysis mechanism of 7-bromo-7-trimethylstannylbicyclo [4.1.0] heptane, in an effort to ascertain whether a cyclopropylidene intermediate is really involved.

I. 1-BROMO-1-LITHIO-2-VINYLCYCLOPROPANE DERIVATIVES

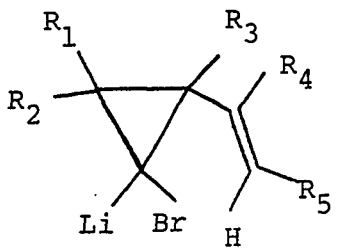
A. Introduction

The direct rearrangement of carbene 1 to carbene 2 is unique in that the divalent carbon atom retains its integrity. This particular type of carbene rearrangement has been dubbed "type II," as opposed to "type I," in which the divalent carbon of the rearranged carbene is different from that of the unrearranged carbene.[4] For simplicity, the 1,3-rearrangement of 2-vinylcyclopropylidenes will sometimes be referred to as the "Skattebol rearrangement," because Skattebol[2,3] discovered this type of reaction.



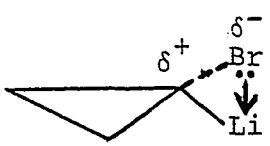
1 2

The remainder of this introduction section will describe the various searches for this rearrangement which have employed 1-halo-1-lithiocyclopropane precursors (3) to the cyclopropylidenes (1). α-Haloalkyllithiums like 3 are

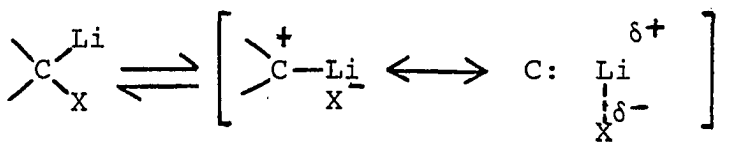


3

often referred to as carbenoids, because they can sometimes undergo reactions typical of the corresponding free carbenes. For simplicity, they are written as monomeric species with purely covalent C-Li and C-Br bonds. First of all, it is well-known that alkyllithium species exist as aggregates in solution. The particular aggregation state involved could conceivably affect the chemistry observed for an intermediate like 3. Secondly, ^{13}C NMR evidence[5,6] indicates that the polar structure shown below



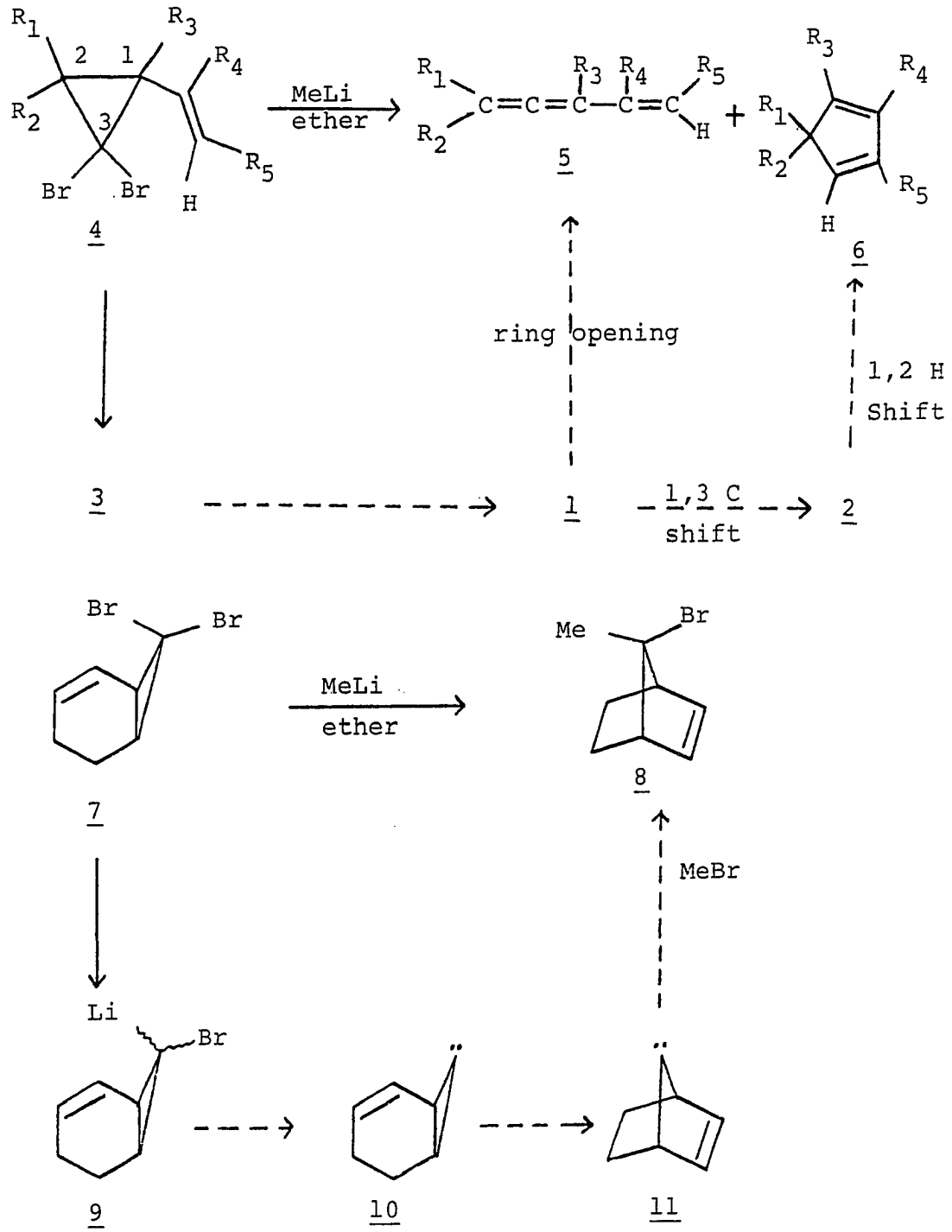
is actually quite important. This structure helps to explain reactions in which compounds like 3 suffer bromine displacement by nucleophiles. In fact, it has been suggested,[7] on the basis of various experimental results, that carbenoid reactions of α-haloalkyllithiums probably proceed through intermediates which are somewhere between the covalent and ionic extremes pictured below.



(covalent) (ionic)

In the 1960s, Skattebol discovered that when dibromides such as 4 (Scheme I) are treated with methyllithium, allenes (5) and cyclopentadienes (6) are formed. Product 5 obviously arises from a cyclopropane ring-opening reaction of carbene 1 (or a carbenoid related to structure 3). Compound 6, however, is most reasonably accounted for by a 1,3-rearrangement of carbene 1 (or a carbenoid related to structure 3). The fact that the 1,3-bond, and not the 1,2-bond, is broken during this rearrangement was proven by ^{12}C labelling experiments.[8] The resulting carbene, 2, could then generate 6 via a 1,2-H-migration. While admitting

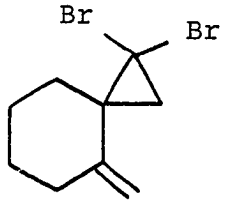
Scheme I:



that carbenoid intermediates might actually be involved, Skattebol,[2,3] for the sake of simplicity, wrote the 1,3-rearrangement as involving the free carbene 1, as illustrated in Scheme I. Even more intriguing was the result obtained from a similar methyllithium treatment of dibromide 7. Instead of an allene or a cyclopentadiene, product 8 was obtained stereoselectively in 80% isolated yield! A sequence of carbene generation and rearrangement, involving intermediates 9, 10, and 11, was again invoked as a possible mechanism. The resulting rearranged carbene 11, however, cannot undergo a 1,2-H-migration in the manner in which carbene 2 can. Instead, it might be expected to insert into methyl bromide, as is proposed in Scheme I. Skattebol[2,3] admitted that the stereoselective formation of 8 is very perplexing within the framework of his proposed carbene rearrangement mechanism. This point will be returned to later.

Reinarz and Fonken[9] observed a very profound dependence of the product distribution upon the stereoconfiguration of the double bond relative to the cyclopropane ring of the cyclopropylidene precursor. They found that methyllithium treatment of 12 (a fixed s-cis isomer) and 13 (which has interconvertible s-cis and s-trans isomers) produced only cyclopentadiene products, while similar treat-

ment of 14 (a fixed s-trans isomer) produced only allene type products. Methyllithium treatment of 15 (a fixed s-cis isomer), on the other hand, resulted in only an allene product, evidently because the expected cyclopentadiene product would be too severely strained.



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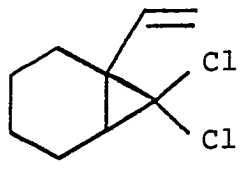

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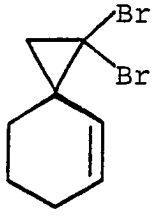

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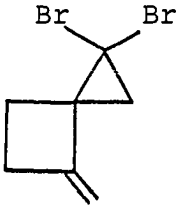
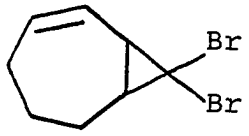


15

Baird and Reese,[10] in 1976, extended the Skattebol rearrangement to include the carbenoid precursors 16 and 17a. They were careful in their study to mention that the reaction could involve either carbene or carbenoid intermediates. In another study, working with an isomer of 16, i.e., 7,7-dibromobicyclo[5.1.0]oct-3-ene (17b), they dis-



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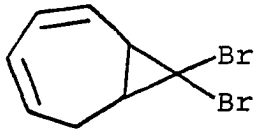
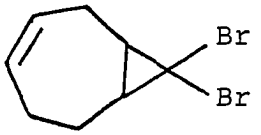


17a



17b

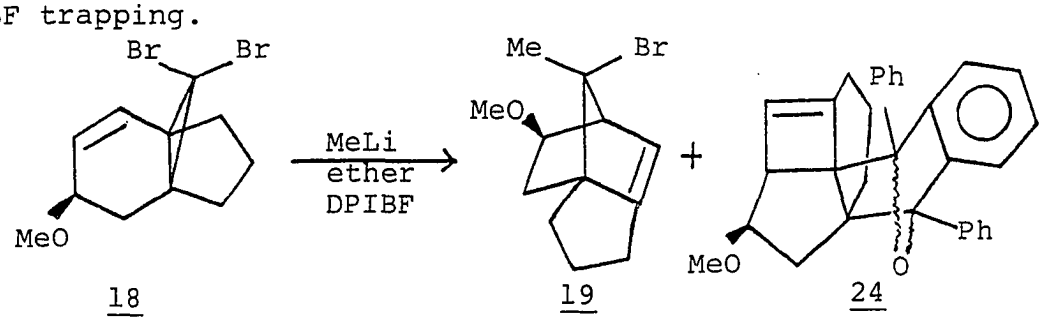
covered an example of a type II carbene (or carbenoid) rearrangement which does not involve a 1,3-alkyl shift.[11]

In recent years, the Skattebol rearrangement has proven to be of some synthetic utility,[12-15] and has also been

extended by Brinker and Fleischhauer[16] to include 1-bromo-1-lithio-2-(buta-1,3-dienyl)cyclopropanes.

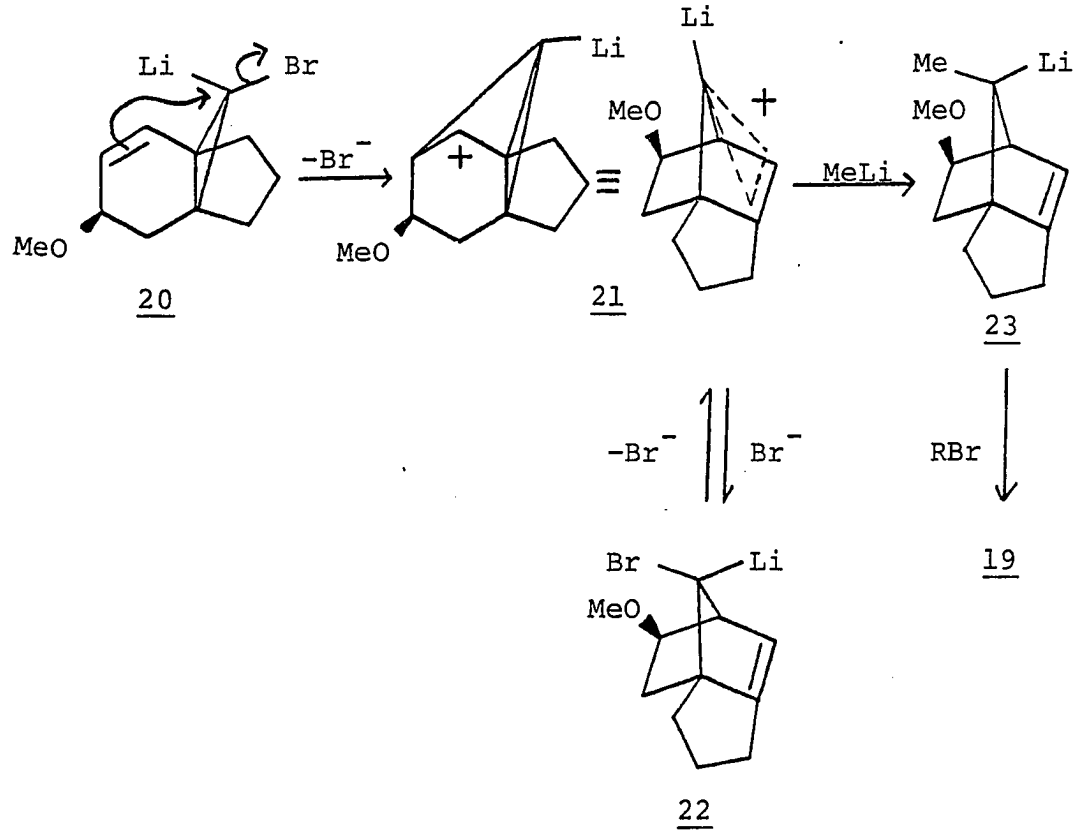
Schoeller and Brinker[17] performed MINDO/3 calculations which suggested that the rearrangement of 2-vinylcyclopropylidene to cyclopent-3-enylidene is initiated by a complexation of the πMO of the double bond with the empty p AO at the carbene cite of 2-vinylcyclopropylidene. Surprisingly, however, investigations into the carbene vs. carbenoid mechanistic question have been extremely rare.

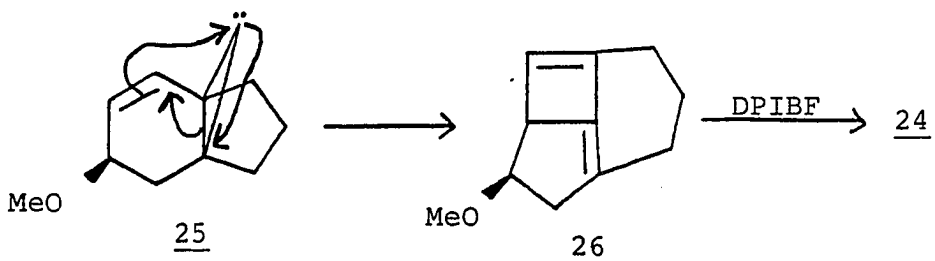
Warner and Chang,[18-20] in the late 1970s, proved compelling evidence that 18 (the tricyclic analogue of 7) reacts with methyllithium, in the presence of DPIBF (1,3-diphenylisobenzofuran), to give 19 (the tricyclic analogue of 8) via a carbenoid rearrangement sequence involving alkyllithium intermediates 20 through 23, as is illustrated in Scheme II. This mechanism quite handily explains the stereoselective generation of 19 (and by implication that of 8 also). There was some evidence that product 24 may have resulted from the direct rearrangement of free carbene 25 to diene 26, followed by DPIBF trapping.



18 19 24

Scheme II:

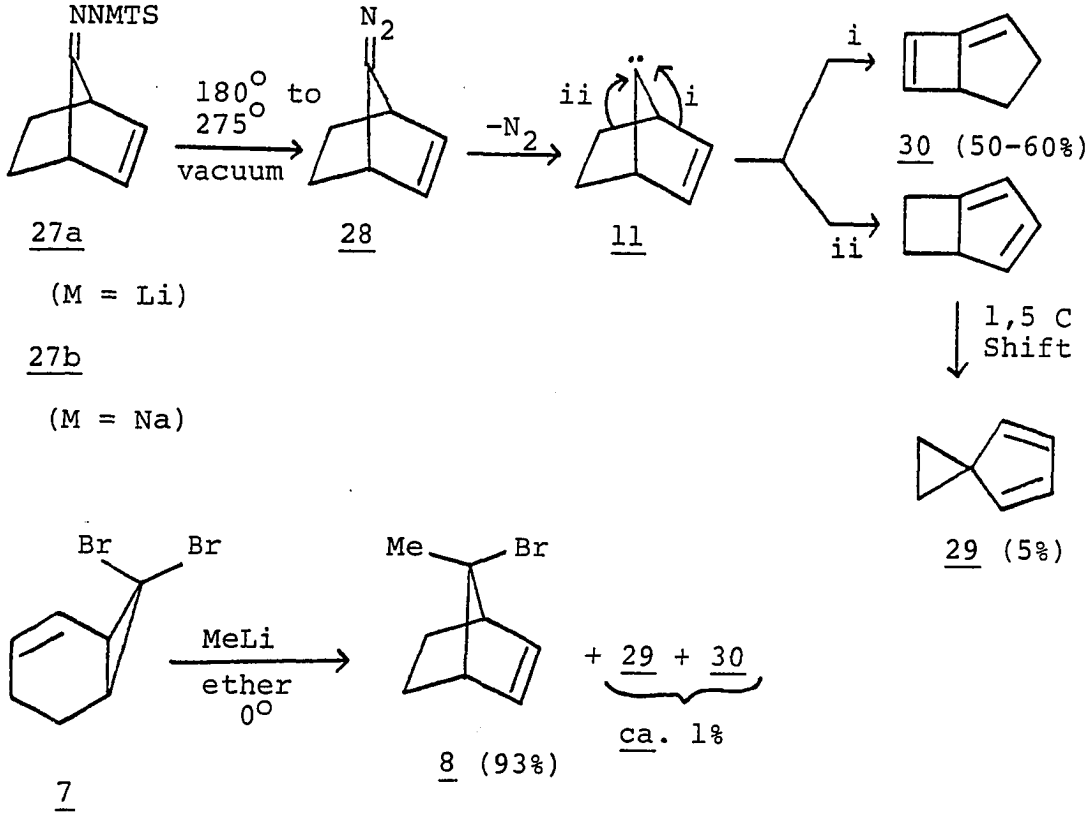




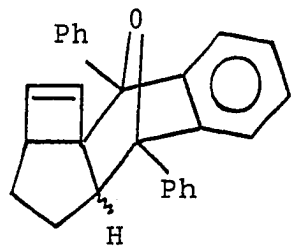
More recently, Brinker and Ritzer[21] carried out a mechanistic study of the methyllithium reaction of dibromide 7. Noting that in the gas phase carbene 11 (generated from 27a or 27b, via diazo compound 28, as shown in Scheme III) was known to produce 29 and 30 as major prod-

ucts.[21-24] Brinker and Ritzer[21] decided to search for such products among those from the methyllithium reaction of 7. In ether solution, only trace amounts (1%) of 29 and 30

Scheme III:



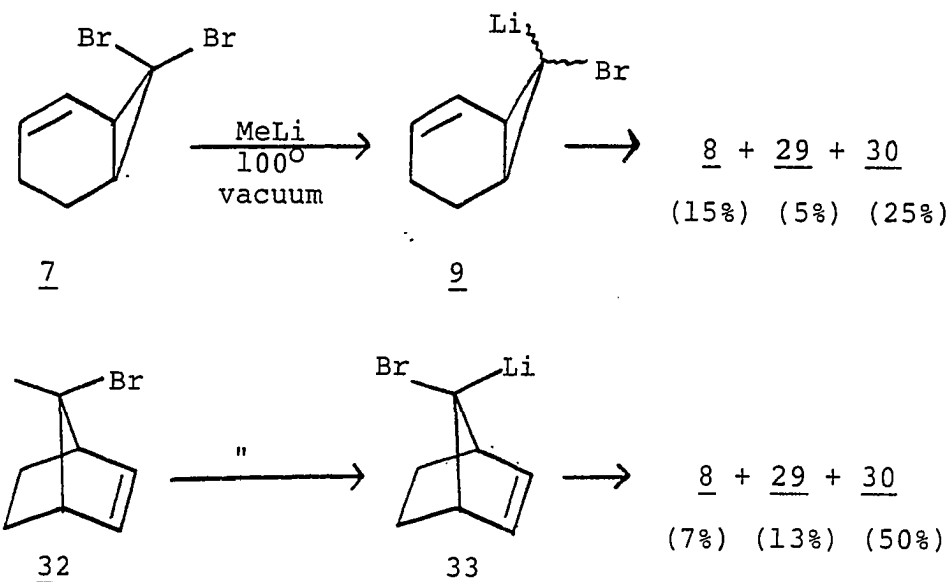
could be detected among the products. The presence of 12-crown-4-ether or N,N,N',N'-tetramethylethylenediamine did not increase the yields of 29 and 30. (Our research group discovered that when both 12-crown-4-ether and DPIBF were present, no more than a trace amount of 31, the expected Diels-Alder trapping product of 30, was formed.[25])



31

By flow pyrolysis through a hot tube packed with methyllithium-coated glass turnings, Brinker and Ritzer[21] were able to study the "gas-phase" methyllithium reaction of 7. As is shown in Scheme IV, 29 and 30 were indeed major products from the reaction of 7 (and also of its norbornenyl isomer 32). They concluded that they had thus

Scheme IV:



succeeded in shifting the chemistry of 9 and 33 away from carbenoid chemistry (in solution), toward free carbene

chemistry (in the gas phase). While they may have been correct, it is, however, quite possible that the rearrangements were actually surface phenomena, involving carbenoid reactions. Since they did not run any pyrolyses in the presence of carbene traps, the mechanisms are still open to question. Thus, there still exists no conclusive evidence that the 1,3-rearrangement of carbene precursors such as 9 involves anything other than carbenoid intermediates (related to structures 9 and 33) under any conditions so far investigated.

Because of the study of systems such as 18, conducted by Warner and Chang,[18-20] it has become more widely accepted[21] that, in solution, the 1,3-rearrangement of carbene precursors such as 9 proceeds by way of a carbenoid rearrangement. We nonetheless desired further evidence in this regard. Warner and Chang[18-20] had, in the course of their investigations, received some indications that the stereoisomer depicted by structure 20 in Scheme II undergoes 1,3-rearrangement more readily than its C^{10} epimer, due to the double bond participation (pictured in Scheme II) which is possible for the former, but not for the latter. Careful studies, however, remained to be carried out. It is the purpose of section B to: a) report the careful product and rate studies which were carried out on the reac-

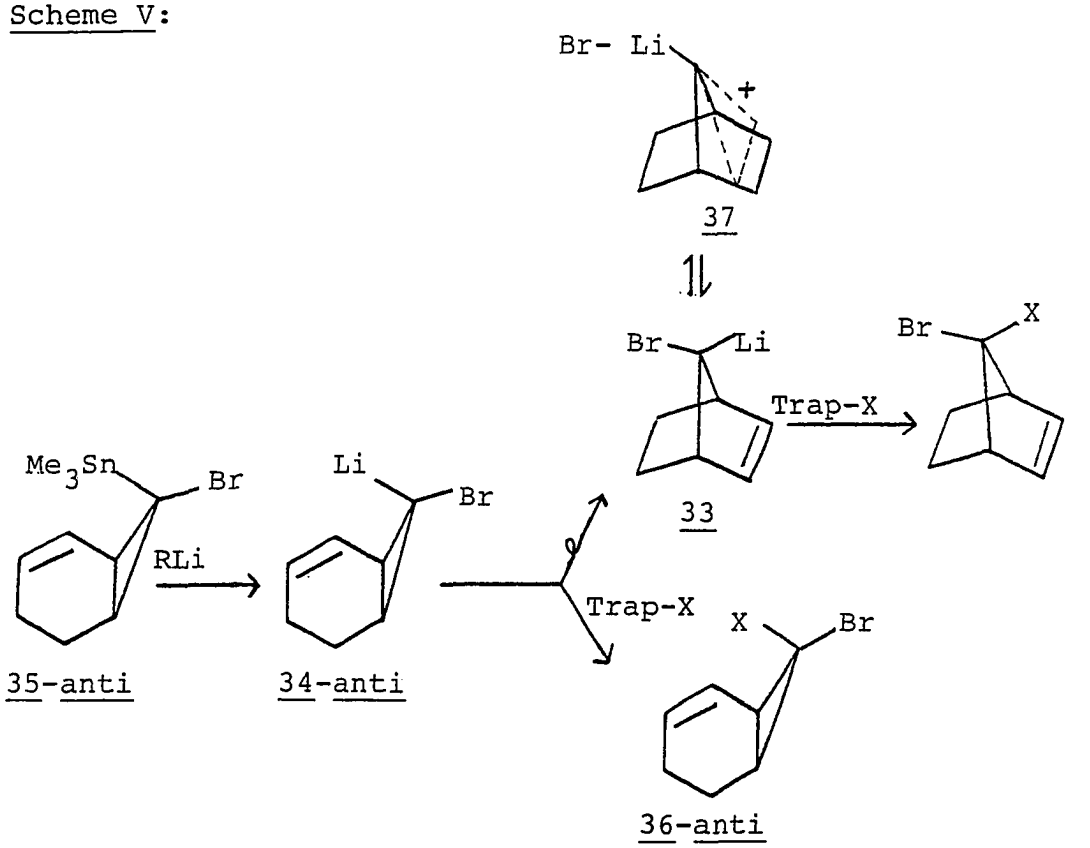
tions of the two epimers of carbene precursor 9, and to b) describe mechanistic studies which were carried out with some derivatives of 9. A discussion of non-alkyllithium precursors of cyclopropylidene 10 will be reserved for Chapter III.

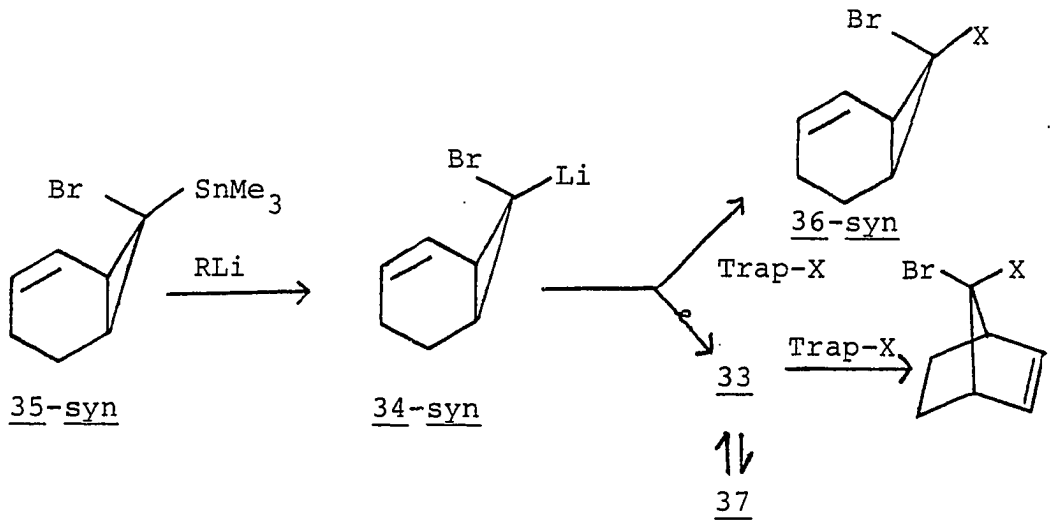
B. Results and Discussion

1. Reactions of 7-bromo-7-lithiobicyclo [4.1.0] hept-2-ene

As shown in Scheme V, in order to stereospecifically generate carbenoids 34-anti and 34-syn, the corresponding trimethylstannyl compounds 35-anti and 35-syn were separately treated with an alkyllithium. It is well-known that alkyllithiums promote trimethylstannyl-lithium exchange more rapidly than they undergo bromine-lithium exchange with compounds such as 35-anti and 35-syn.[26,27] It was anticipated that, under the proper conditions, 34-anti and 34-syn (the unrearranged carbenoids) could be trapped as 36-anti and 36-syn, respectively, and that the rearranged carbenoid 33/37 could be trapped. The resulting trapping yields of unrearranged and rearranged carbenoids could then be used to estimate the relative rearrangement rates of 34-anti and 34-syn. If the rates were different, evidence would then have been obtained that the 1,3-rearrangement really does involve carbenoid intermediates, and

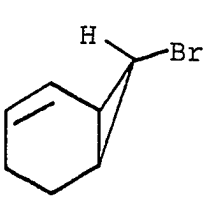
Scheme V:


Br- Li
+
37
Br
Li
Trap-X
Br
X
33
Me3Sn
Br
RLi
Li
Br
35-anti
34-anti
Trap-X
X
Br
36-anti

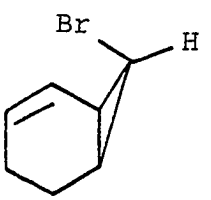

Br
SnMe3
RLi
Br
Li
Br
X
36-syn
Trap-X
Br
X
Trap-X
33
35-syn
34-syn
37

not free carbenes. (One must worry, of course, that different rearrangement rates might merely signal different rates for forming the same carbene from 34-anti and 34-syn, followed by carbene-carbene rearrangement. Thus, some additional evidence concerning the intermediacy of free carbenes would be fruitful.)

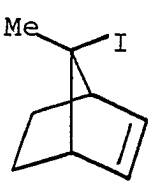
The preliminary set of conditions investigated (Conditions A) involved the treatment of 35-anti or 35-syn with n-butyllithium in ether at -78°, followed by the addition of methyl iodide as a carbenoid trap. In each experiment, the crude NMR spectrum and the GC-MS indicated that the major product was a bicyclo [2.2.1] hept-2-ene derivative. Along with n-butyltrimethyltin, GC-MS analysis detected variable amounts of 38-anti, 38-syn, 39 through 41, 42-syn, and 42-anti. Compounds 39 through 41 were only tentatively



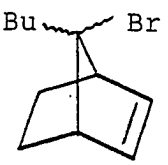
38-anti



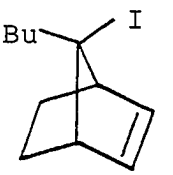
38-syn



39



40



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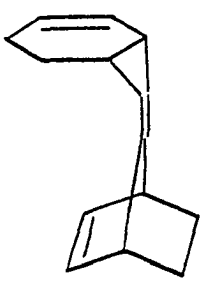
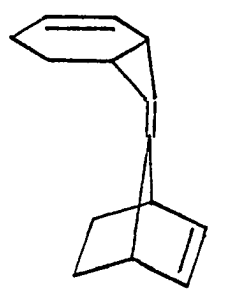


42-syn



42-anti

identified by a combination of crude NMR spectra and GC-MS analyses. Their stereochemistries were tentatively assigned on the basis of mechanistic considerations (Scheme VI). The structure proofs for 42-syn and 42-anti will be discussed later. The reaction times and the relative amounts of these products for several experiments are listed in Table I. It is clear from the data in Table I that the major product obtained from 35-anti after a 60 minute reaction time (experiments 1 and 2) was compound 40, while the major product after only a 6 minute reaction time (experiments 3 and 4) was compound 39. When 35-syn was reacted for 6 minutes (experiment 5), 41 was the major product, but a significant amount of 40 was also formed.

Possible mechanisms for the formation of 38 through 41 are depicted in Scheme VI. Precedence for the proposed mechanisms can be found in the work of Warner and Chang.[18-20] The mechanism for the formation of 42-syn and 42-anti will be deferred to a later part of this section. It is clear that carbenoids 34-anti and 34-syn stereorandomize under Conditions A, since stereorandomized (38-anti + 38-syn), presumably formed via proton abstraction from solvent, was observed. This effect might merit more careful future study. Since, in the 60 minute reaction of 35-anti, there are two reasonable ways to form product 40 (path a through intermedi-

Table I. Reaction of carbenoids 34-anti and 34-syn under Conditions A[a]

Expt.	SM	No. mg SM	No. equiv. n-BuLi	Time (min.)[b]
1	35-anti	44.6	2.0	60
2	35-anti	35.5	3.0	60
3	35-anti	46.0	2.5	6
4	35-anti	56.4	2.5	6
5	35-syn	47.9	2.6	6

[a]For description of Conditions A, see text and experimental section.

[b]Reaction time prior to the methyl iodide quench.

[c]Uncorrected (assuming all the relative GC response factors to be 1.0) mass ratios from GC-MS (Column C) quantitation.

[d]Determined by GC-MS (Column C) quantitation.

[e]Measured by NMR integration of the bridgehead protons vs. an internal standard.

[f]Measured as in footnote e, but using the trimethylstannyl protons of 35-anti.

[g]Not entirely clear because the mass spectra of some of the small GC peaks were not investigated.

Amt. recov. SM[c]	Amt. (38-anti +38-syn)[c]	Amt. 39[c]	Amt. 40[c]	Amt. 41[c]	Amt. 42-syn +42-anti[c]	Ratio 38-syn:38-anti[d]
3.7	4.4	0.6	46(49)[e]	3.0	4.9	1:1.8
0.7	1.4	1.3	39	9.2	16	1:1.2
22(23)[f]	3.4	44(45)[e]	8.8	4.2	5.5	1:1.5
0	2.0	55(60)[e]	8.6	3.1	3.3	1:1.2
0	ca.4.5[g]	2.9	6.9	23(17)[e]	25	?[g]

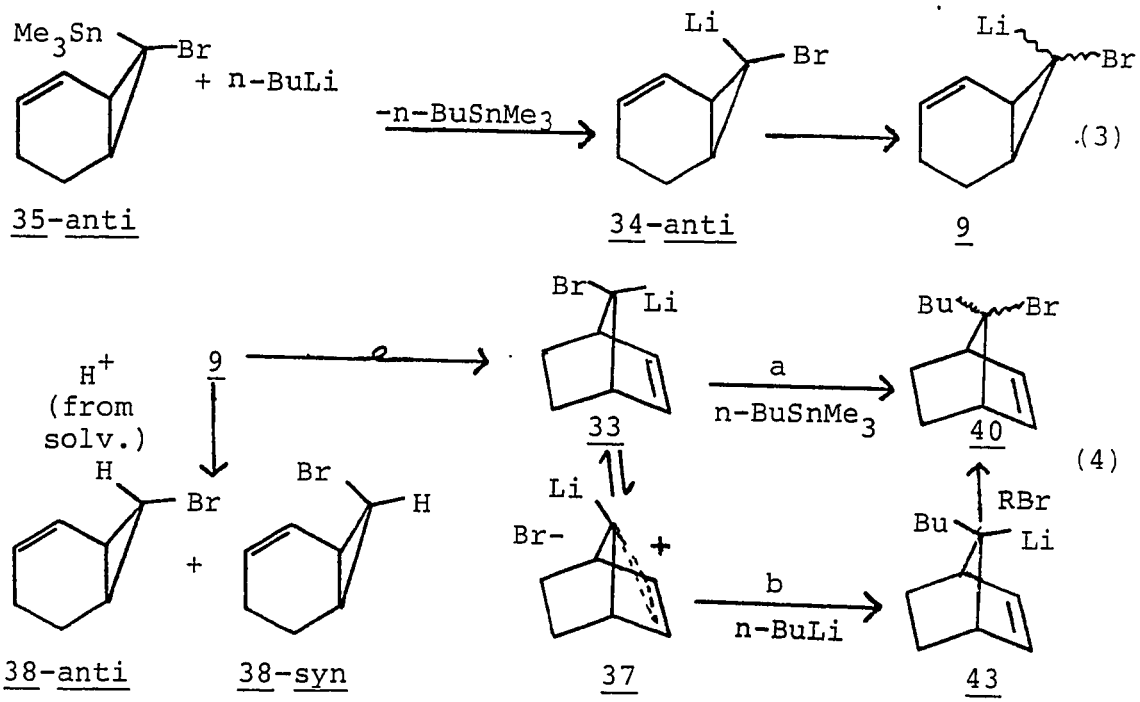
ate 33, and path b through intermediate 43), shown in equation (4), one expects stereorandomized 40 to be formed. For the 6 minute reaction of 35-anti, as shown in equations (5) through (7), the very slow initial trimethylstannyl-lithium exchange causes the entire reaction to evidently occur during the warmup after the methyl iodide addition. (Excess n-butyllithium was necessary in order to get a reasonable rate of trimethylstannyl-lithium exchange. Treatment of an ether solution of 35-anti with 1.1 equivalents of n-butyllithium for 10 minutes at -78° prior to the methyl iodide quench resulted in a ca. quantitative recovery of starting material. Treatment with 1.6 equivalents of n-butyllithium for 6 minutes at -78° prior to the methyl iodide quench gave a 39% recovery of starting material, along with a 23% yield of 39, both measured by NMR. Finally, treatment of 35-syn with 1.6 equivalents of n-butyllithium for 6 minutes at -78° prior to the methyl iodide quench gave a 41% recovery of starting material, along with an 11% yield of 41, both measured by NMR.) The intermediacy of 44 implies that 39 should be formed stereoselectively during the 6 minute reaction of 35-anti. Equations (8) and (9) demonstrate how a mixture of 40 and 41 can be formed from 35-syn.

Complete characterizations of 39 through 41 and corrected yield measurements were not obtained, because

it was obvious that, due to the slow initial trimethylstannyl-lithium exchange, and the resulting stereorandomization of carbenoids 34-anti and 34-syn, Conditions A could allow no differentiation to be made between 34-anti and 34-syn.

Scheme VI:

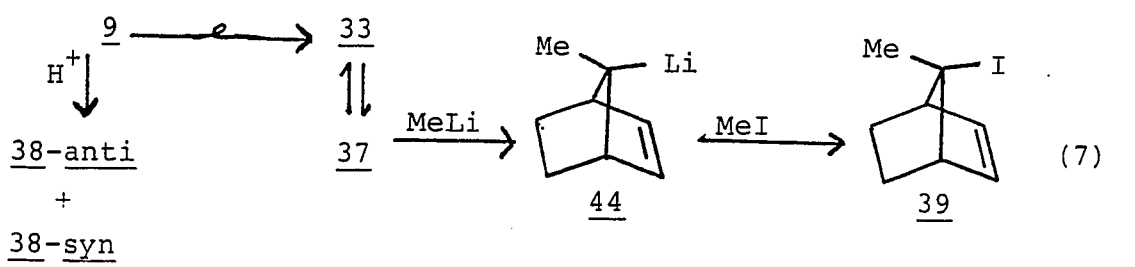
35-anti, 60 min. rxn.:



35-anti, 6 min. rxn.:

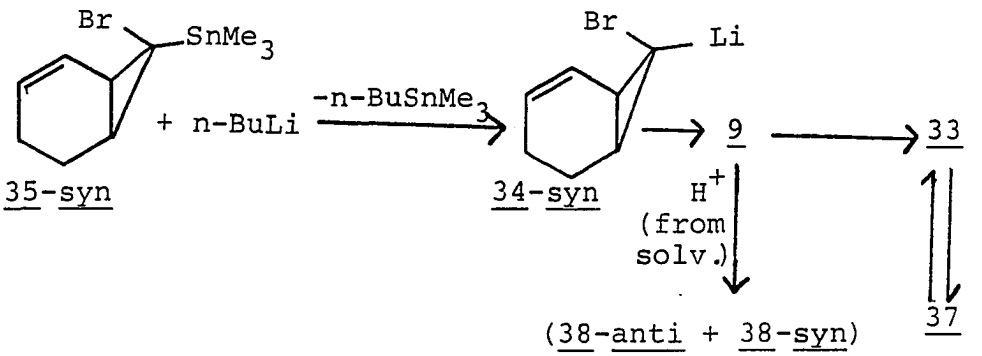
n-BuLi + MeI ⟶ n-BuI + MeLi (5)

35-anti + MeLi ⟶ 34-anti ⟶ 9 (6)

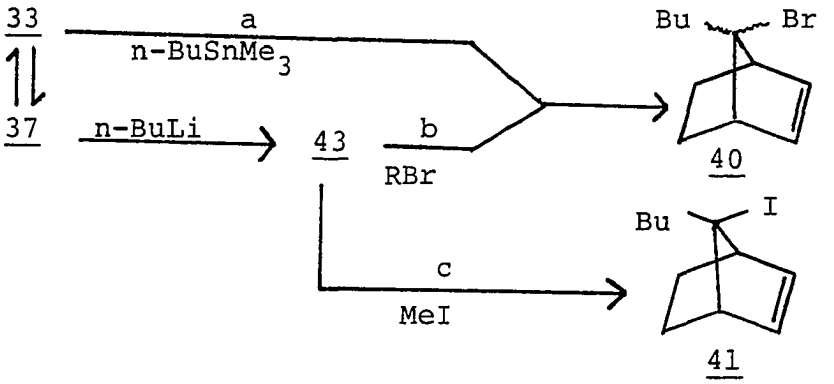


Scheme VI (Continued):

35-syn, 6 min. rxn.:



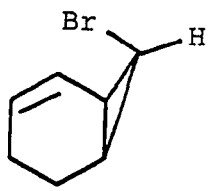
(8)



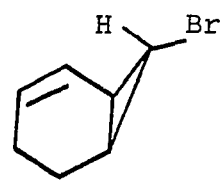
(9)

It was felt, on the basis of precedent,[7] that changing the solvent from ether to THF would cause a faster initial trimethylstannyl-lithium exchange, and thereby allow for a differentiation of the chemistry of 34-anti from that of 34-syn. The second set of experiments (Conditions B) was, therefore, conducted in THF with 35-anti and 35-syn and n-butyllithium at -90° to -95°, with methyl iodide as the carbenoid trap. The major products obtained were 38-anti, 38-syn, 42-syn, and 42-anti. It

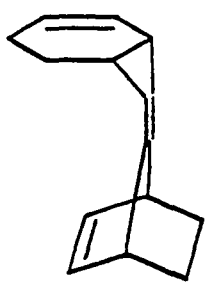
was very clear that the methyl iodide was not functioning as a carbenoid trap, and that the carbenoids 34-anti and 34-syn were reacting during the warmup after the methyl iodide addition. Nevertheless, closer scrutiny of the data (Table II) reveals that 34-anti actually generates 42-syn and 42-anti faster than does 34-syn.



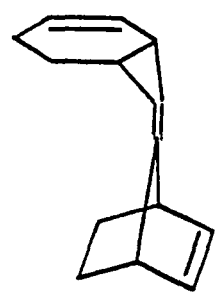
38-syn



38-anti



42-syn



42-anti

In order to obtain more quantitative information concerning the relative reaction rates of carbenoids 34-anti and 34-syn, it was decided to utilize a much more efficient carbenoid trap, i.e., methanol-O-d, but to still use the n-butyllithium/THF reaction system (Conditions C) at either -90° to -95°, or -78°. These new conditions did finally allow for the convenient differentiation of the chemistry of 34-anti from that of 34-syn.

Table II. Reaction of carbenoids 35-anti and 35-syn under Conditions B[a]

Expt.	SM	No. mg SM	No. eq. n-BuLi	Time[b] (min.)
1[d]	35-anti	45.8	1.6	15
2[d]	35-anti	50.6	1.6	5.5
3[d]	35-syn	50.3	1.6	5
4[d]	35-anti	40.4	1.4	5
5[d]	35-syn	39.8	1.4	6
6[h]	35-syn	47.9	1.5	5

[a]For description of Conditions B, see text and experimental section.

[b]Reaction time prior to the methyl iodide quench.

[c]Yield measured by NMR integration of the olefinic hydrogens vs. an internal standard.

[d]The methyl iodide was added as a THF solution.

[e]Not analyzed by GC-MS.

[f]Ratio obtained from GC-MS quantitations, with the appropriate GC correction factors.

[g]Ratio obtained from NMR integration.

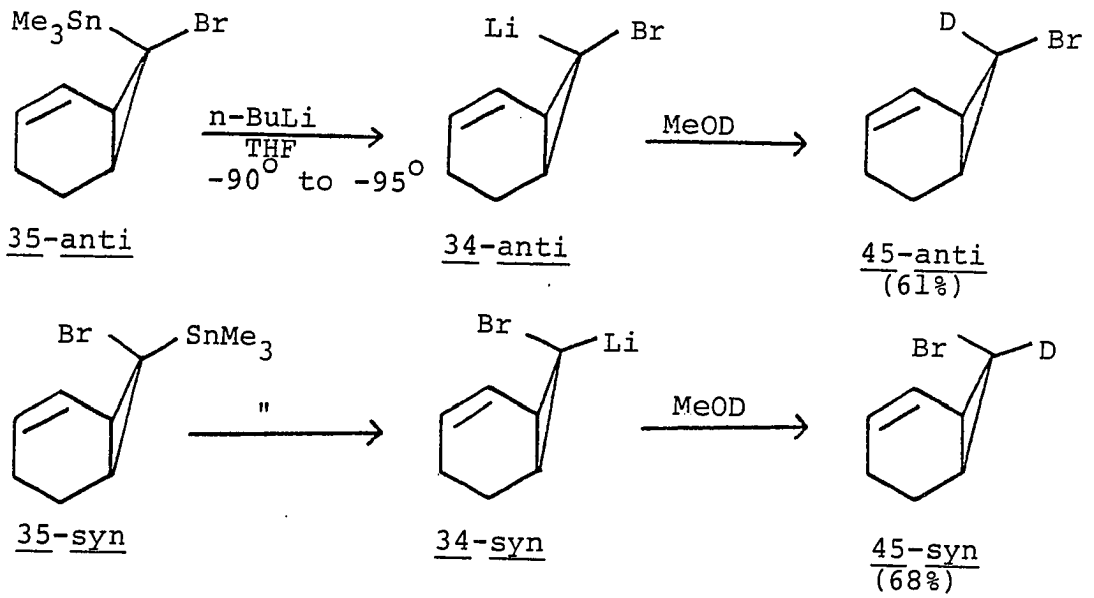
[h]The methyl iodide was added as a hexane solution.

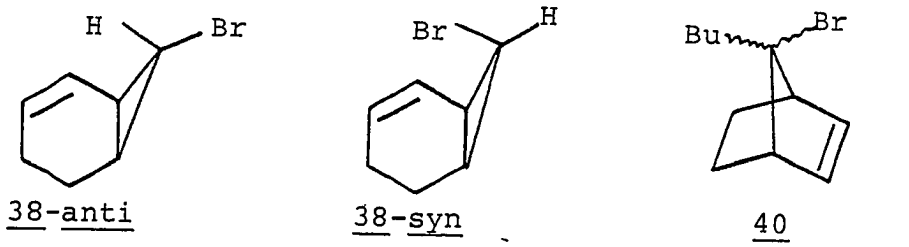
%Yield[c] 38-syn	%Yield[c] 42-syn + 42-anti	Ratio 38-anti: (42-syn+ 42-anti)	Ratio 38-syn: (42-syn+ 42-anti)	Ratio 38-syn: 38-anti
	59	?[e]		?[e]
	54	1:3.3[f]		1:5.7[f]
28	22		2.5:1[g]	?[e]
	56	1:5[f]		1:18[f]
41	17		4.8:1[g]	53:1[f]
25	35		1.4:1[g]	37:1[f]

Treatment of 35-anti or 35-syn under Conditions C at -90° to -95° (Scheme VII) resulted in either 45-anti or 45-syn, respectively, as the major product (Table IIIa). These results demonstrate the stereospecificity of the initial trimethylstannyl-lithium exchange, which was expected on the basis of precedent.[26,27] Minor amounts of 40, 46 and 47 (all tentatively identified by GC-MS analysis), as well as 42-syn and 42-anti were also formed (Table IIIb). The formation of product 47 is significant, since it implies that a small amount of bromine-lithium exchange does occur in 35-anti.

Then, n-butyllithium treatment of 35-anti or 35-syn under Conditions C at -78° produced major amounts of 42-syn and 42-anti admixed with either 45-anti (plus 38-anti) or 45-syn (plus 38-syn), respectively. The structures of 42-syn and 42-anti were elucidated by the usual spectral and analytical techniques. Table IV is a compilation of portions of their 300 MHz NMR spectra. In isomer 42-syn, the double bond of the norcarenyl moiety evidently produces a sufficient distortion of the norbenyl π-system to cause a much larger $\Delta\delta_{AB}$ for this isomer (0.046 ppm) than for 42-anti (0.022 ppm). Considering the data in Table Va, it is noteworthy that the %D incorporations for 38-anti/45-anti are generally much higher than for 38-syn/45-syn. This result implies that 34-syn suffers

Scheme VII:


Me3Sn
Br
n-BuLi
THF
-90° to -95°
Li
Br
MeOD
D
Br
35-anti
34-anti
45-anti
(61%)
Br
SnMe3
"
Br
Li
MeOD
Br
D
35-syn
34-syn
45-syn
(68%)


H
Br
Br
H
Bu
Br
38-anti
38-syn
40

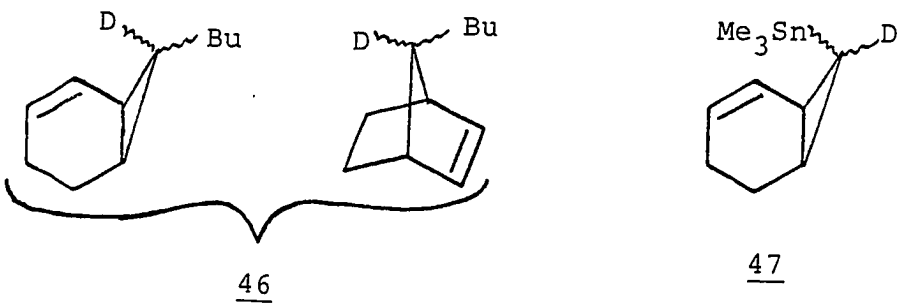

D
Bu
D
Bu
Me3Sn
D
46
47

Table IIIa. Reaction of carbenoids 34-anti and 34-syn under Conditions C at -90° to -95°[a]

Expt.	SM	No. mg SM	No. eq. n-BuLi	Time[b] (min.)
1	35-anti	55.1	1.5	5
2	35-syn	49.7	1.5	5

[a]For description of Conditions C, see text and experimental section.

[b]Reaction time prior to the methanol-O-d quench.

[c]Yield measured by GC integration vs. an internal standard, with correction factors applied. (Structure shown in Scheme VII).

[d]%D incorporation was calculated from mass spectral data as follows (P-1 was negligible):

$$\%D = \frac{^{175}\text{intens.} - \left[\frac{(P+1)^*}{P} \times {}^{172}\text{intens.}\right] + {}^{176}\text{intens.}}{^{174}\text{intens.} + {}^{175}\text{intens.} + {}^{176}\text{intens.}}$$

* Exptl. natural $(\frac{P+1}{P})$ ratio

%Yield[c,d] 45-anti	%Yield[c,d] 38-anti	%Yield[c,d] 45-syn	%Yield[c,d] 38-syn
61.2	10.1	1.2	0
2.0	0	67.5	10.1

Table IIIb. Yield data for 40, 42-syn, 42-anti, 46, and 47 (formed from 34-anti and 34-syn) under Conditions C at -90° to -95°[a]

Expt.	%Yield[b] (42-syn + 42-anti)	%Yield 46[c]	%Yield 47[c]	%Yield 40[c]
1	8	0.5[d] (53%D)[e] (2 GC peaks)	2.7[d] (84%D)[f]	0.2[d]
2	0	0.4[g] (100%D)[e] (1 GC Peak)	0.07[g] (?%D)[h]	0[g]

[a]For description of Conditions C, see text and experimental section.

[b]Yield measured by GC integration vs. an internal standard, with correction factors applied.

[c]Structure (Scheme VII) tentatively assigned from GC-MS data.

[d]Uncorrected GC yield, measured from the GC-MS (column C) ratio of the compound relative to (38-anti + 45-anti), assuming relative correction factors to be 1.0:1.0.

[e]%D incorporation calculated from the relative m/e 150 and 151 intensities, assuming the (P+1)/P ratio to be equal to the natural value of 12.18/100.

[f]%D incorporation calculated from the relative m/e 93 and 94 intensities, assuming the (P+1)/P ratio to be the same as the experimental value measured for the C_7H_8 portion of 38-anti and 38-syn.

[g]Uncorrected GC yield measured as in footnote d, but using (38-syn + 45-syn) as a reference. (The relative GC-MS response factors of 38-anti and 38-syn were measured as 1.0:1.0).

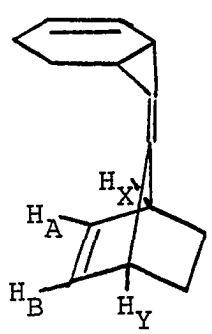
[h]GC peak too small to permit accurate %D calculation.

Table IV. 300 MHz NMR data ($CDCl_3$) for 42-syn and 42-anti

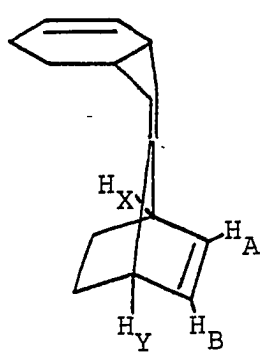
Compd.	δB,δA[a] or δA,δB	δY,δX[a] or δX,δY	ΔδAB (ppm)	ΔδXY (ppm)	J_{AB} (Hz)	J_{AX} (Hz)	J_{AY} (Hz)
42-syn[b]	6.148, 6.194	3.067, 3.134	0.046	0.067	5.9[c]	2.8[d]	0[e]
42-anti[b]	6.211 6.233	3.181	0.022	ca.0	6.0[c]	2.4[d]	1.1[e]

[a]In ppm downfield from tetramethylsilane.

[b]



42-syn



42-anti

[c,d,e]These coupling constants were measured via a decoupling study, and compare favorably with some average literature coupling constants (5.5, 2.9, and 0.7 Hz, respectively) for a series of 8 norbornenyl derivatives.[28]

Table Va. Reaction of carbenoids 34-anti and 34-syn under Conditions C at -78°[a]

Expt.	SM	No. mg SM	No. eq. n-BuLi	Time[b] (min.)
1 (VIII-14)[c]	35-anti	44.2	1.5	3
2 (VIII-11)[c]	35-anti	47.3	1.5	5
3 (VIII-44)[c]	35-anti	41.0	1.5	5
4 (VIII-13)[c]	35-syn	43.1	1.5	3
5 (VIII-12)[c]	35-syn	44.2	1.5	5
6 (VIII-45)[c]	35-syn	39.4	1.5	5
7 (VIII-22)[c]	35-syn	41.9	1.5	20
8 (VIII-46)[c]	35-syn	40.0	1.5	20

[a]For description of Conditions C, see text and experimental section.

[b]Reaction time prior to the methanol-O-d quench.

[c]Notebook number, followed by page number.

[d]Yield measured by NMR integration of the olefinic hydrogens vs. an internal standard. The ratio of stereoisomers was determined by GC-MS quantitation on Column C.

[e]Yield measured by GC integration (Column G) vs. an internal standard, with the appropriate correction factors applied. The ratio of stereoisomers was measured as in d.

[f]%D incorporation calcd. as in footnote d, Table IIIa.

[g]Yield measured by GC-MS quantitation (Column C) vs. an internal standard, with correction factors.

[h]Approx. %D incorp. from mass spectral data:

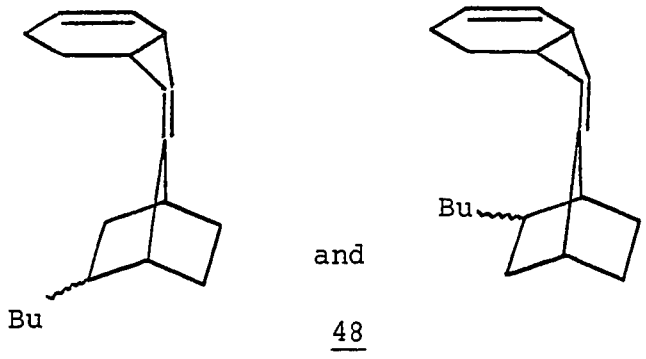
$$\%D = \frac{^{173}\text{intens.} - \left[\frac{(P+1)}{P}^{*} \times {}^{172}\text{intens.}\right]}{^{172}\text{intens.} + {}^{173}\text{intens.} - \left[\frac{(P+1)}{P}^{*} \times {}^{172}\text{intens.}\right]}$$

*Experimental natural $\frac{(P+1)}{P}$ ratio

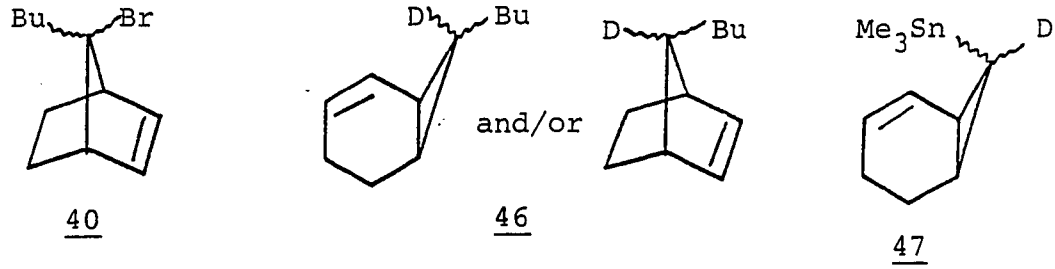
%Yield 42-syn	%Yield 42-anti	%Yield (38-anti + 45-anti)	%Yield (38-syn + 45-syn)
49[d](38)[e]	6.7[d](5.2)[e]	8.4[e](78%D)[f]	0.1[g]
56[d](43)[e]	7.5[d](5.7)[e]	11[e](12%D)[f]	0.4[g]
54[d](42)[e]	7.4[d](5.8)[e]	7.5[e](75%D)[f]	0.2[g](38%D)[h]
13[d](11)[e]	9.8[d](8.1)[e]	2.7[g](39%D)[h]	61[d](57)[e](55%D)[f]
14[d](13)[e]	10[d](9.4)[e]	1.9[g](21%D)[h]	52[d](49)[e](68%D)[f]
14[d](11)[e]	8.0[d](6.7)[e]	0.5[g](3.0%D)[h]	49[d](52)[e](74%D)[f]
23[d](22)[e]	17[d](17)[e]	0[g]	39[d](82%D)[f]
22[d](20)[e]	15[d](13)[e]	0.3[g](0%D)[h]	36[d](33)[e](68%D)[f]

protonation by solvent to a much greater extent than does 34-anti, probably due to steric effects.

Minor quantities of 40 and 46 through 48 (all tentatively identified by GC-MS analysis) were also obtained from the reaction of carbenoids 34-anti and 34-syn under Conditions C at -78°, as shown in Table Vb.



48



40 46 47

The reaction of 35-anti under Conditions C at -78°, in the presence of 2 equivalents of DPIBF, gave virtually none of the Diels-Alder trapping product (31) expected from diene 30 (described in the Introduction to this chapter).

Table Vb. Yield data for 40, and 46 through 48 (in the reaction of 34-anti and 34-syn) under Conditions C at -78°[a] (See Table Va)

Expt.	%Yield 46[a] (1 to 3 GC peaks)	%Yield 47[a]	%Yield 40[a]	%Yield 48[a] (4 GC peaks)
1	2.9[b,c] (57%D)[d]	2.8[b,c] (80%D)[e]	1.2[b,c]	2.2[b,c]
2	0.5[b,c] (71%D)[d]	1.6[b,c] (36%D)[e]	0.8[b,c]	3.6[b,c]
3	3.1[b,c] (89%D)[d]	4.7[b,c] (67%D)[e]	1.6[b,c]	3.9[b,c]
4	2.0[f,c] (70%D)[d]	0.3[f,c]	0.3[f,c]	0.1[f,c]
5	2.2[f,c] (93%D)[d]	0.2[f,c] (21%D)[e]	0.1[f,c]	1.1[f,c]
6	3.2[f,c] (93%D)[d]	0.4[f,c] (9.0%D)[e]	0.2[f,c]	1.7[f,c]
7	1.7[f,c] (82%D)[d]	0.1[f,c]	0.3[f,c]	6.6[f,c]
8	1.8[f,c] (67%D)[d]	0.2(9.0%D)[e]	0.2[f,c]	3.4[f,c]

[a]The structure (previous page) was tentatively identified by GC-MS analysis.

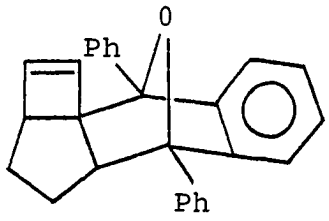
[b]Uncorrected GC yield measured from the GC-MS (Column C) ratio of the compound relative to (38-anti + 45-anti), assuming the relative GC correction factors to be 1:1.

[c]The relative GC-MS response factors of 38-anti and 38-syn were measured as 1:1.

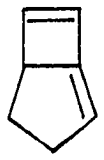
[d]%D incorporation was calcd. from the relative m/e 150 and 151 intensities. The natural (P+1)/P ratio was taken to be the theoretical value of 12.18/100.

[e]%D incorporation was calculated from the relative m/e 93 and 94 intensities. The natural (P+1)/P ratio was taken to be the same as the experimental value for the C_7H_8 portion of 38-anti and 38-syn.

[f]Uncorrected GC yields measured as in footnote b, but using (38-syn + 45-syn) as a reference.



31



30

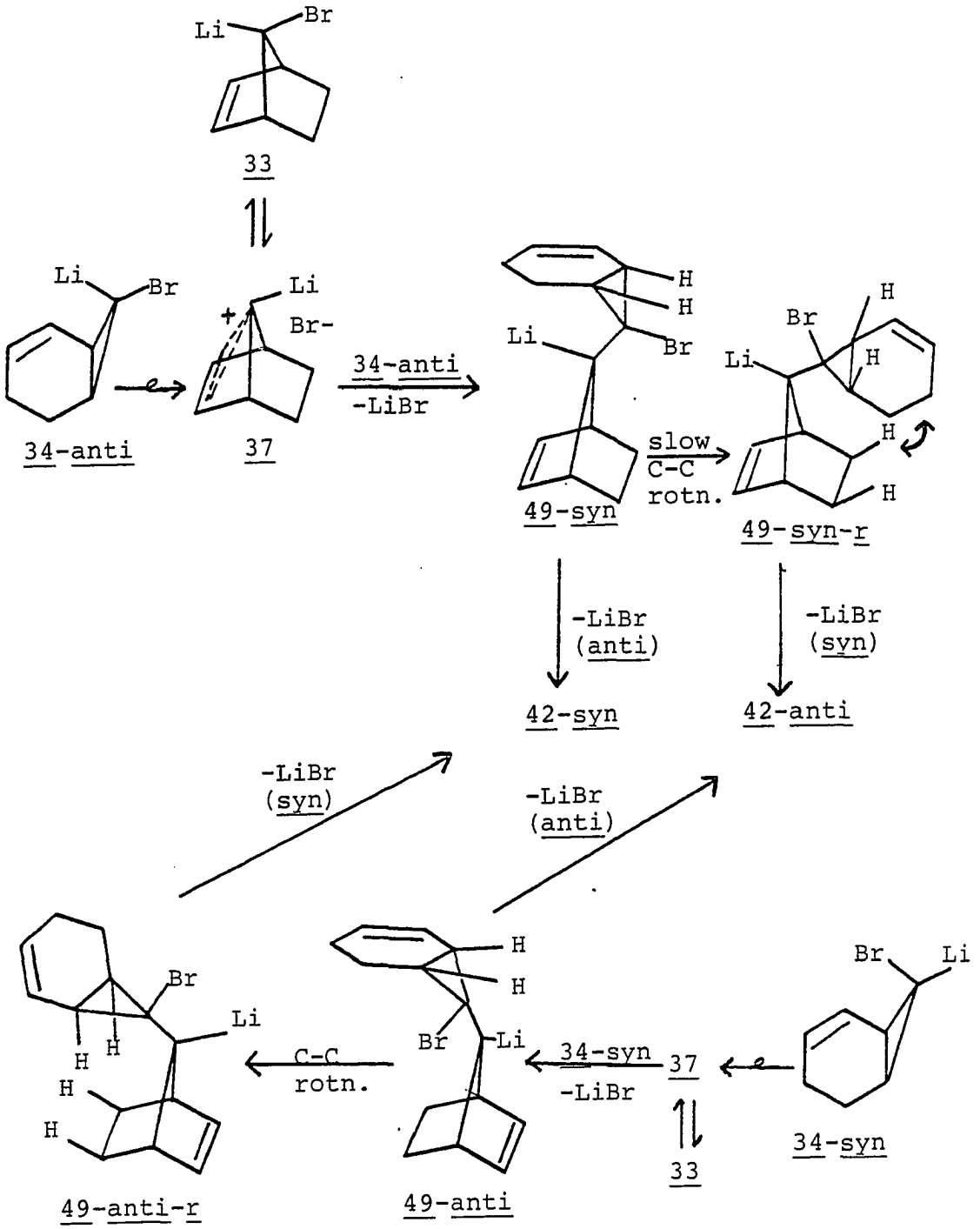
The mechanistic implications of the above reactions of 35-anti and 35-syn will now be discussed. The generation of the norbornenyl moieties of 42-syn and 42-anti must obviously involve the 1,3-rearrangement either of carbenoids 34-anti and 34-syn, or of cyclopropylidene 10. A convincing argument against any free carbene involvement in the reactions of 34-anti and 34-syn under Conditions C can be constructed by combining: a) a lack of any carbene trapping by isobutylene (210 equivalents), cyclohexene (180 equivalents), or triethylsilane (12.4 equivalents), during reactions of 34-anti, b) the fact that the saturated analogues of 34-anti and 34-syn apparently do not generate bicyclo[4.1.0]hept-7-ylidene under Conditions C at -78° (discussed in Chapter II), and c) the very different product distributions derived from 34-anti and 34-syn (Table Va).

Possible mechanisms which account for the dimers 42-syn and 42-anti (Table IV) are outlined in Schemes VIIIa and VIIIb. Scheme VIIIa demonstrates how the products could arise if carbenoid 37 acts as an electrophile and carbenoid 34-anti or 34-syn acts as a nucleophile. (THF solvent might, through

cation solvation, enhance the nucleophilic character of 34-anti and 34-syn more than ether does, thus causing much different product distributions to be obtained in THF than in ether.[7]) The syn-elimination of lithium bromide might, in the absence of any other effects, be expected to be more favorable than anti-elimination. However, in the reaction of 34-anti, the C-C bond rotation which is necessary for 49-syn to undergo such a syn-elimination is difficult because of a severe steric interaction in the resulting intermediate 49-syn-r. Therefore, a 7.5 to 1 ratio of 42-syn to 42-anti seems quite reasonable. For the reaction of 34-syn, however, intermediate 49-anti-r doesn't suffer such a severe steric interaction, so that the C-C bond rotation leading to syn- elimination of lithium bromide from 49-anti-r is quite competitive with anti-elimination from 49-anti, and a 1.5 to 1 ratio of 42-syn to 42-anti is very understandable.

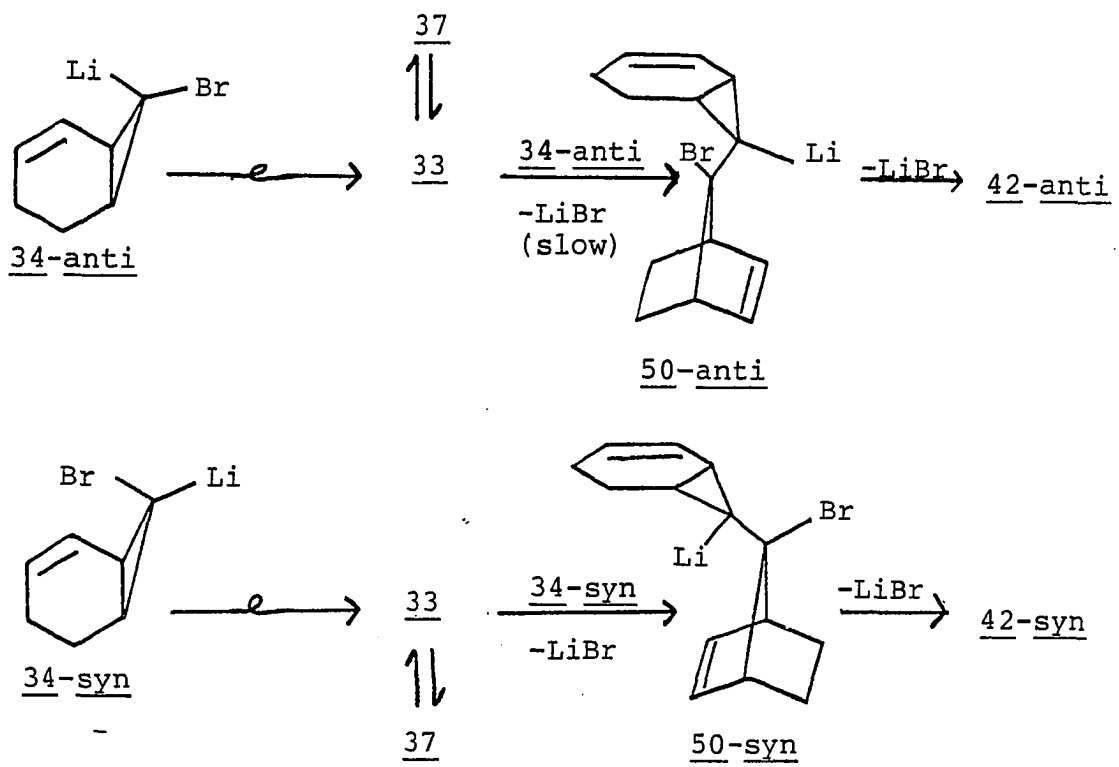
An alternative mechanistic explanation is offered in Scheme VIIIb, which shows carbenoid 33 acting as a nucleophile, and 34-anti or 34-syn acting as an electrophile. (THF solvent might, through cation solvation, enhance the nucleophilic character of 33 more than ether does, thereby bringing about the very different product distributions obtained in these two solvents.[7]) Nucleophilic attack of 33 on 34-anti, which would be expected to result in 42-anti,

Scheme VIIIa:



via intermediate 50-anti, would be sterically more difficult (due to an interaction between the norcarenyl moiety of 34-anti and the bromine of 33) than would electrophilic attack of 37 on 34-anti (Scheme VIIIa), which would result in 42-syn. Thus, electrophilic attack of 37 on 34-anti (Scheme VIIIa) would be the preferred reaction mode, and the 7.5 to 1 ratio of 42-syn to 42-anti would not be at all surprising.

Scheme VIIIb:



On the other hand, nucleophilic attack of 33 on 34-syn, (Scheme VIIIb) resulting in intermediate 50-syn, would have about the same steric demands as electrophilic attack of 37 on 34-syn (Scheme VIIIa), so that the two reaction modes

should be competitive. The 1.5 to 1 ratio of 42-syn to 42-anti is also not surprising in this case.

The two mechanistic possibilities just discussed would be extremely difficult to distinguish experimentally.

A very significant point expressed by the data in Table Va is that 34-anti generates the dimers much more rapidly than 34-syn does. (A faster rearrangement of 34-anti than of 34-syn to 33/37 must therefore be invoked.) This point is even more emphatically expressed by the calculations shown in Table VI.

Note that the %rearrangement of carbenoid 34-syn after a 5 minute reaction time (experiments 4 and 5) was 22%, and after 20 minutes (experiments 6 and 7) it was 40%. The first order rate for the 20 minute experiment($k = 4.3 \times 10^{-4}$ sec^{-1})is only about one-half that for the 5 minute experiment($k = 8.3 \times 10^{-4}$ sec^{-1}). This discrepancy is probably due to a fast initial reaction due to local heating during the n-butyllithium addition. (Note that, for both 34-anti and 34-syn, the results for the 3 and 5 minute runs in Table Va were almost the same.)

The data in Table VI make it clear that 34-anti rearranges much faster than 34-syn does, even though 34-anti is thermodynamically more stable. (As can be seen in the experimental section of this chapter, under entry 3, when 7 was treated with a slight deficiency of n-butyllithium,

Table VI. %Rearrangement of 34-anti and 34-syn[a]

Expt.	SM	Time (min.)	%Rearr.[b] of 34-anti to (33/37)	%Rearr.[c] of 34-syn to (33/37)
1(VIII-14)[d]	35-anti	3	77	N/A
2(VIII-44)[d]	35-anti	5	81	N/A
3(VIII-13)[d]	35-syn	3	N/A	23
4(VIII-12)[d]	35-syn	5	N/A	25
5(VIII-45)[d]	35-syn	5	N/A	19
6(VIII-22)[d]	35-syn	20	N/A	38
7(VIII-46)[d]	35-syn	20	N/A	42

[a] Conditions C at -78°. (See text and Experimental.)

[b] $\frac{(1/2)X(\%42\text{-syn} + \%42\text{-anti})}{\%45\text{-anti} + (1/2)X(\%42\text{-syn} + \%42\text{-anti})}$

(Based on the GC yields in Table V.)

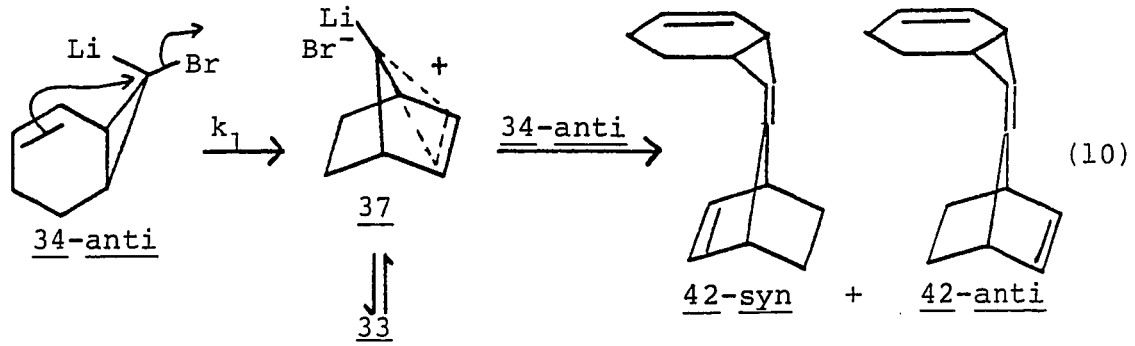
[c] $\frac{(1/2)X(\%42\text{-syn} + \%42\text{-anti})}{\%45\text{-syn} + (1/2)X(\%42\text{-syn} + \%42\text{-anti})}$

[d] Notebook number, followed by page number.

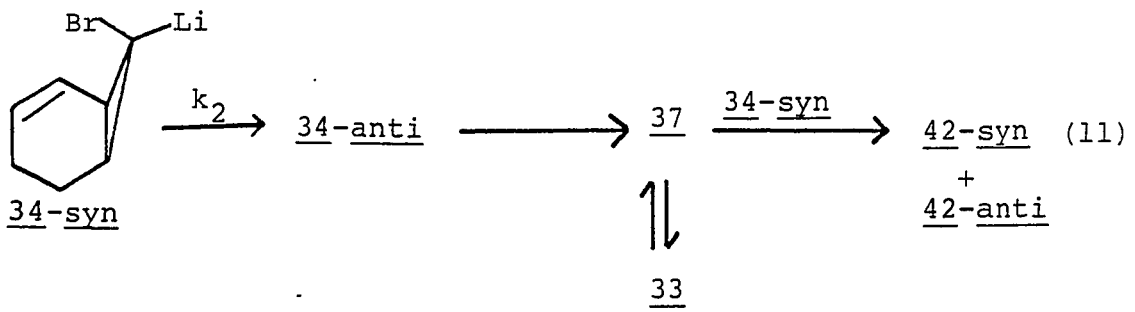
the initial carbenoid, 34-syn, was rapidly transformed into the more stable 34-anti. This pattern is the same as Seyferth and Lambert[26] found for the saturated counterparts of 34-anti and 34-syn.) The only realistic interpretation for this is

that the double bond participates effectively in 34-anti, but not in 34-syn. Furthermore, the different dimer distributions (7.5:1, 42-syn:42-anti, from 34-anti, and 1.5:1 from 34-syn) make it clear that 42-syn and 42-anti are products of carbenoid dimerization (as was already discussed in connection with Schemes VIIIa and VIIIb). If carbenes are to be invoked, then a carbenoid to carbene to carbenoid sequence would be required, and the less stable carbenoid must produce a carbene more slowly. The more economical explanation involves the sequences shown in Scheme IX. For simplicity, the electrophilic mechanism, involving 37 is written for the generation of 42-syn and 42-anti. Thus, as shown in equation (10) of Scheme IX, double bond participation in 34-anti aids ionization of the bromine (k_1), leading directly to 37. With 34-syn, there are two possibilities. As shown in equation (11), epimerization (k_2) could precede the ionization to 37, or as depicted in equation (12), 34-syn could rearrange directly (k_2') to 37. Assuming first order rearrangements for the sake of simplicity, kinetic analysis of the data in Table VI estimates k_1 as 5.7×10^{-3} sec^{-1} (correlation factor $r = 0.95$) and k_2 (or k_2') as 0.34×10^{-3} sec^{-1} ($r = 0.92$). The value of k_1/k_2 (or k_1/k_2') can thus be estimated as 17.

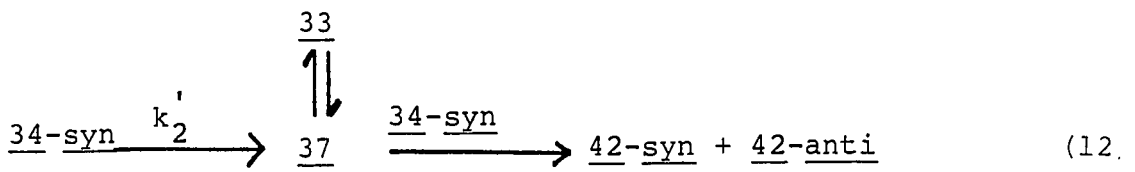
Scheme IX:



(10)



(11)



(12)

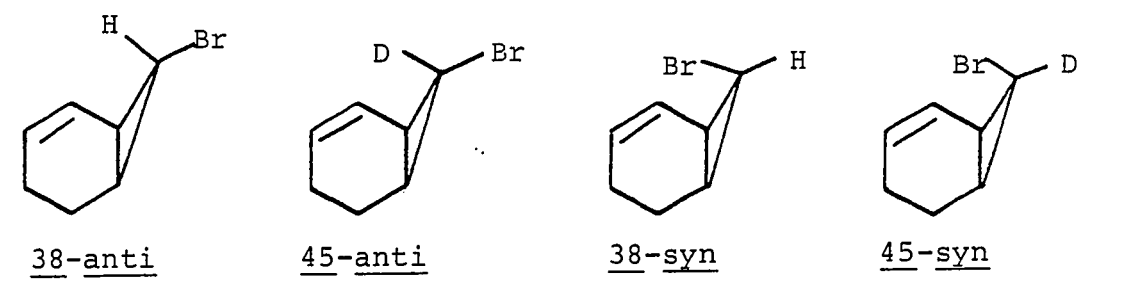


Table VIIa. Reaction of carbenoid 34-syn (Conditions C, -78°)[a] in the presence of an excess and a deficiency of n-butyllithium

Expt.	SM	No. mg SM	No. eq. n-BuLi	Time[b] (min.)	% Conversion of SM
1[c]	35-syn	45.1	0.8	3	81
2[g]	35-syn	44.9	0.9	20	80
3[c]	35-syn	34.8	3.1	10	100
4[g]	35-syn	35.1	5.2	10	100

[a]For description of Conditions C, see text and experimental section. For product structures, see Scheme IX.

[b]Time prior to the methanol or methanol-O-d quench.

[c]Methanol was used as the quench.

[d]Yield measured by NMR integration vs. internal std.

[e]These NMR yields are probably magnified, since the GC yields of 42-syn and 42-anti in Table Va were consistently lower than the corresponding NMR yields.

[f]Yield measured by GC-MS quantitation (Column C), vs. internal standard, with correction factors.

[g]Methanol-o-d was used as the quench.

[h]%D incorporation calcd. as in footnote h, Table V.

[i]%D incorporation calcd. as in footnote d, Table III.

[j]Yield measured by GC integration (Column G) vs. an internal standard, with correction factors.

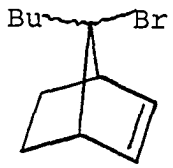
%Yield (42-syn + 42-anti)	%Yield (38-anti + 45-anti)	%Yield (38-syn + 45-syn)
16[d,e]	1.2[f]	64[d]
40[d,e]	1.5[f] (0%D)[h]	46[d] (54%D)[i]
13[j]	0.2[f]	42[d] (50)[j]
14[j]	0[f]	38[d] (37)[j] (92%D)[i]

Equation (11) of Scheme IX seems to be a more likely mechanism than equation (12) for the rearrangement of carbenoid 34-syn. The miniscule yields of 38-anti and 45-anti (Table Va) from the reactions of 35-syn, however, show that there was no substantial build-up of unreacted 34-anti. However, this is probably a result of the much more rapid rearrangement of 34-anti than of 34-syn. Since, as has already been discussed, 34-syn was known to rapidly epimerize to 34-anti in the presence of traces of dibromide 7, one might expect a slight excess of unreacted 35-syn to also accelerate the epimerization of 34-syn to 34-anti, thereby accelerating the rearrangement of 34-syn to 33/37. It was also felt that a large excess of n-butyllithium might also, through aggregation effects, accelerate the epimerization. The results of some experiments with deficiencies and large excesses of n-butyllithium are shown in Table VIIa.

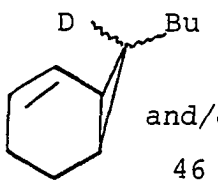
The data in Table VIIa gave no evidence for a faster epimerization of carbenoid 34-syn with either a deficiency or a large excess of n-butyllithium. One cannot, therefore, draw any conclusion regarding the relative importance of equations (11) and (12) of Scheme IX.

Table VIIb shows the yields of products 40 and 46 through 48 in the presence of a slight deficiency or a large excess of n-butyllithium. Excess n-butyllithium

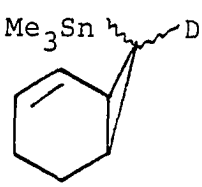
resulted in a much larger yield of 46. This is understandable, since 46 most likely arises from a reaction between n-butyllithium and 33/37 and/or 34-syn.



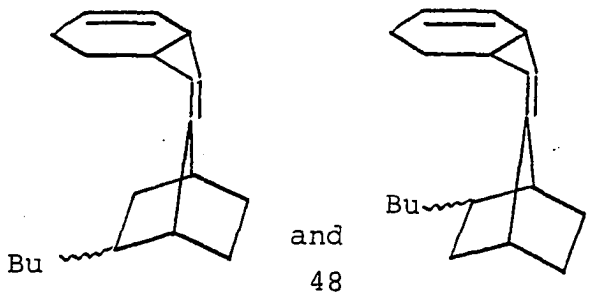
40



46



47



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Because the reaction of 34-anti had been carried out at two different temperatures, approximate values for ΔH‡ (enthalpy of activation), ΔG‡ (free energy of activation), and ΔS‡ (entropy of activation) could be calculated, using the standard set of equations. The yield data and rate constants at two different temperatures are presented in Table VIII. In this way, ΔH‡ was calculated as ca. 15 kcal-mol^{-1}, and ΔG‡ as ca. 13 kcal-mol^{-1}. The ΔS‡ value calculated by this method is ca. + 10 eu. A positive ΔS‡ is not consistent with the solvent reorganization which would be expected for an ionization process. The results are also inconsistent with the 1,3-rearrangement being the rate determining step, since the ΔS‡ for that process should

Table VIIb. Yield data for 40, and 46 through 48 (from the reaction of 34-syn in the presence of an excess and a deficiency of n-butyllithium[a])

Expt.	%Yield 46[b]	%Yield 47[b]	%Yield 40[b]	%Yield 48[b]
1	0.2[c] 1 GC peak	0.6[c]	0.01[c]	0[c]
2	0.1[c](0%D)[d] 1 GC peak	0.2[c](59%D)[e]	0[c]	0[c]
3	14[c] 2 GC peaks	0.1[c]	0.2[c]	2.8[c] 4 GC peaks
4	30[c](95%D)[d] 3 GC peaks	0.1[c]	0.2[c]	3.2[c] 4 GC peaks

[a]Run under Conditions C (described in text and experimental section).

[b]See previous page for structure (tentatively assigned by GC-MS).

[c]Uncorrected GC yield calculated from the GC-MS ratio (Column C) of the compound relative to (38-syn + 45-syn), assuming the relative GC correction factors to be 1.0:1.0.

[d]%D incorporation was calculated from the m/e 150 and 151 relative intensities. The natural (P+1)/P ratio was taken to be the theoretical value of 12.18/100.

[e]%D incorporation was calculated from the m/e 93 and 94 relative intensities. The natural (P+1)/P ratio was taken to be the same as the measured value for the C_7H_8 portion of 38-anti and 38-syn.

Table VIII. Reaction of carbenoid 34-anti at two different temperatures[a]

Temperature	k(sec^{-1})[b]
-78^{o}	5.7×10^{-3}[c]
-95^{o}	2×10^{-4}[d]

[a]Under Conditions C (described in text and experimental section).

[b]From least squares analysis of ln[SM] vs. time (assuming a first order reaction).

[c]Average from the data in Table VI.

[d]Experiment 1 of Tables IIIa and IIIb. The % rearr. (6%) was calculated as in footnote b, Table VI, and in turn led to the value of k as 2×10^{-4} sec^{-1} through a first order analysis.

be very close to zero. At any rate, the accuracy of the $\Delta S^{\ddagger}$ value just calculated is open to question, since the reaction is probably not cleanly first order in 34-anti, due to aggregation effects, and the local heating during the initial n-butyllithium addition. These effects all require more careful experiments, in order to obtain an accurate $\Delta S^{\ddagger}$ value.

2. Reaction of 42-syn with DPIBF

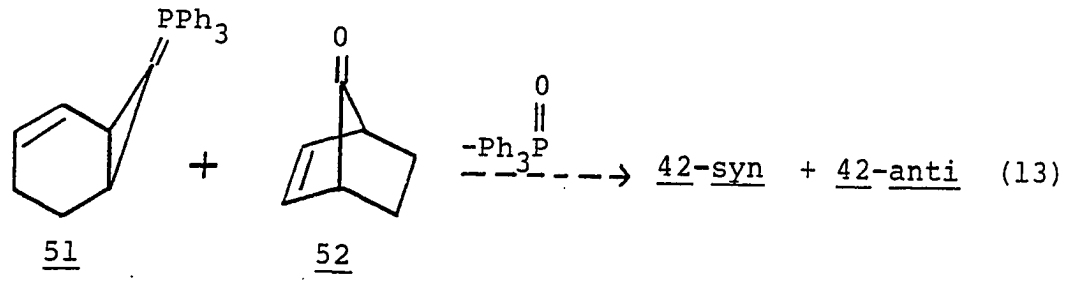
Crystalline derivatives of 42-syn and 42-anti were desired so that X-ray crystal structures could be obtained. Treatment of 42-syn with DPIBF (1,3-diphenyl-isobenzofuran)

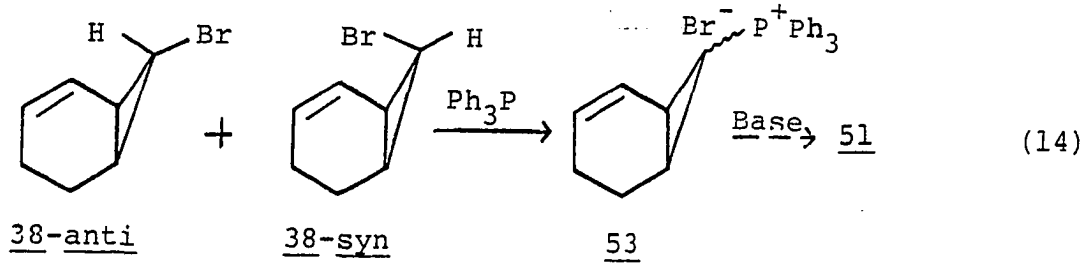
at 70° gave no reaction. After 3 hours of heating at 120°, however, two isomeric DPIBF adducts were obtained in good yield. Their mass spectra indicated that they were either the two expected diastereomeric Diels-Alder adducts of 42-syn, or isomers thereof. Because of the harsh conditions required for their generation, however, it seemed quite unlikely that the 42-syn had really been trapped without attendant rearrangements. (Note that attempted isolation of 42-syn by preparative GC resulted in extensive isomerization, as discussed in the Experimental.) This approach was therefore not pursued.

3. Alternative synthesis of 42-syn and 42-anti

In order to conveniently secure large amounts of 42-syn and 42-anti, so that crystalline derivatives of them could be sought, work was aimed toward developing a rational synthetic route. The first methodology which was investigated centered around the hypothetical Wittig reaction between 51 and 52, pictured in equation (13) of Scheme X. The difficulty in generating the required Wittig reagent, 51, by the normal method, shown in equation (14), stems from the virtually nonexistent yields of cyclopropylphosphonium salts such as 53 which are obtained when cyclopropyl bromides are treated with triphenylphosphine.[29] An alternative strategy for generating 54, a derivative of

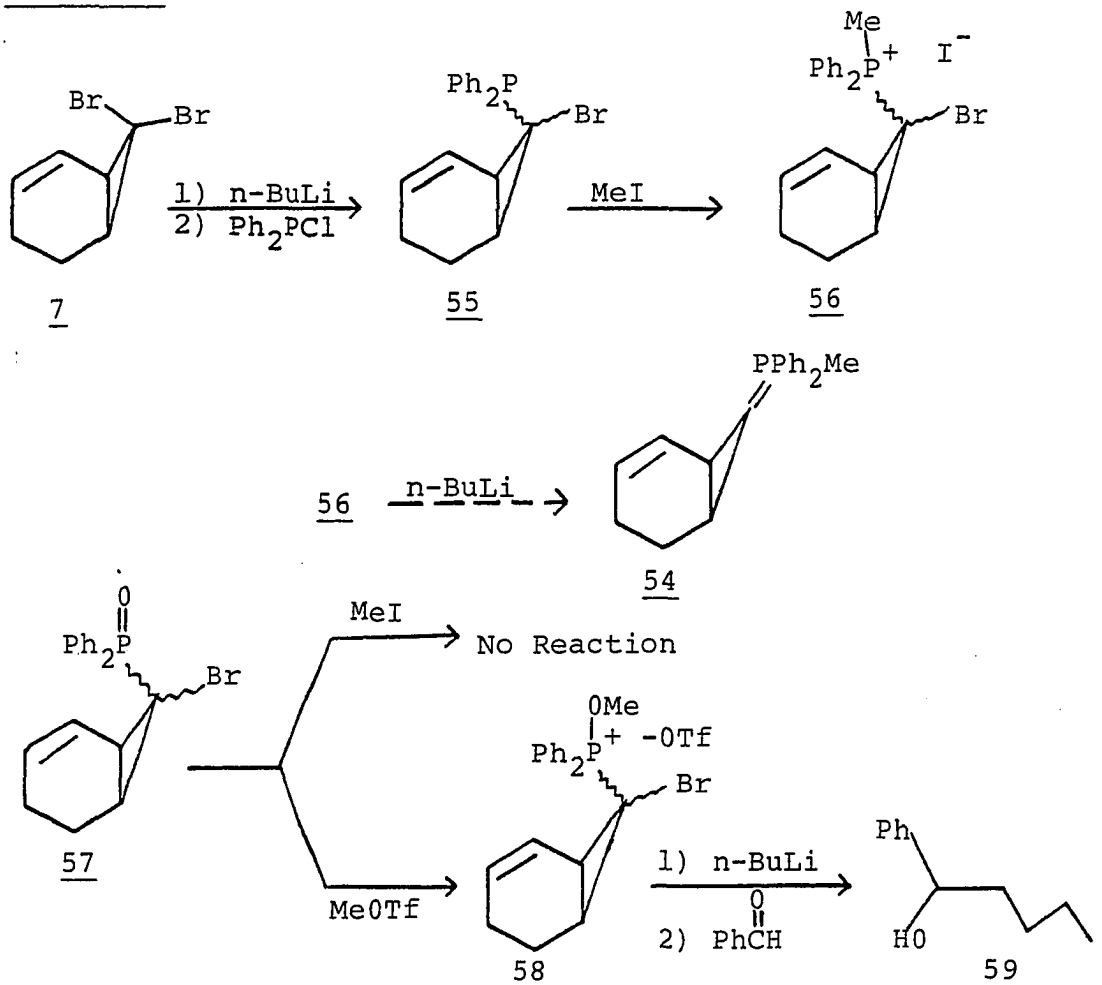
Scheme X:





51, which takes advantage of the special stability of cyclopropyl anions, is depicted in Scheme XI. The alkyllithium compound obtained from n-butyllithium treatment of 7 is alkylated with diphenylchlorophosphine, to generate phosphine 55, which is then methylated, resulting in phosphonium salt 56. A second bromine-lithium exchange on 56 then generates the desired Wittig reagent, 54. This strategy has not been previously reported in the literature. During the first attempts to synthesize phosphine 55, phosphine oxide 57 was obtained instead. The synthesis of 55 was quite capricious in this regard, for reasons which have remained obscure (as described in the Experimental). Before it was realized that the undesired phosphine oxide, 57, had been

Scheme XI:



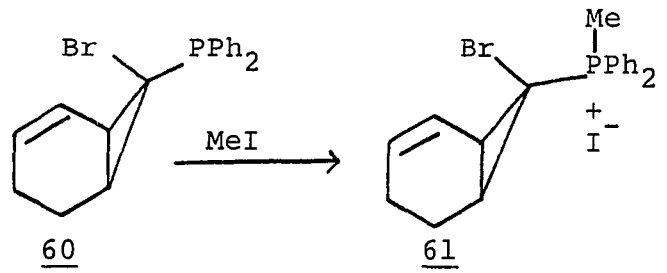
obtained, attempts were made to methylate it. Methyl iodide treatment understandably gave no reaction. However, methyl triflate treatment of 57 did result in a salt, tentatively identified as 58 on the basis of its NMR spectrum. The attempted modified Wittig reaction of 58 with n-butyllithium and benzaldehyde simply gave 59, the product from a reaction between n-butyllithium and benzaldehyde.

It was found, in two separate experiments, that simply switching from ether to benzene solvent during the workup allowed the desired phosphine 55 to be isolated. (However, as is discussed in the experimental section of this chapter, a third attempt to prepare 55 with this workup procedure again resulted in phosphine oxide 57.) As is indicated in Scheme XII, the methylation of 60 (the major epimer of 55 isolated) gave 61 smoothly. The modified Wittig reaction of 61 with n-butyllithium and benzaldehyde did not, however, proceed very well. A very substantial amount of 38-syn (the product of n-butyllithium-phosphorous cleavage) was observed. Only a very small amount of the desired product 62 was obtained. Evidently, interaction between n-butyllithium and the phosphorous group is too competitive with bromine-lithium exchange (especially for stereoisomer 60) for this method to be of synthetic value.

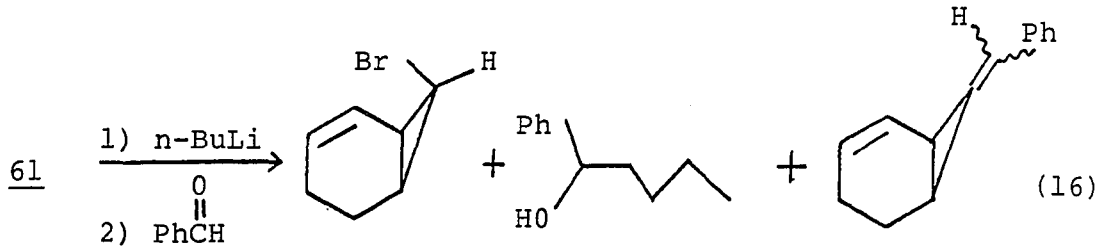
In a final effort to react both 60 and its C^7-epimer, 7 was subjected to the one pot procedure shown in equation (17) of Scheme XII. Predictably, a very complicated product mixture resulted, which included only a trace of 62.

This modified Wittig procedure was abandoned in favor of a Peterson olefination sequence (Scheme XIII). The trimethylsilylbromo compound 63 was treated sequentially with n-butyllithium and bicyclo [2.2.1] hept-2-en-7-one (52),

Scheme XII:

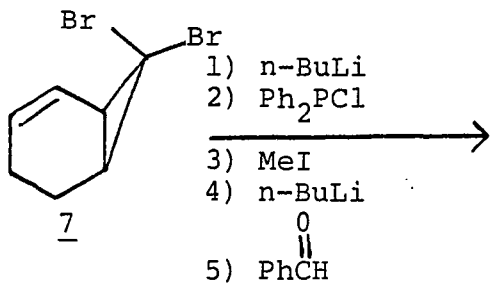


60 61 (15)



38-syn (14 % yield) 59 62 (16)

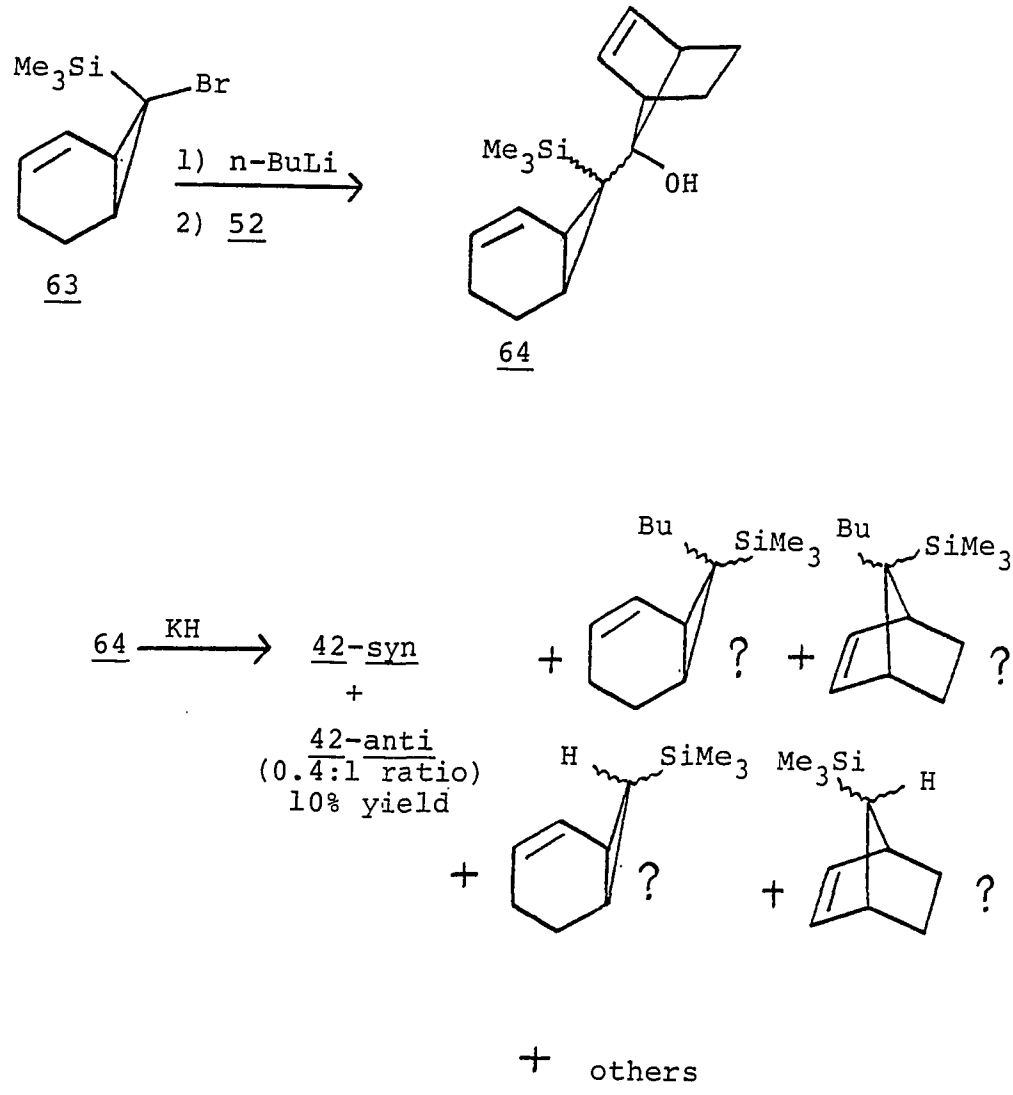
Uncorrected GC-MS mole ratios: 0.4 0.5 0.1



7 → tr. 62 + complex mixture (17)

to generate an intermediate tentatively identified as 64. Subsequent treatment of 64 with potassium hydride (according to literature precedent[30]) resulted in only very small amounts (10% combined yield) of the dimers 42-syn and 42-anti,

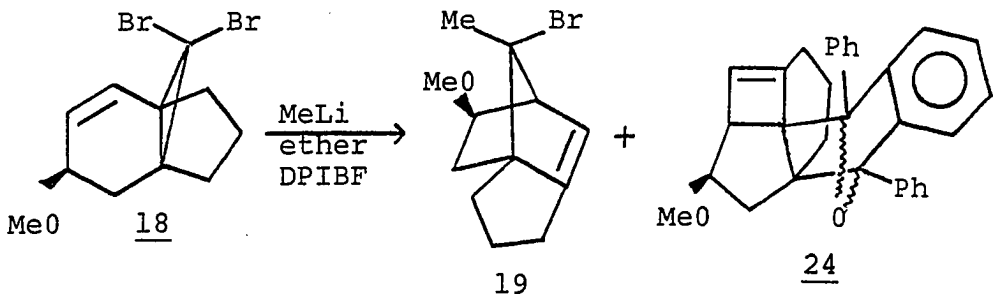
Scheme XIII:



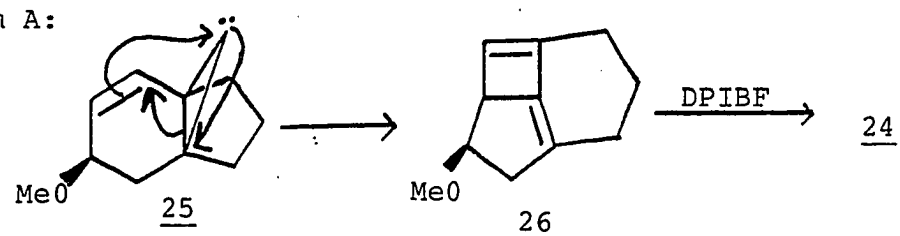
along with much larger amounts of a number of other compounds (Scheme XIII). It was decided at this point to abandon any further attempts to synthesize the dimers.

4. Reaction of 10-bromo-10-lithio-exo-4-methoxytricyclo-[4.3.1.$0^{1,6}$]dec-2-ene

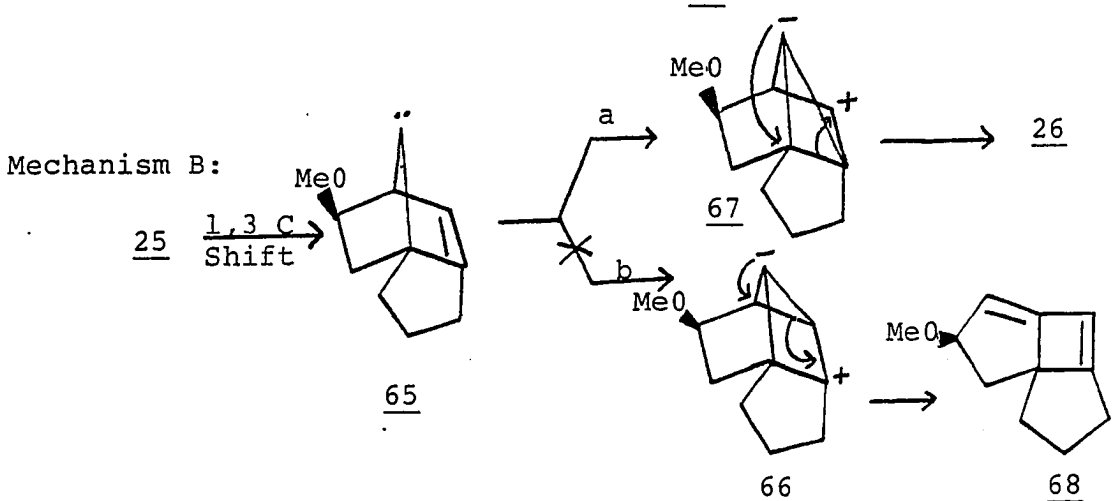
As was discussed in the Introduction to this chapter, Warner and Chang[18-20] identified 19 and 24 (Scheme XIV) as Scheme XIV:



Mechanism A:



Mechanism B:



the major products from the methyllithium treatment of 18 in the presence of DPIBF. Product 19 was proven to be formed via a carbenoid rearrangement (Scheme II). Product 24 most reasonably arises from the trapping of diene 26 by DPIBF. When the reaction was run with 12-crown-4-ether present, product 24 was favored at the expense of 19, implying that 26 might be derived from a free carbene. Mechanism A of Scheme XIV (the direct rearrangement of carbene 25 to diene 26) was favored over Mechanism B (the 1,3-rearrangement of carbene 25 to carbene 65) because the latter would require that carbene 65 react via pathway a, but not pathway b. If anything, one would expect intermediate 66 to be more stable than intermediate 67. Furthermore, diene 68 should be less strained than diene 26. At any rate, one would be very hard-pressed indeed to explain the complete absence of a DPIBF trapping adduct of diene 68.

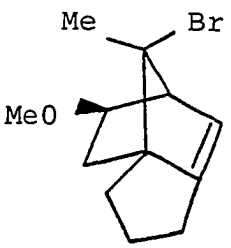
Running the reaction in the presence of cis-2-butene or isobutylene resulted in no trapping products.[18-20] Therefore, in the present work, it was decided to run the methyllithium reaction of 18 in the presence of triethylsilane, in hopes of obtaining either 69 or 70 (see Table IX, footnote b). However, the presence of triethylsilane at either a 1 molar or a 3 molar concentration resulted in no 69 or 70 (Table IX).

Table IX. Reaction of 18 with methyllithium in the presence of triethylsilane

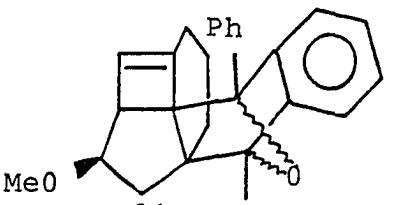
Expt.	No. eq. MeLi	SM M	Ether M	Triethylsilane M	DPIBF M
1	11	0.024	6.1	1.0	0.029
2	10	0.024	3.1	3.0	0.030
3[c]	10	0.025	9.5	0	0.028

[a]Yield measured by NMR integration vs. an internal standard.

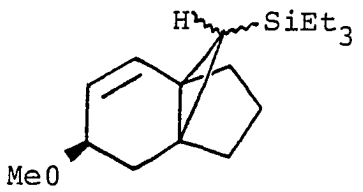
b



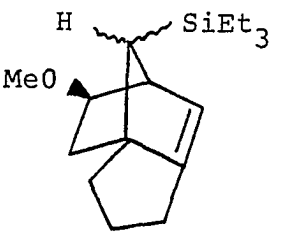
19



24



69

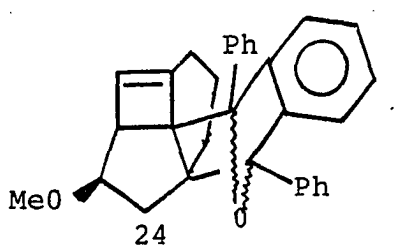


70

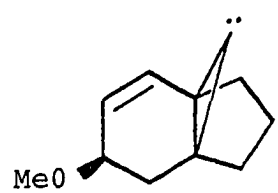
[c]This experiment was taken from S.-C. Chang's Ph.D. Dissertation.[20]

%Yield[a] 24[b]	%Yield[a] 19[b]	%Yield[a] 69[b] or 70[b]
64	33	0
59	41	0
62	34	N/A

It must be concluded from the triethylsilane results that either a) carbene 25 rearranges too rapidly to be trapped by olefins and triethylsilane, or b) there is actually no carbene involvement in the generation of 24, despite the 12-crown-4-ether results. This point will most likely be the object of further investigation in the future.



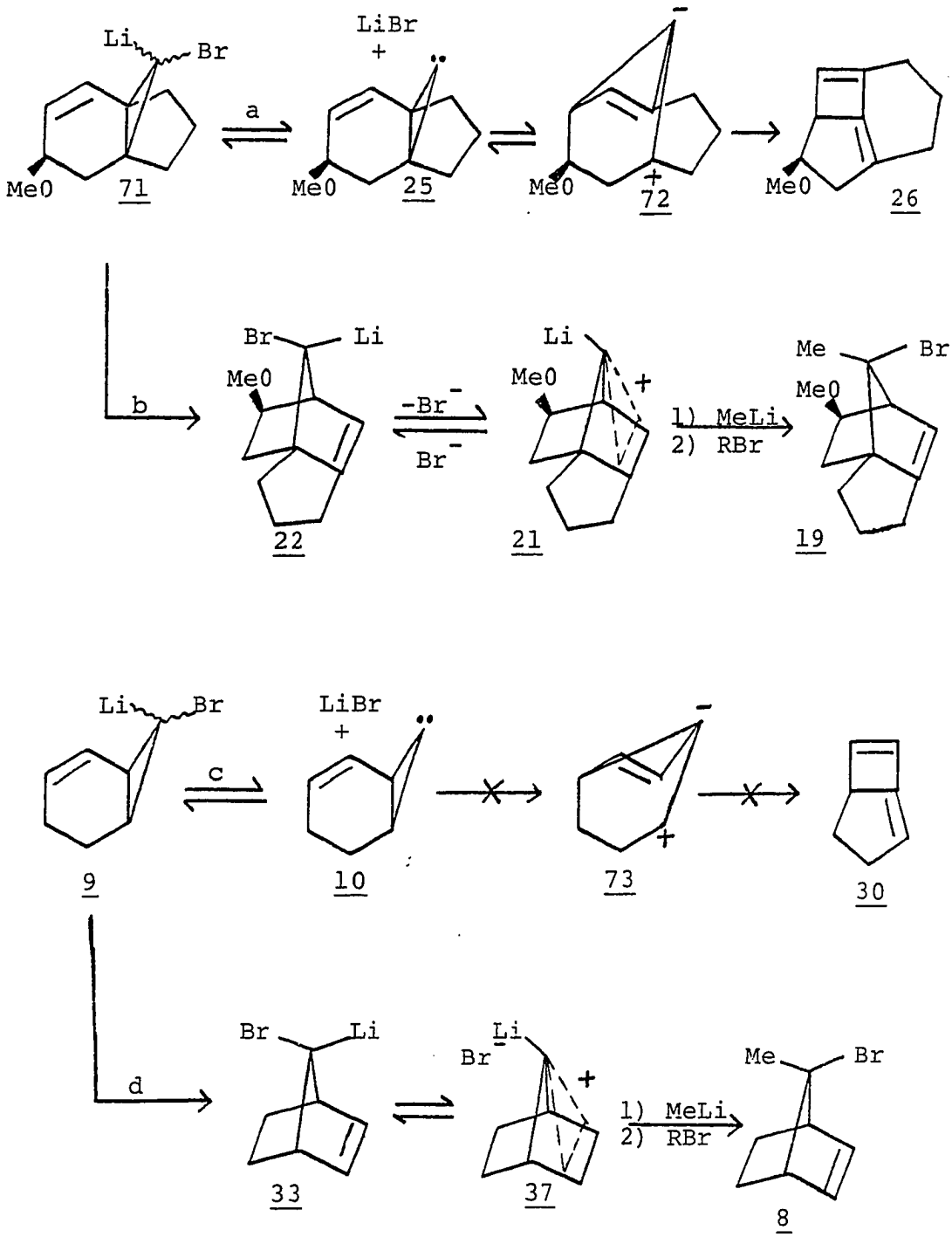
24



25

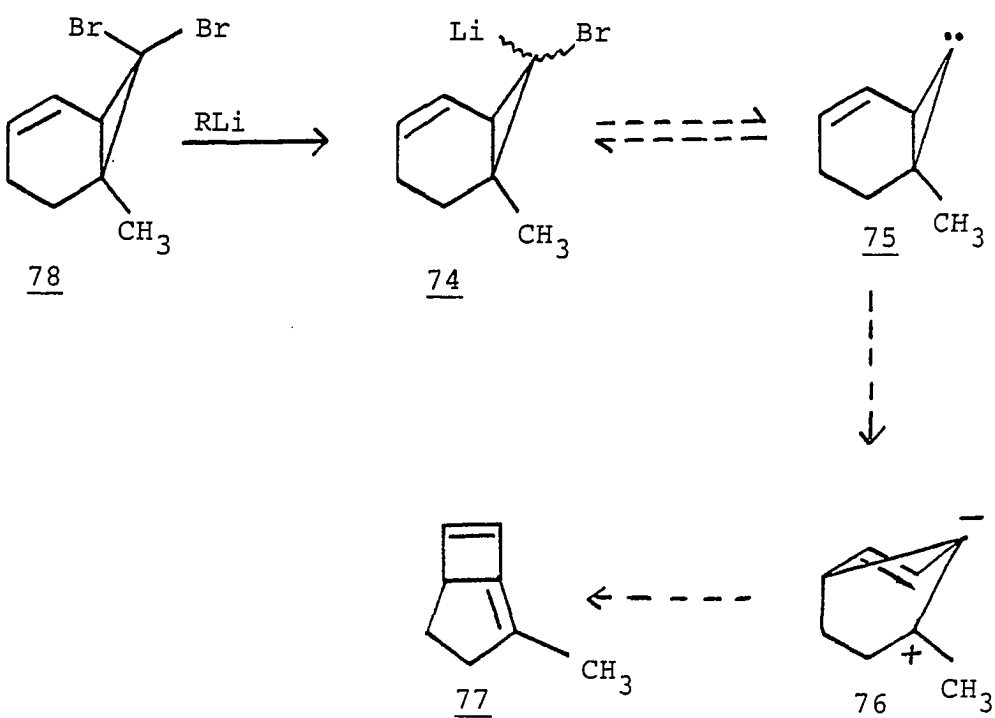
It is very intriguing that such a difference exists between the chemistry of carbenoids 71 and 9 (Scheme XV). Carbenoid 71 generates both a bicyclo [3.2.0] hepta-1,6-diene derivative (26), and a bicyclo [2.2.1] hept-2-ene derivative (19), whereas carbenoid 9 generates only a bicyclo [2.2.1] hept-2-ene derivative (8) in its methyl-

Scheme XV:


Li
Br
LiBr
a
MeO
71
25
72
26
b
-Br⁻
Br⁻
22
21
1) MeLi
2) RBr
19
Me
c
9
10
73
30
d
33
37
8

lithium reaction. Scheme XV offers a mechanistic explanation for this diversity. For the reaction pathway a of carbenoid 71, the cationic center of zwitterion 72 is a tertiary carbonium ion. For the reaction pathway c of carbenoid 9, however, the cationic center of zwitterion 73 is only secondary. Since the cation center in this case is just as strained as in 72, but is only a secondary carbonium ion, carbene 10 might choose not to form 73 at all, but to simply recombine with lithium bromide, and revert to the starting carbenoid 9. The key compound required in order to test this hypothesis is carbenoid 74.

Scheme XVI:

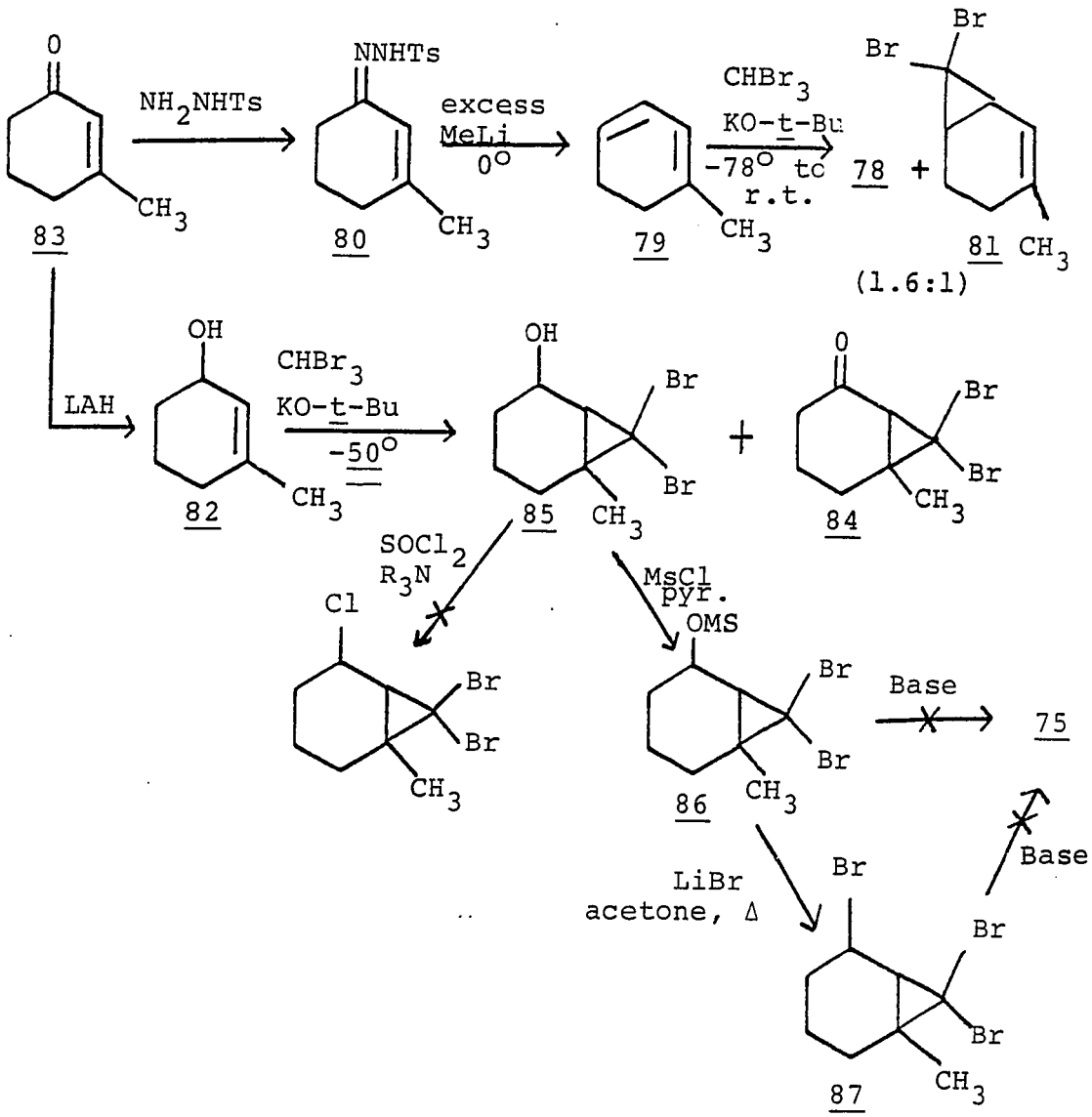


As shown in Scheme XVI, carbenoid 74 could possibly form carbene 75, which might, in turn, generate zwitterion 76. Zwitterion 76, which would be more stable than 73 (Scheme XV) because it has a tertiary carbonium ion center, could then generate diene 77. The precursor of carbenoid 74, i.e., dibromide 78, was an unknown compound, so that a synthetic route had to be established.

5. Preparation of 7,7-dibromo-6-methylbicyclo[4.1.0]hept-2-ene (75)

Scheme XVII shows some unsuccessful attempts to synthesize 78. Dibromocarbene addition to diene 79 (generated from tosylhydrazone 80) was, unfortunately, unselective, resulting in a 1.6 to 1 mixture of 78 and 81, respectively. The mixture of 78 and 81 was not easily separable. Dibromocarbene addition to alcohol 82 (synthesized from ketone 83) was accomplished, but the reaction conditions had to be chosen very carefully, because the dibromocarbene polymerized faster than it reacted with 82 (which would be present in the form of its potassium alkoxide under the reaction conditions). A ketone side product, 84, was also obtained. (Note that an analogous ketone side product was obtained from a similar dibromocarbene addition to 1-hydroxy-1,2,3,4-tetrahydroindane.[20]) All attempts to chlorinate alcohol 85 with thionyl chloride failed miserably, but

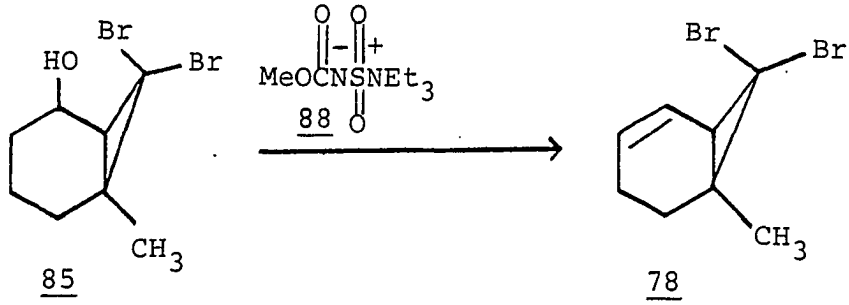
Scheme XVII:



mesylation, to give 86, went very smoothly. Disappointingly, however, treatment of 86 with a variety of bases (DBU, sodium hydride, and potassium tert-butoxide) under various condi-

tions (0°, room temperature, and 56°) resulted in either recovered starting material, or a horrendous mixture of unidentified products, none of which possessed any olefinic hydrogens. The bromide 87 was easily obtained by treating mesylate 86 with lithium bromide, but all attempts at dehydrobromination of 87 again resulted in a bad mixture of compounds, which did not contain any 78.

The method which finally did work was simpler than any of those shown in Scheme XVII. It was found that 85 was very smoothly transformed into 78 by the Burgess reagent 88. It will be very interesting to see the results from the treatment of 78 with n-butyllithium. (This experiment is in the planning stage at the time of writing of this manuscript.)



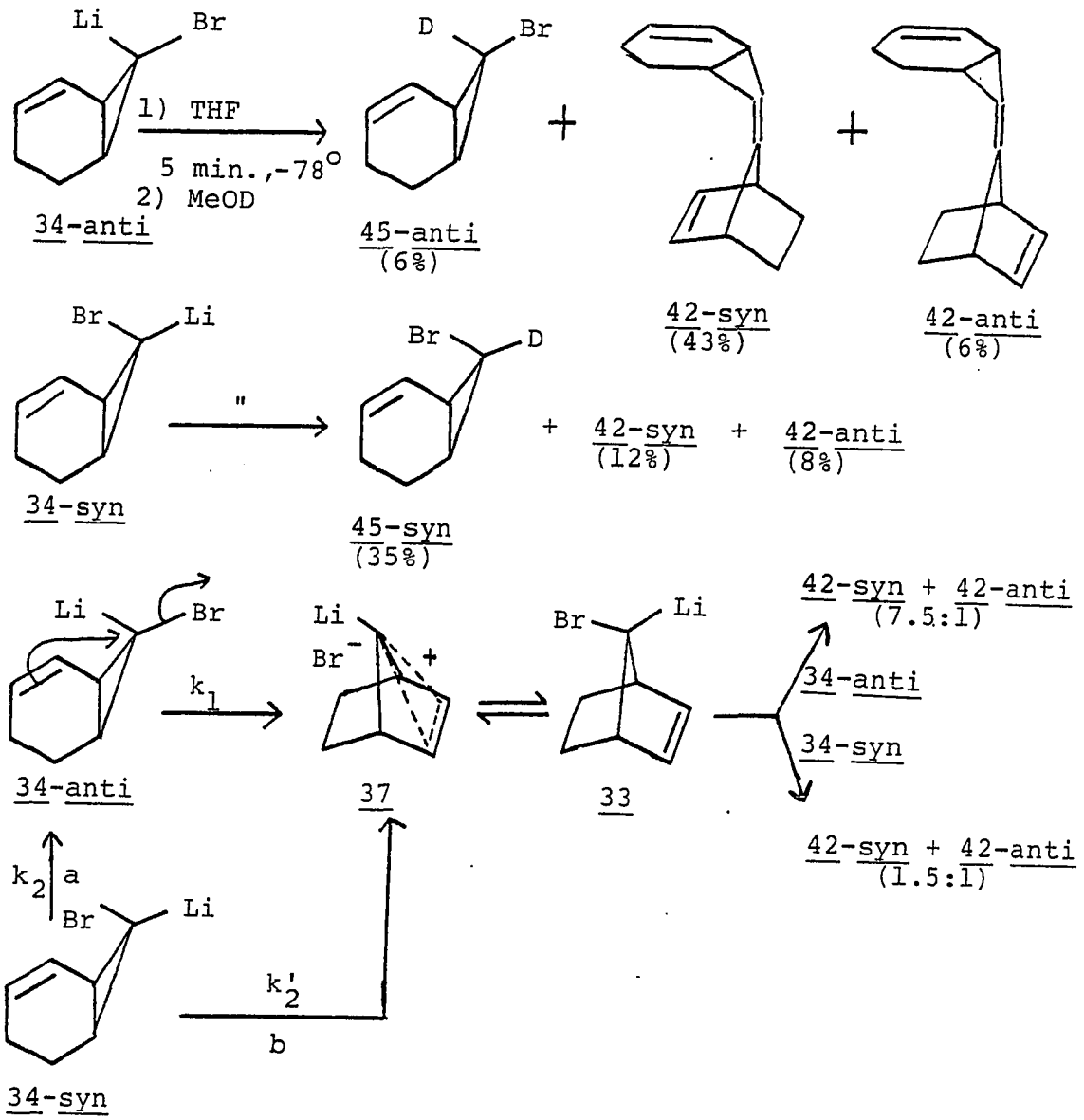
85 78

C. Conclusion

The chemistry of 34-anti and 34-syn was not differentiated by experiments using ether as the solvent and methyl iodide as the carbenoid trap, because their 1,3-rearrangements proceeded at virtually the same rate. This happened

for two reasons: a) the initial trimethylstannyl-lithium exchange between n-butyllithium and 7-bromo-7-trimethylstannylbicylo [4.1.0] hept-2-ene (35-anti and 35-syn) was rather slow in ether solvent, and b) methyl iodide was a very poor trap for 34-anti, 34-syn, and the rearranged carbenoid 33/37. When the experiments were run in THF solution, with methyl iodide as the carbenoid trap, the initial trimethyltin-lithium exchange was sufficiently rapid, but the study was still unsuccessful because of the poor quality of methyl iodide as a carbenoid trap. In THF solution, with methanol-O-d as the carbenoid trap, however, the chemistry of 34-anti and 34-syn was differentiated quite conveniently. The major products and their yields are shown in Scheme XVIII. Possible mechanisms for the formation of 42-syn and 42-anti can be found in Schemes VIIIa and VIIIb. Isomer 34-anti rearranges to 33/37 faster than 34-syn does, even though the former is thermodynamically more stable, which is not in keeping with a carbene mechanism. Furthermore, the different distributions of dimers 42-syn and 42-anti demonstrate very clearly that they are products of carbenoid dimerization (Schemes VIIIa and VIIIb). If carbenes are to be invoked, then a carbenoid to carbene to carbenoid sequence would be required, and the less stable carbenoid must produce carbene more slowly. The more economical sequence involves double bond participation (Scheme XVIII),

Scheme XVIII:



which is possible for 34-anti, but not for 34-syn. (It could not be determined whether the rearrangement of 34-syn

follows pathway a or b of Scheme XVIII, but the k_1/k_2, or k_1/k_2', ratio was estimated as 17.) A further convincing argument against any free carbene involvement can be constructed by combining a) a lack of any carbene trapping by large excesses of isobutylene, cyclohexene, or triethylsilane with b) the fact that the saturated analogues of 34-anti and 34-syn do not generate the corresponding free carbene, bicyclo[4.1.0]heptan-7-ylidene under the same reaction conditions (Chapter II). These results can be combined with those of Warner and Chang[18,19], discussed in the introduction section, to state unequivocally that the 1,3-rearrangement reactions of 1-lithio-1-bromo-2-vinylcyclopropanes (in solution) proceed strictly via carbenoid rearrangements.

In order to conveniently secure large quantities of 42-syn and 42-anti, work was aimed toward developing a rational synthetic route. The first route involved an unsuccessful attempt to develop a new Wittig reaction modification, i.e., reaction of a α-lithiocyclopropyltriarylphosphonium salt with a ketone, in an attempt to generate the corresponding cyclopropane alkylidene derivative (Scheme XII). The second route was a Peterson olefination sequence (Scheme XIII), i.e., the reaction of 7-lithio-7-trimethylsilylbicyclo[4.1.0]hept-2-ene with bicyclo[2.2.1]hept-2-en-7-one (52), followed by treatment

of the resulting vicinal hydroxy-trimethylsilyl compound (64) with potassium hydride. The reaction was very messy, yielding large quantities of many unidentified products. Traces of 42-syn and 42-anti (3% and 7% yields, respectively) could, however, be identified within the crude product mixture. In view of the low yields of the desired products, the reaction was not pursued.

D. Experimental

1. General considerations

Infrared spectra were recorded on a Beckman IR-4250 or Acculab 2 spectrophotometer. The 60 MHz ^{1}H NMR (proton magnetic resonance) spectra were obtained on a Varian HA-60, a Hitachi Perkin-Elmer R-20B, or a Varian EM-360 spectrometer, the 90 MHz ^{1}H NMR on a Jeol FX-90Q spectrometer, the 100 MHz ^{1}H NMR spectra on a Varian HA-100 spectrometer, and the 300 MHz ^{1}H NMR spectra on a Bruker WM-300 or a Nicolet NT-300 spectrometer, using the solvents indicated, and tetramethylsilane as the internal standard. "NMR yield" refers to a yield measured by 60 MHz ^{1}H NMR integration of the compound relative to a known amount of an internal standard. ^{13}C NMR (carbon magnetic resonance) spectra were recorded on a Bruker HX-90, a Jeol FX-90Q, or a Bruker WM-300 spectrometer, as indicated. The GC-MS studies were conducted on a Finnegan 4023 GLC-Mass Spectrometer, and the high res-

olution mass spectra were measured on an AEI MS 902 Mass Spectrometer. Analytical GC studies were conducted on a Varian 3700 Gas Chromatograph. "Corrected GC yield" refers to a yield measurement by GC integration of a compound relative to a known amount of an internal standard, with the appropriate correction factors applied. Preparative GC isolations were carried out on a Varian Aerograph Model 90-P. (The inlet port contained a glass insert.) The melting points were taken on a Thomas-Hoover capillary melting point apparatus or on a Spencer microscope slide apparatus (as indicated), and are uncorrected. Elemental analyses were performed by either Spang Microanalytical Laboratory (Eagle Harbor, Michigan) or Galbraith Laboratories, Inc. (Knoxville, Tennessee).

The following GC columns were used for GC-MS studies:

A-- 6 ft x 2 mm, 3% OV-101 on Supelcoport, glass

B-- 1.5 ft x 2 mm, 3% OV-101 on Supelcoport, glass

C-- SE-30 glass capillary

D-- DB-1 glass capillary

E-- DB-1701 glass capillary

The following GC columns were used for analytical GC studies:

F-- 6 ft x 2 mm, 3% OV-1 on Chromosorb W, glass

G-- 12 ft x 2 mm, 3% OV-1 on Chromosorb W, glass

H-- 12 ft x 2 mm, 8% OV-17 on Chromosorb W, glass

I-- 50 cm x 3 mm, 5% OV-101 on Chromosorb G stainless steel

The GC columns which were employed for preparative GC isolations are described within the experimental sections.

2. Preparation of 7,7-dibromobicyclo [4.1.0] hept-2-ene(7)

Compound 7 was previously prepared from 1,3-cyclohexadiene and dibromocarbene by Lindsay and Reese.[31] The following is a more detailed procedure than that described by those authors.

A 100 ml 3-neck round-bottom flask was equipped with an addition funnel, a magnetic stirring bar, and a nitrogen inlet, and was nitrogen-flushed and dried. Then, it was charged with 3.33 g (29.7 mmol) of commercial potassium tert-butoxide powder, followed by 25 ml of hexane. A solution of 2.4 ml (25.2 mmol) of cyclohexa-1,3-diene and 2.2 ml (25.1 mmol) of bromoform in 10 ml of hexane was next placed in the addition funnel. The flask and its contents were cooled to -78° (dry ice-acetone), and the solution in the addition funnel was added dropwise over a 40 minute period to the stirred potassium tert-butoxide suspension. (It is important to add the bromoform/olefin solution through the center neck of the flask to avoid its freezing as it runs down the side of the flask. Stirring the potassium tert-butoxide suspension

is sometimes difficult, especially if the reaction is run on a larger scale than that described here. The addition of a small amount of extra hexane usually makes stirring easier in such an event. If the preparation is to be run on much more than twice the scale described here, an overhead mechanical stirrer should be used.) The resulting mixture was allowed to slowly warm while being stirred under nitrogen for 19 hours. The mixture was poured into an ice-cold mixture of 30 ml of water plus 30 ml of ether, transferred to a separatory funnel, and shaken. The aqueous layer was withdrawn and re-extracted with 3 x 20 ml of ether. The combined organic layers were washed with 3 x 5 ml of water and 1 x 5 ml of saturated sodium chloride solution, and then dried (anh. magnesium sulfate), filtered, and concentrated in vacuo, yielding 5.6 g of yellow oil. Distillation through a short path distillation head at 0.2 to 0.25 mm afforded, after a brief forerun, a 76% yield of 7 as a colorless liquid (b.p. 45-47°, 0.25 mm). Its NMR spectrum matched the literature spectrum.[31] 60 MHz NMR (CCl_4): δ 5.86 (m, 2H), 2.00 (m, 6H).

3. Preparation of anti-7-bromo-syn-7-trimethylstannylbicyclo[4.1.0]hept-2-ene (35-anti) and syn-7-Bromo-anti-7-trimethylstannylbicyclo[4.1.0]hept-2-ene (35-syn).

These compounds were prepared from 7,7-dibromobicyclo[4.1.0]hept-2-ene (7) by a slight modification (differing

mainly in the method of temperature control) of the procedure used by Seyferth et al.[26] for their saturated analogues.

a. Using 1.18 equivalents of n-butyllithium A 100 ml 3-neck round-bottom flask was equipped with a magnetic stirring bar, an addition funnel, and a nitrogen inlet, and was nitrogen-flushed and dried. Then, a solution of 0.503 g (1.99 mmol) of 7 in 30 ml of dry (freshly distilled from LAH) THF was placed in the flask, and a solution of 0.427 g (2.14 mmol) of trimethyltin chloride in 15 ml of dry THF was placed in the addition funnel. The flask was next cooled to -100° to -105° ("Skelly B" hexane slush bath) for 15 minutes before 1.08 ml (2.36 mmol) of a 2.187 M n-butyllithium/hexane solution was slowly syringed in down the side of the flask over a 2 minute period. After the resulting solution had been stirred at -100° to -105° for 20 more minutes, the solution in the addition funnel was a added dropwise over a 2.5 minute period. After the solution had been stirred at -100 to -105° for 10 more minutes, it was allowed to slowly warm while being stirred under nitrogen for 2.5 more hours. The cooling bath was removed, and the stirring was continued another 75 minutes. The solution was then quenched with 5 drops of water, followed by 10 ml of saturated ammonium chloride solution, and concentrated via rotary evaporator. The residue was extracted with 50 ml of ether, and the organic layer was then washed sequentially with 5 ml of water, and 5 ml of satu-

rated sodium chloride solution, and then dried (anhydrous magnesium sulfate), filtered, and concentrated *in vacuo* to give 0.636 g of slightly yellow oil. NMR analysis showed that a 1.5 to 1 mixture of *35-anti* and *35-syn*, respectively, had been obtained. The two products were isolated by preparative TLC on silica gel (hexane). *35-anti* (rf=0.58) was isolated in 37% yield. The NMR and IR spectral data agreed quite well with those reported by Brinker and Ritzer[21] for their compound, whose stereochemistry was unspecified. *60 MHz ^{1}H NMR* (CCl_4): δ5.84 (br dd, spacings = 29, 14 Hz), 2.4-1.3 (complex m, 6H), 0.24 (s, 9H, with $Sn^{117,119}$ satellites, J_{HCSn} = 53,55 Hz). *IR (CCl_4)*: 3070 (sh), 3040 (m), 2987 (m), 2938 (br s), 2875 (m, 2857 (sh), 1642 (w), 1452 (w), 1440 (sh), 1395 (w), 1350 (w), 1325 (w), 1217 (w), 1201 (sh), 1193 (m), 1175 (sh), 1128 (w), 1090 (w), 1070 (m), 1048 (w), 997 (w), 955 (br w), 930 (w), 870 (w), 718 (br s) cm^{-1}. *^{13}C NMR ($CDCl_3$)*: δ129.670 (rel. intens. 8552), 126.223 (6257), 36.352 (2467), 26.857 (7837), 25.491 (8412), 22.368 (8929), 21.003 (7554), - 6.306 (8399). *Analysis*: Calcd. for $C_{10}H_{17}BrSn$: 35.76%C, 5.10%H, 23.79%Br, 35.34% Sn; Found: 35.81%C, 5.11%H, 23.85%Br, 35.22%Sn.

35-syn (rf=0.42) was isolated in 25% yield. *60 MHz ^{1}H NMR* (CCl_4): δ5.75 (br s, 2H), 2.3-1.1 (complex m, 6H), 0.17 (s, 9H, with $Sn^{117,119}$ satellites, J_{HCSn} = 52,54 Hz). *IR (CCl_4)*: 3070 (sh), 3035 (s), 2982 (s), 2922 (s), 2850 (m),

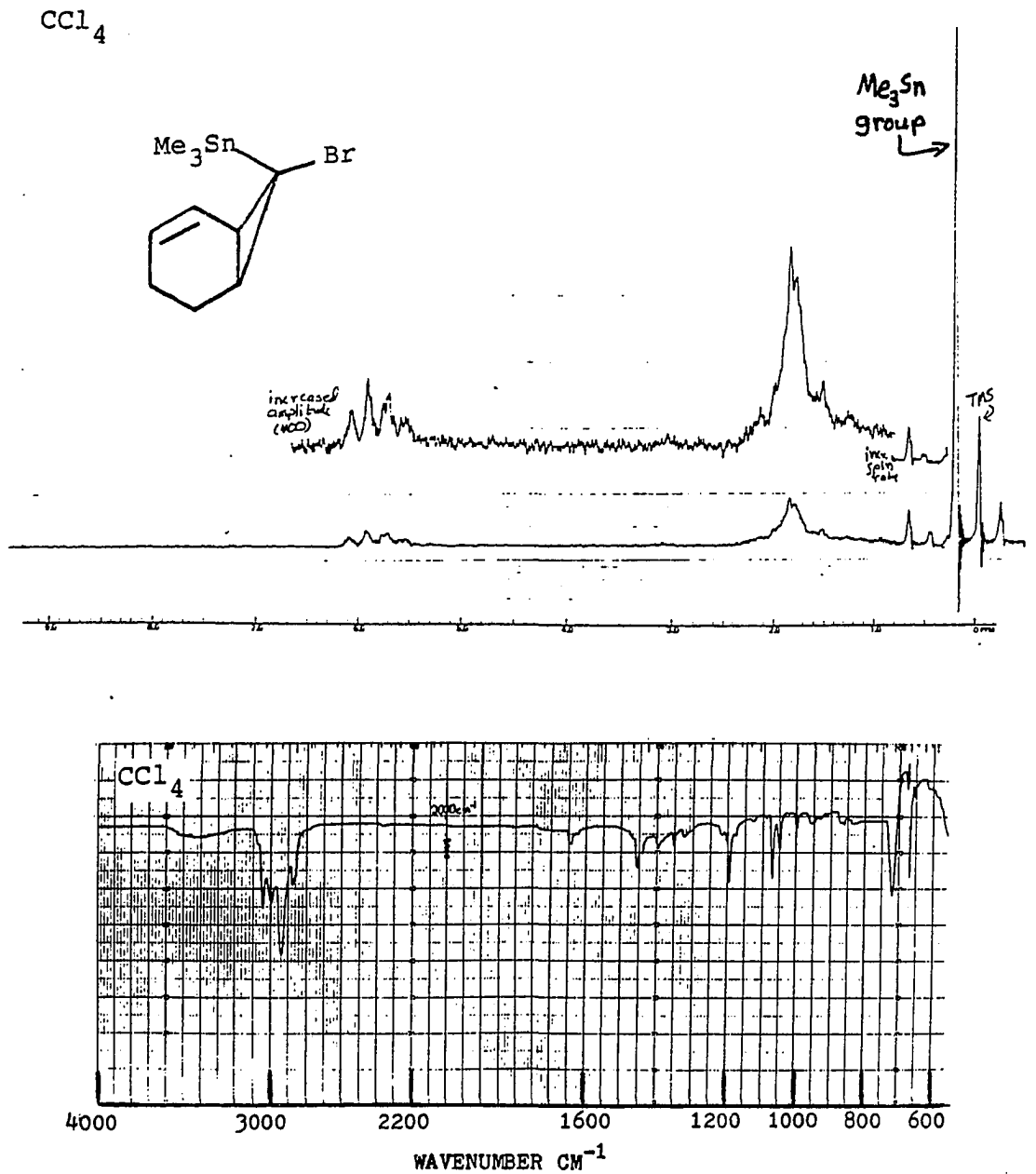
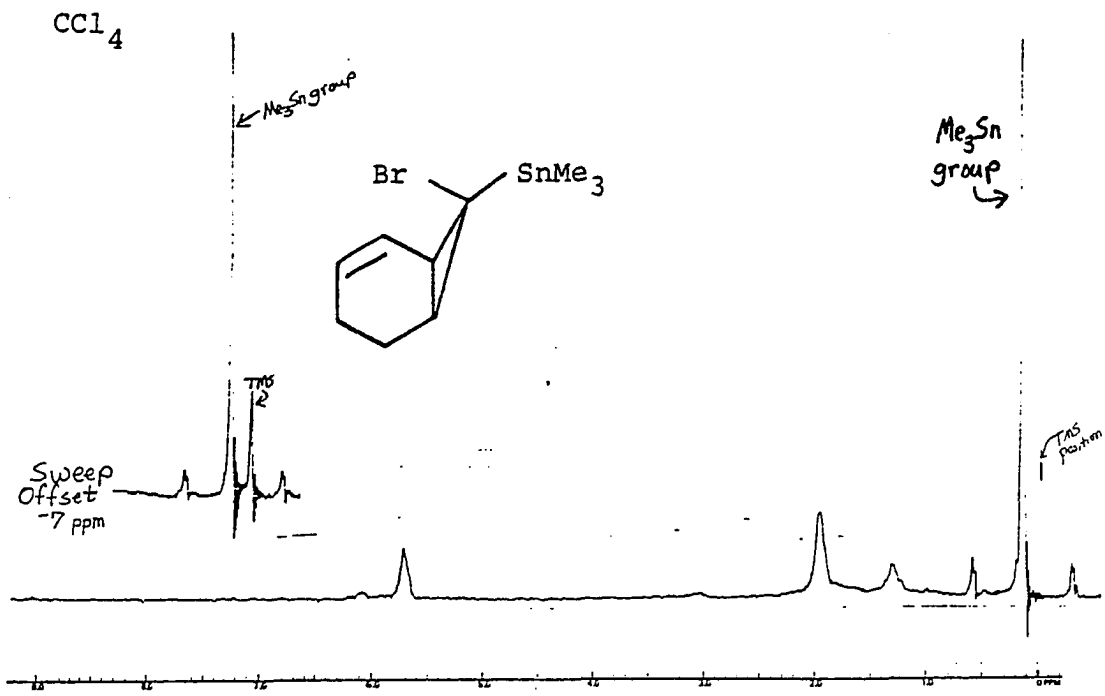


Figure 1. ^{1}H NMR and IR spectra of 35-anti (anti-7-bromo-syn-7-trimethylstannylbicyclo[4.1.0]hept-2-ene)



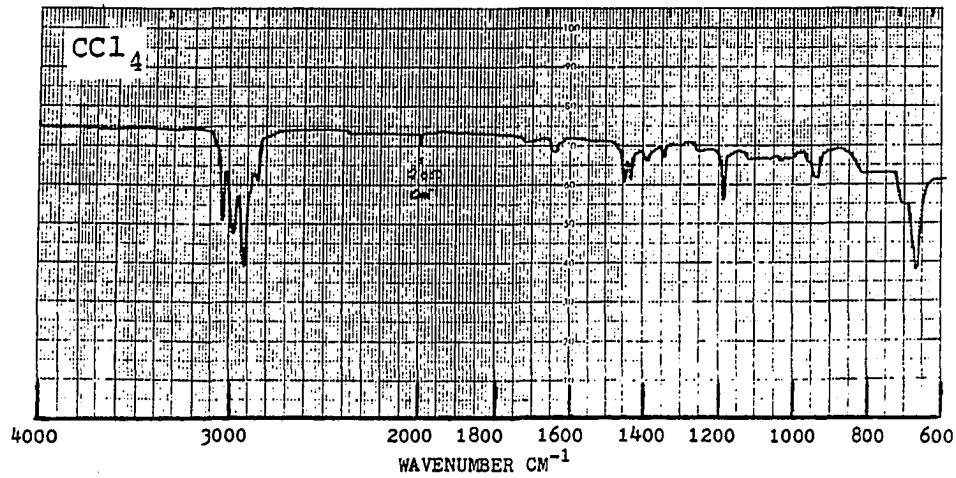


Figure 2. ^1H NMR and IR spectra of 35-syn (syn-7-bromo-anti-7-trimethylstannylbicyclo [4.1.0]hept-2-ene)

1642 (br w), 1625 (sh), 1450 (m), 1432 (m), 1392 (w), 1348 (w), 1255 (w), 1190 (s), 1032 (w), 963 (sh), 940 (br m), 702 (sh), 670 (br s) cm^{-1}. ^{13}C NMR ($CDCl_3$): δ128.174 (rel. intens. 6369), 123.752 (6277), 40.449 (1917), 22.303 (5691), 19.312 (6669), 18.792 (6745), 17.881 (6386), -9.623 (6845). Analysis: Calcd. for $C_9H_{14}BrSn$ (P-15): m/e 320.93008. Found: m/e 320.92907. (The parent peak was visible, but too weak to be accurately measured.)

b. 0.69 equivalents of n-butyllithium A procedure similar to a) was followed, but with only 0.69 equivalents of n-butyllithium. The result was a mixture of starting material and 35-anti. There was not detectable 35-syn.

c. 1.06 equivalents of n-butyllithium A 100 ml 3-neck round-bottom flask, equipped with an addition funnel, a magnetic stirring bar, and a nitrogen inlet, was nitrogen-flushed and dried prior to being charged with a solution of 1.01 g (4.02 mmol) of 7 in 20 ml of dry (freshly distilled from LAH) THF. The addition funnel was next charged with a solution of 0.845 g (4.22 mmol) of trimethyltin chloride in 20 ml of dry THF, and the flask was then cooled to -95 to 100°. After 1.95 ml (4.26 mmol) of a 2.187 M n-butyllithium/hexane solution had been slowly syringed in down the side of the flask, the mixture was stirred at -95° to -100° for 35 minutes. The solution in the addition funnel was added dropwise over an 8 minute period. The resulting mixture was

stirred at -95° to -100° for a few more minutes, and then allowed to slowly warm over a 2.5 hour period. The solution was quenched with a few drops of water, concentrated in vacuo, and partitioned between 10 ml of water and 70 ml of ether. The ether layer was washed sequentially with 10 ml of water and 20 ml of saturated sodium chloride solution, and then dried (anhydrous magnesium sulfate), filtered, and concentrated on a rotary evaporator to afford 1.08 g of yellowish oil. NMR analysis revealed that it contained a 9 to 1 mixture of 35-anti and 35-syn. Purification by preparative TLC on silica gel (hexane) gave a 49% yield of 35-anti (rf=0.59).

4. Hydrogenation of 35-anti and 35-syn

Hydrogenation of 35-anti and 35-syn to their known saturated analogs provided further structural proof. A 37.0 mg sample of 35-anti was dissolved in 3 ml of cyclohexane, and added to a mixture of 16 mg of platinum oxide and 7 ml of cyclohexane, which had been previously saturated with hydrogen. The resulting stirred mixture was kept under one atmosphere of hydrogen for 25 minutes. Filtration and concentration in vacuo gave 27 mg of an oil. Aside from a very small amount of an impurity (singlet at δ0.83), the NMR spectrum matched that of an authentic sample of anti-7-bromo-syn-7-trimethylstannylbicyclo[4.1.0]heptane.[26]

A 29.5 mg sample of a 1.8 to 1 mixture of 35-anti and 35-syn, respectively, was similarly hydrogenated for 15

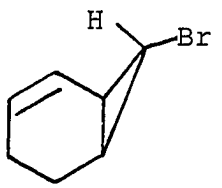
minutes. In addition to a small amount of an impurity (singlet at δ0.23), NMR analysis showed that a 1.7 to 1 mixture of anti-7-bromo-syn-7-trimethylstannylbicyclo [4.1.0] heptane and its C^7-epimer, respectively, had been obtained. Purification by preparative TLC on silica gel (hexane) gave samples of the saturated analogs of 35-anti (rf=0.60) and of 35-syn (rf=0.70), whose NMR spectra matched those of authentic samples.[26]

5. n-Butyllithium treatment of 35-anti and 35-syn under conditions A

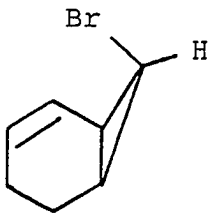
a. 60 Minute procedure A 3-neck 25 ml round-bottom flask was equipped with a magnetic stirring bar, an addition funnel, and an argon inlet, and was dried and argon-flushed. A solution of a measured amount (40 to 60 mg) of 35-anti or 35-syn in 6 ml of dry (freshly distilled from LAH) ether was placed in the flask, and the addition funnel was then charged with 1 to 2 ml of a dry ether solution of a measured amount of methyl iodide (equal to the number of mmoles of n-butyllithium). The flask was next cooled with a dry ice-acetone bath (-78°) for 8 minutes prior to the slow addition (via syringe) down the side of the flask of the desired amount of a 2.46 M n-butyllithium/hexane solution. The n-butyllithium (1.6 to 3 times the number of mmoles of 35-anti or 35-syn) was added over a 1 minute period. Stirring at

-78° under argon was continued for 60 minutes, followed by the dropwise addition over a ca. 1 minute period of the solution in the addition funnel. After 10 more minutes at -78°, the solution was allowed to warm slowly to room temperature over a 1.5 to 2 hour period. After it had been quenched with 3 ml of water, the solution was diluted with 8 ml of ether, and partitioned. The organic layer was washed with 5 ml of saturated sodium chloride solution, dried over anhydrous sodium sulfate, filtered, and concentrated on a rotary evaporator to an oil.

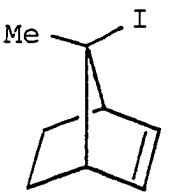
b. 6 Minute procedure This procedure was the same as the "60 Minute procedure" above, except that, after the n-butyllithium addition, the solution was stirred at -78° for only 6 minutes prior to the addition of the methyl iodide solution. The solution was next stirred under argon at -78° for 9 to 10 minutes, the dry ice bath was removed, and the stirring was continued for 15 more minutes. The workup was the same as in the "60 Minute procedure." The product mixtures were analyzed by NMR and GC-MS, and found to contain 38-anti, 38-syn, 39 through 41, 42-syn, and 42-anti. Compounds 38-syn and 38-anti were identified by comparison of their GC retention times and GC-MS data with those of authentic samples. The isolation and spectral data for 42-syn and 42-anti are given under entries 7 and 8 below. n-Butyl-



38-anti



38-syn



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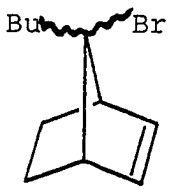

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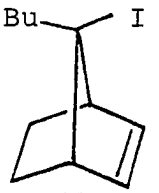
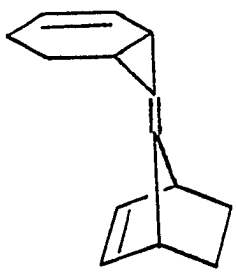
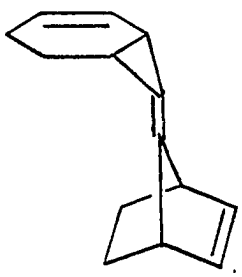


41



42-syn



42-anti

trimethyltin and 39 through 41 were tentatively identified by their GC-MS and NMR spectra. The spectral data for 39 through 41 follow. 7-Iodo-7-methylbicyclo [2.2.1] hept-2-ene (39)--crude 60 MHz ^{1}H NMR (CCl_4): δ6.07 (t, J=2.3Hz), 2.75 (m), 1.80 (s), 2.0-0.6 (complex m). 70 eV MS (Finnegan GC-MS) m/e (%RIC): 234 (P, 1.00), 206 (P-28, 0.11), 127 (P-107, 0.86), 107 (P-127, 21.59), 93 (0.12), 92 (1.42), 91 (10.23), 79 (23.24), 77 (11.41), 65 (2.76), 51 (3.72). 7-Bromo-7-n-butylbicyclo [2.2.1] hept-2-ene (40)--crude 60 MHz ^{1}H NMR (CCl_4): δ5.84 (t, J=2.3 Hz), 2.53 (m), 1.9-0.4 (complex m). 70eV MS (Finnegan GC-MS) m/e (%RIC): 230 (P+2, 0.10), 228 (P, 0.10), 202 (P+2-28, 0.27), 200 (P-28, 0.28), 188 (0.11), 186 (0.12), 160 (0.63), 158 (0.68), 149 (8.36), 120 (2.45), 107 (2.87), 105 (2.30), 93 (11.43), 92 (1.87), 91 (8.43), 79 (13.21), 77 (6.79), 67 (2.90), 65 (3.41), 55 (3.23), 51 (2.25). 7-Iodo-7-n-butylbicyclo [2.2.1] hept-2-ene (41)--crude 60 MHz ^{1}H NMR (CCl_4): δ 6.06 (t, J=1.9 Hz), 2.85 (m), 2.1-0.7 (complex m). 70eV MS (Finnegan GC-MS) m/e (%RIC): 276 (P, 0.09), 248 (P-28, 0.01), 149 (P-127, 11.52), 107 (2.57), 105 (1.78), 93 (8.66), 92 (1.47), 91 (8.08), 79 (18.61), 78 (6.15), 77 (7.05), 71 (2.97), 67 (2.87), 65 (2.86), 55 (4.41), 51 (1.90).

For compounds 39, 40, and 41, the NMR spectra (a triplet near δ6, and a multiplet at δ2 to 3) strongly suggest bicyclo-[2.2.1] hept-2-ene structures.

6. Preparation of anti-7-bromobicyclo [4.1.0] hept-2-ene (38-anti) and syn-7-bromobicyclo [4.1.0] hept-2-ene (38-syn)

These compounds are known, and can be prepared by the tri-n-butyltin hydride reduction of 7,7-dibromobicyclo-[4.1.0]hept-2-ene (7).[32]

An alternative (and in the author's opinion more convenient) procedure is as follows: A 50 ml 3-neck round-bottom flask was equipped with a magnetic stirring bar, and an argon inlet, and was dried and argon-flushed. The flask was next charged with a solution of 0.2 g (0.8 mmol) of 7 in 14 ml of dry (freshly distilled from LAH) THF, and then cooled to -100° to -105° with a hexane ("Skelly B") slush bath. Then 0.9 mmol of 1.47 M n-butyllithium/hexane solution was slowly added via syringe, over a 2 minute period, down the side of the flask. The solution was stirred at -100° to -105° for 18 minutes, followed by the slow addition (15 second period) down the side of the flask (via syringe) of 0.5 ml of methanol. After the solution had been stirred at -100° to -105° under argon for another 8 minutes, the solution was allowed to slowly warm to room temperature. After it had been quenched with 7 drops of water, 5 ml of saturated ammonium chloride solution was added, and the resulting mixture was concentrated on a rotary evaporator, and extracted with

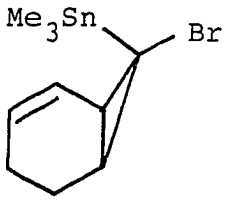
50 ml of ether. The organic layer was washed with 5 ml of water and 5 ml of saturated sodium chloride solution, dried over anhydrous magnesium sulfate, filtered, and concentrated on a rotary evaporator to give 0.16 g of yellow oil. The product mixture was purified by preparative TLC on two 1 mm silica gel plates, using hexane as the developing solvent. Compound 38-anti had an rf of 0.7. 60 MHz ^{1}H NMR (CCl_4): δ 6.22-5.91 (complex m, 1H), 5.67-5.31 (complex m, 1H), 2.80 (t, J = 3.2Hz, 1H), 2.35-1.15 (complex m, 6H). 70eV MS (Finnegan GC-MS) m/e (%RIC): 174 (P+2, 0.54), 172 (P, 0.56), 94 (2.15), 93 (P-79, 28.37), 92 (2.41), 91 (15.90), 77 (19.35), 65 (5.89), 51 (3.94). Compound 38-syn had an rf of 0.6. 60 MHz ^{1}H NMR (CCl_4): δ 5.78 (m, 2H), 3.34 (t, J = 7.5 Hz, 1H), 2.5-1.1 (complex m, 6H). 70eV MS (Finnegan GC-MS), m/e (%RIC): 174 (P+2, 0.28), 172 (P, 0.26), 94 (2.21), 93 (P-79, 28.56), 92 (2.60), 91 (17.20), 77 (19.23), 65 (5.81), 51 (4.00).

The two products prepared by this method had spectral data matching those prepared by the known tri-n-butyltin hydride reduction procedure.[32]

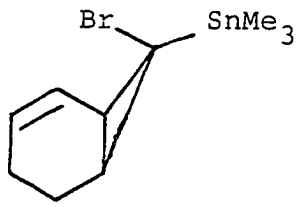
7. n-Butyllithium treatment of 35-anti and 35-syn under conditions B

An argon-flushed, dried 25 ml 3-neck round-bottom flask (equipped with a magnetic stirring bar, an argon inlet, and

an addition funnel) was charged with a solution of a measured amount (45 to 50 mg) of 35-anti or 35-syn in 6 ml of dry



35-anti

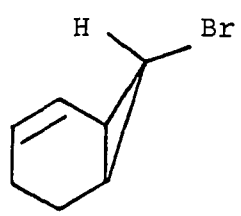


35-syn

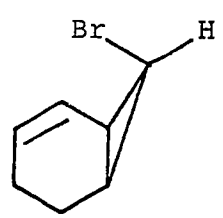
(freshly distilled from LAH) THF. A solution of a measured amount of methyl iodide, which was equal to the number of mmoles of n-butyllithium used for the particular experiment (1.4 to 1.6 times the number of mmoles of 35-anti or 35-syn), was next placed in the addition funnel, and the flask was then cooled to -90° to -95° (15% "Skelly B"/85% toluene slush bath) for 15 minutes prior to the addition (over a 1 minute period) down the side of the flask (via syringe) of the desired amount of a 2.46 M n-butyllithium/hexane solution. After the solution had been stirred at -90° to -95° under argon for the appropriate length of time (5 to 15 minutes), the methyl iodide solution was added dropwise over a 2 minute period. After another 10 to 15 minutes of stirring, the cooling bath was removed, and the solution was again stirred for 15 minutes under argon. Next, 3 ml of water were added as a quench, and the resulting mixture was concentrated on a rotary evaporator. The addition of 0.5 ml of saturated sodium

chloride solution was followed by extraction with 35 ml of ether. The organic layer was washed with saturated sodium chloride solution, dried over anhydrous sodium sulfate, filtered, and concentrated on a rotary evaporator to yield an oil.

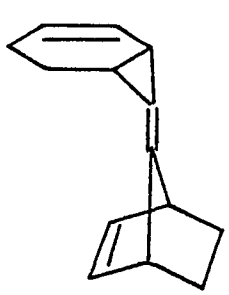
The product mixtures were analyzed by NMR, GC, and GC-MS, and the major products were found to be 38-anti, 38-syn, 42-syn, and 42-anti. 42-syn and 42-anti, crude 60 MHz ^{1}H NMR (CCl_4): δ 6.10 (t, J = 1.9 Hz), 3.10 (m). Complete characterizations of the two isomers are given under entry 8 below.



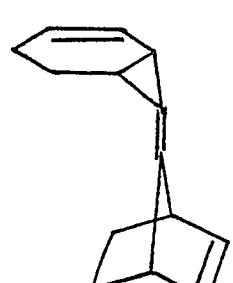
38-anti



38-syn



42-syn



42-anti

8. n-Butyllithium treatment of 35-anti and 35-syn under conditions C

a. -90° to -95° Reaction A 25 ml 3-neck round-bottom flask equipped with a magnetic stirring bar, an addition funnel, and an argon inlet, was argon-flushed and dried. It was then charged with a solution of a measured amount (50 to 55 mg) of 35-anti or 35-syn in 6 ml of dry (freshly distilled from LAH) THF. The addition funnel was charged with a solution of 50 µl (1.23 mmol) of methanol-0-d (99.5+ atom %D) in 1.5 ml of dry THF. The solution in the flask was cooled to -90° to -95° (15% "Skelly B" hexane/85% toluene slush bath) for 15 minutes prior to the slow (1 minute period) addition down the side of the flask, via syringe, of the desired quantity (1.5 equivalents) of a 2.46 M n-butyllithium/hexane solution. After the solution was stirred at -90° to -95° under argon for 5 minutes, the solution in the addition funnel was added dropwise over a 1 to 2 minute period. The solution in the flask was again stirred at -90° to -95° for 15 minutes. The cooling bath was then removed, and stirring was continued for 15 more minutes, followed by quenching with 6 drops of water. Concentration on a rotary evaporator was followed by partitioning between 3 ml of water, 2 ml of saturated sodium chloride solution, and 35 ml of ether. The organic layer was washed with 3 ml of saturated sodium chloride solution, dried over anhydrous sodium sulfate, filtered, and carefully

concentrated on a rotary evaporator, followed by a cautious (to avoid volatilization of the products) nitrogen-flush.

Treatment of 35-anti under these conditions gave anti-7-bromo-syn-7-deuteriobicyclo[4.1.0]hept-2-ene (45-anti) as the major product (71.3% yield by GC, 86% D by MS). The position of the deuterium was assigned to H^7 by the lack of the normal H^7 absorption at δ 2.80 in the NMR spectrum.

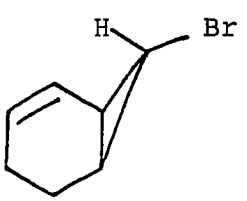
Similar treatment of 35-syn gave syn-7-bromo-anti-7-deuteriobicyclo[4.1.0]hept-2-ene (45-syn) as the major product (77.6% by GC, 87% D by MS). The position of the deuterium was established as the H^7 by the absence of the normal H^7 absorption of δ 3.34.

More detailed analyses of these two product mixtures are given within the text.

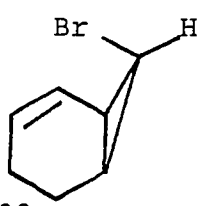
b. -78° Reaction This procedure was similar to that for the -90° to -95° reaction. The differences follow: The flask was not equipped with an addition funnel. Also, the range of the amounts of 35-anti or 35-syn used was 35 to 50 mg. The solution was cooled to -78°, instead of -90° to -95°, with a dry ice-"Skelly B" hexane bath. The number of equivalents of n-butyllithium ranged from 0.8 to 3.1. After the n-butyllithium addition, the solution was stirred for the appropriate length of time (3 to 20 minutes) at -78° prior to the dropwise addition, via syringe, of 0.3 ml (7.4 mmol) of

methanol-O-d (99.5^{+} atom %D) over a 15 to 20 second period. After the solution had been stirred under argon at -78^{o} for 10 more minutes, it was quenched with 10 drops of water, and carefully concentrated on the rotary evaporator, followed by a cautious nitrogen flush. The workup was the same as that for the -90^{o} to -95^{o} reaction.

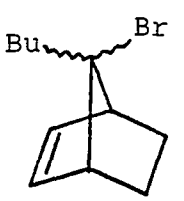
The product mixtures were analyzed by NMR, GC, and GC-MS. Products 38-anti and 38-syn were identified by comparison of their GC retention times, GC-MS data, and, in some cases, NMR spectra with those of authentic samples. The %D contents were measured by MS. Compound 40 was tentatively identified by comparison of its GC-MS data with those of the same product described under entry 5 above. Compounds 46, 47, and 48 were tentatively identified by



38-anti



38-syn



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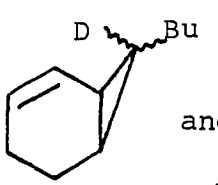

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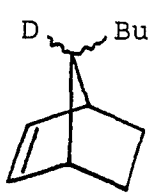

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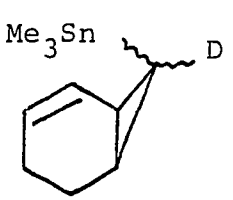

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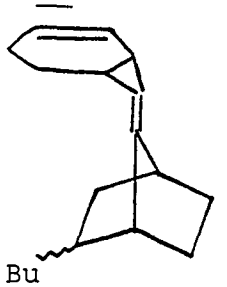

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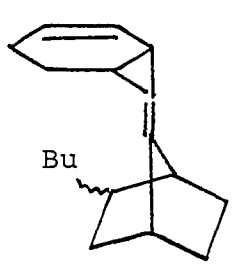
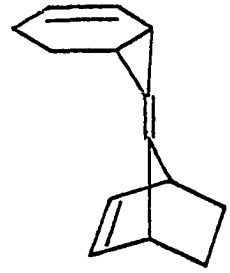


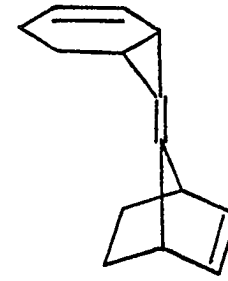
48

GC-MS. 70eV MS (Finnegan GC-MS) for 7-n-butyl-7-deuterio-bicyclo [4.1.0] hept-2-ene or -bicyclo [2.2.1] hept-2-ene (46), ~100%D, m/e (%RIC): 151 (P, 0.35), 136 (P-15, 0.13), 123 (P-28, 1.26), 122 (P-29, 0.49), 109 (0.77), 108 (P-43, 1.05), 95 (3.19), 94 (P-57, 13.52), 92 (6.56), 81 (22.24), 80 (13.97), 67 (2.96), 53 (1.14). 70eV MS (Finnegan GC-MS) for 7-trimethylstannyl-7-deuteriobicyclo [4.1.0] hept-2-ene (47), ~68%D, m/e (%RIC): FPTC (first peak of a Sn^{120}, 118, 116 cluster) at 244 ($P^{Sn, 120}$-15, 0.29), FPTC at 212 (0.09), FPTC at 185 (0.08), FPTC at 165 ($P^{Sn,120}$-94, 13.57), FPTC at 150 (1.56), FPTC at 135 (2.71), FPTC at 120 (Sn^{120}, 1.01), 94 ($P^{Sn,120}$-165, 7.12), 93 (3.39), 92 (5.25), 91 (3.12), 78 (2.47), 77 (3.13), 66 (1.13), 65 (1.27), 53 (0.54), 51 (0.69). (The fragmentation pattern of 47 was very different from those for the two epimers of the corresponding bicyclic [2.2.1] derivative, which were available in the Iowa State University Chemistry Department mass spectrum library.) There were 4 GC peaks assigned as isomers of 48 (the product of a reaction between 42-syn and n-butyllithium). The following 70eV MS (Finnegan GC-MS) is representative for 48, m/e (%RIC): 242 (P, 0.22), 214 (P-28, 0.76), 185 (0.34), 173 (0.54), 171 (0.31), 157 (2.25), 132 (11.65), 117 (5.26), 115 (1.82), 104 (20.69), 94 (3.14), 93 (0.98), 92 (1.00), 91 (4.88), 79 (3.63), 67 (2.79), 57 (1.13), 55 (1.02), 53 (0.97). The order

of elution of the products from Column C or D was: 38-anti, 38-syn, 46, 47, 40, 42-syn, 42-anti, 48.



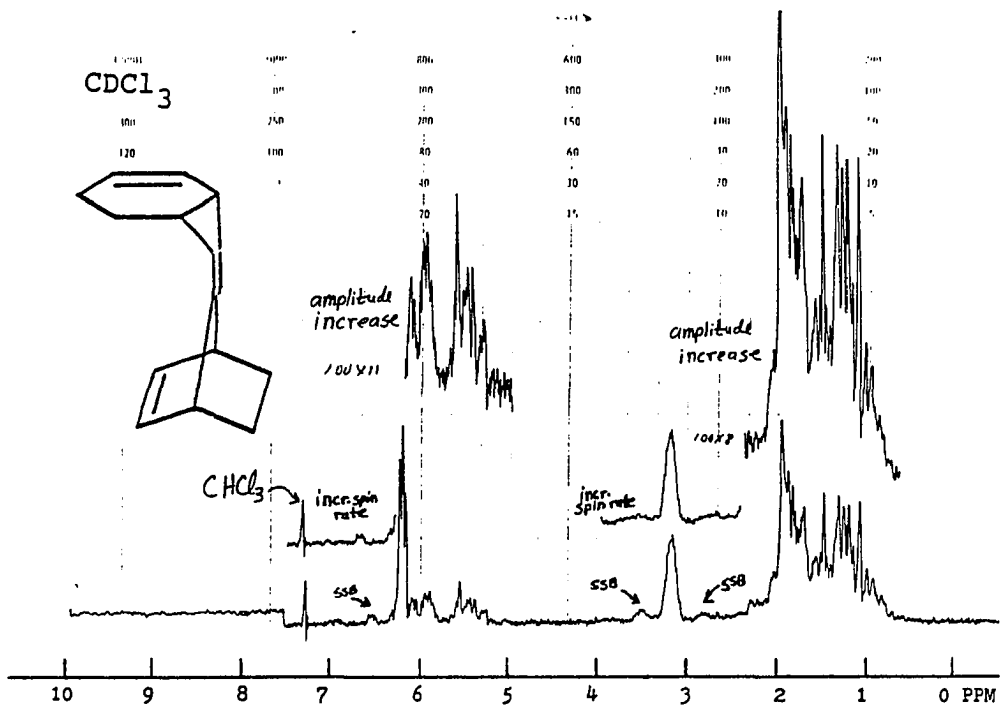
42-syn



42-anti

Attempted preparative GC isolation of 42-syn on either a 12 ft OV-1 glass column, or a 26 ft DEGS glass column (injector 150°, column 140°, detector 175° to 195°) gave two fractions with complex NMR spectra which were much different from the crude spectra of 42-syn and 42-anti. GC-MS analysis showed that each was an isomer of 42-syn. (It was later discovered that in order to get a single GC peak for 42-syn and for 42-anti during GC-MS analysis, it was necessary to use an injector temperature of 180° rather than the temperature of 260° normally used for GC-MS work.)

Products 42-syn and 42-anti could be isolated by preparative TLC on silica gel, with hexane (developed twice) as the eluting solvent. For NMR spectra, chloroform-d was preferable to carbon tetrachloride, because the former caused a larger chemical shift difference between the olefinic pro-



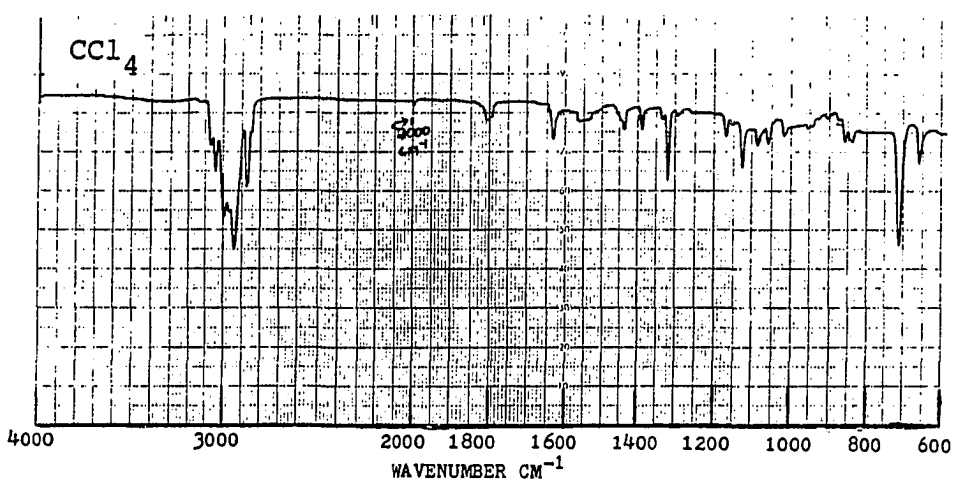


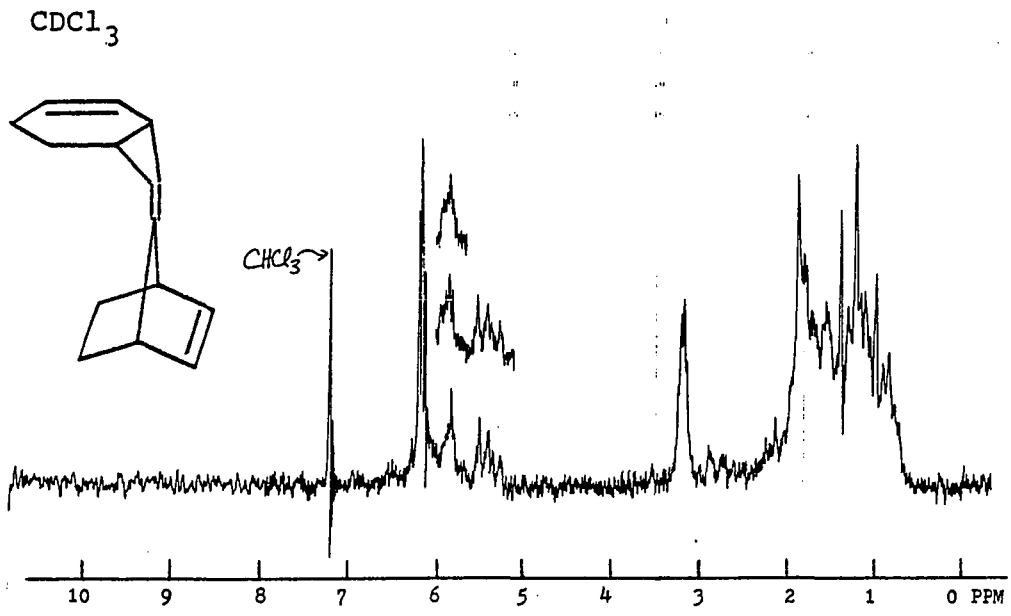
Figure 3. 60 MHz ^{1}H NMR and IR spectra of 42-syn

tons of 42-syn and 42-anti. 42-syn (rf=0.38) 60 MHz ^{1}H NMR ($CDCl_3$): δ 6.18 (t, 2H, J = 2.5 Hz), 6.13-5.78 (complex m, 1H), 5.64-5.23 (complex m, 1H), 3.16 (m, 2H), 2.32-0.69 (complex m, 10H). 300 MHz ^{1}H NMR, Bruker WM-300 ($CDCl_3$): δ 6.171 (AB portion of an ABXY pattern, 2H, $\delta_{A \text{ or } B}$ = 6.148, $\delta_{B \text{ or } A}$ = 6.194, J_{AB} = 5.9 Hz, J_{AX} = 2.8 Hz, J_{AY} = 0), 5.955 (complex 7-line pattern, 1H), 5.408 (t, 1H, J = 8.1 Hz, with further splitting of 2.0 Hz), 3.134 and 3.067 (2 br singlets, XY portion of an ABXY pattern, 2H), 1.858-0.867 (complex m, 10H). A decoupling study (300 MHz ^{1}H NMR) of 42-syn gave the following results: Irradiation of the broad singlet at δ 3.067 caused the left half of the olefinic multiplet at δ 6.171 to collapse to a doublet (J_{AB} = 5.9 Hz), and the right half to collapse to a doublet of doublets (J_{AX} = 2.8, and J_{AB} = ca. 6 Hz). There were no changes in the olefinic multiplets at δ 5.995 and δ 5.408. Similarly, irradiation of the broad singlet at δ 3.134 caused the right half of the olefinic multiplet at δ 6.171 to collapse to a doublet (J = 5.9 Hz) and the left half to collapse to a doublet of doublets (J = 2.8 Hz, and ca. 6 Hz). Again, there were no changes in the olefinic multiplets at δ 5.955 and δ 5.408. Irradiation of the multiplet at δ 5.408 caused some small ill-defined changes in the multiplet at δ 5.955, but no changes in the multiplet at δ 6.171 or in the broad singlets at δ 3.134 and δ 3.067. Similarly, irradiation of the

multiplet at δ 5.955 caused some small changes only in the multiplet at δ 5.408. In all cases, the aliphatic multiplet at δ 1.858 to 0.867 was too complex to detect any changes during the decoupling study. This decoupling study allowed the olefinic chemical shifts (δ_A and δ_B) to be calculated by using the center of gravity method: for two doublets with peaks numbered 1, 2, 3, and 4: (δ1-δ3) = (δ2-δ4) = $\sqrt{(\Delta\upsilon)^2 + J^2}$.[33] 42-syn, IR ($CCl_4$): 3135 (w), 3065 (m), 3045 (m), 3000 (m), 2970 (m), 2940 (s), 2875 (m), 2860 (sh), 2845 (sh), 1810 (br w), 1795 (br sh), 1640 (m), 1630 (sh), 1567 (br w), 1470 (br sh), 1460 (br sh), 1448 (sh), 1439 (m), 1395 (m), 1380 (sh), 1339 (w), 1325 (sh), 1297 (w), 1288 (sh), 1260 (w), 1230 (w), 1202 (w), 1175 (m), 1158 (br w), 1128 (m), 1090 (m), 1080 (sh), 1065 (m), 1027 (m), 980 (w), 960 (w), 945 (w), 930 (w), 910 (w), 880 (w), 862 (m), 849 (m), 718 (s), 665 (s) cm^{-1}. ^{13}C NMR, Jeol FX-90Q ($CDCl_3$): δ 144.128 (967), 136.056 (4550), 135.190 (5476), 126.576 (5408), 123.813 (5492), 101.276 (1015), 44.395 (5184), 43.528 (5377), 25.162 (6892), 24.837 (6738), 21.315 (5925), 18.065 (5650), 16.927 (5177), 14.601 (4154). 70eV MS (Finnegan GC-MS) m/e (%RIC): 184 (0.41), 183 (0.47), 169 (2.60), 156 (3.15), 155 (4.53), 141 (6.95), 129 (4.45), 128 (7.45), 115 (7.44), 105 (0.82), 103 (0.84), 102 (0.85), 93 (1.19), 92 (1.12), 91 (6.64), 89 (1.06), 78 (2.92), 77 (4.82), 65 (2.51),

63 (2.16), 51 (3.04). Analysis: Calcd. for $C_{14}H_{16}$: m/e 184.12520. Found: m/e 184.12513. Calcd. for $C_{14}H_{16}$: 91.25% C, 8.75% H. Found (average of 3 measurements): 89.91% C, 8.82% H. (Evidently there was some degradation during transit for the elemental analysis.)

42-anti (rf=0.30), 60 MHz ^{1}H NMR ($CDCl_3$): δ 6.24 (t, 2H, J = 2.5 Hz), 6.12-5.68 (complex m, 1H), 5.60-5.20 (complex m, 1H) 3.19 (m, 2H), 2.40-0.67 (complex m, 10H). 300 MHz ^{1}H NMR, Bruker WM-300 ($CDCl_3$): δ 6.222 (AB portion of an ABXY pattern, 2H, $\delta_{A \text{ or } B}$ = 6.211, $\delta_{B \text{ or } A}$ = 6.233, J_{AB} = 6.0 Hz, J_{AX} = 2.4 Hz, J_{AY} = 1.1 Hz), 5.989 (complex 7-line pattern, 1H), 5.407 (t, 1H, J = 7.8 Hz), with further splitting of 2.3 Hz), 3.181 (complex m, 2H), 1.951-0.776 (complex m, 10H). Strong irradiation of the multiplet at δ 3.181 caused the olefinic multiplet at δ 6.222 to collapse to two doublets (J_{AB} = 6.0 Hz), with no change in the multiplets at δ 5.989 and δ 5.407. Weaker irradiation of the multiplet at δ 3.181 caused the olefinic multiplet at δ 6.222 to collapse to two doublets of doublets (J_{AX} = 2.4 Hz, and J_{AB} = ca. 6 Hz). In the undecoupled spectrum, the smallest spacing within the multiplet at δ 6.222 was 1.1 Hz (J_{AY}). The next larger spacing was ca. 2.4 Hz (J_{AX}). Irradiation of the multiplet at δ 5.407 caused small changes in the multiplet at δ 5.989, but no changes in the multiplets



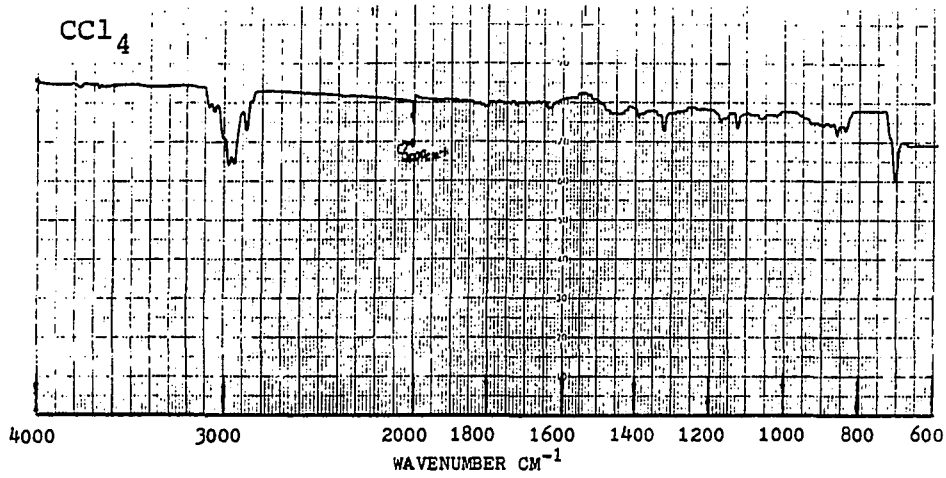


Figure 4. 60 MHz ^{1}H NMR and IR spectra of 42-anti

at δ 6.222 or δ 3.181. Similarly, irradiation of the multiplet at δ 5.989 caused small changes only in the multiplet at δ 5.407. This decoupling study allowed the olefinic chemical shifts (δ_A and δ_B) to be calculated by using the center of gravity method: for two doublets with peaks numbered 1, 2, 3, and 4: $(\delta 1 - \delta 3) = (\delta 2 - \delta 4) = \sqrt{(\Delta\upsilon)^2 + J^2}$.[33] IR ($CCl_4$): 3130 (w), 3070 (w), 3042 (w), 2995 (sh), 2970 (s), 2940 (s), 2910 (sh), 2878 (m), 2868 (sh), 2845 (sh), 2810 (sh), 1810 (br w), 1795 (br sh), 1638 (m), 1632 (sh), 1625 (sh), 1472 (br sh), 1467 (sh), 1458 (w), 1445 (w), 1437 (w), 1395 (w), 1380 (w), 1338 (w), 1325 (m), 1172 (w), 1157 (w), 1127 (m), 1090 (w), 1062 (w), 1020 (w), 928 (w), 908 (w), 898 (sh), 880 (w), 862 (m), 848 (sh), 837 (w), 705 (s), 666 (m), 652 (w) cm^{-1}. ^{13}C NMR, Jeol FX-90Q ($CDCl_3$): δ 144.073 (749), 136.001 (4479), 135.622 (4780), 127.063 (3862), 123.595 (4441), 102.196 (862), 44.719 (4496), 44.015 (4565), 25.757 (5695), 24.511 (6488), 21.585 (5587), 18.010 (4832), 17.197 (4522), 14.600 (4002). 70eV MS (Finnegan GC-MS) m/e (%RIC): 184 (0.44), 183 (0.61), 169 (3.41), 156 (3.45), 155 (4.54), 141 (6.58), 129 (4.36), 128 (7.05), 115 (6.80), 105 (0.87), 103 (0.80), 102 (0.82), 93 (1.32), 92 (1.16), 91 (6.87), 89 (1.05), 78 (2.89), 77 (4.88), 65 (2.47), 63 (2.00), 51 (2.92). Analysis: Calcd. for $C_{14}H_{16}$: m/e 184.12520. Found: m/e 184.12460.

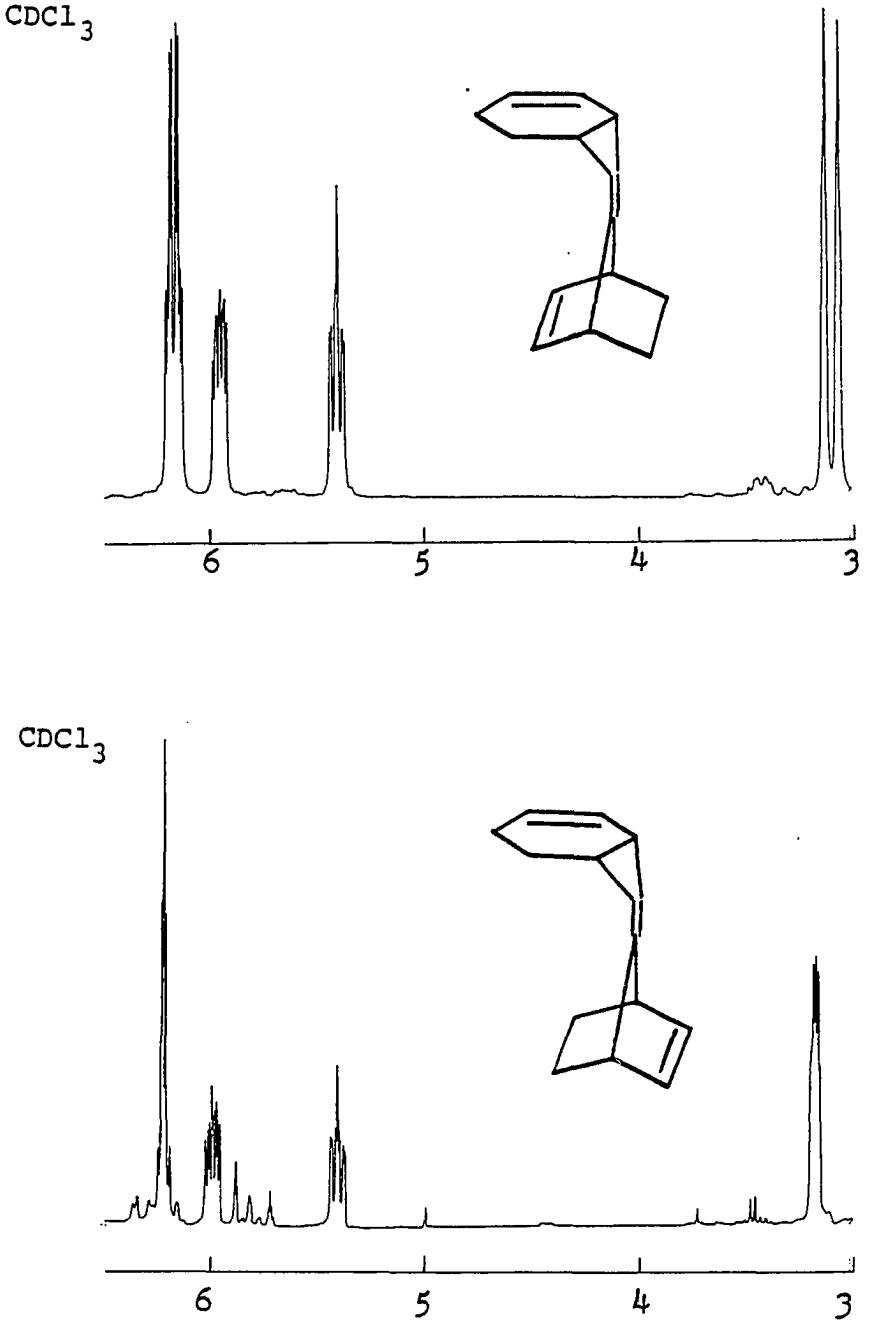


Figure 5. 300 MHz ^{1}H NMR spectra of 42-syn and 42-anti

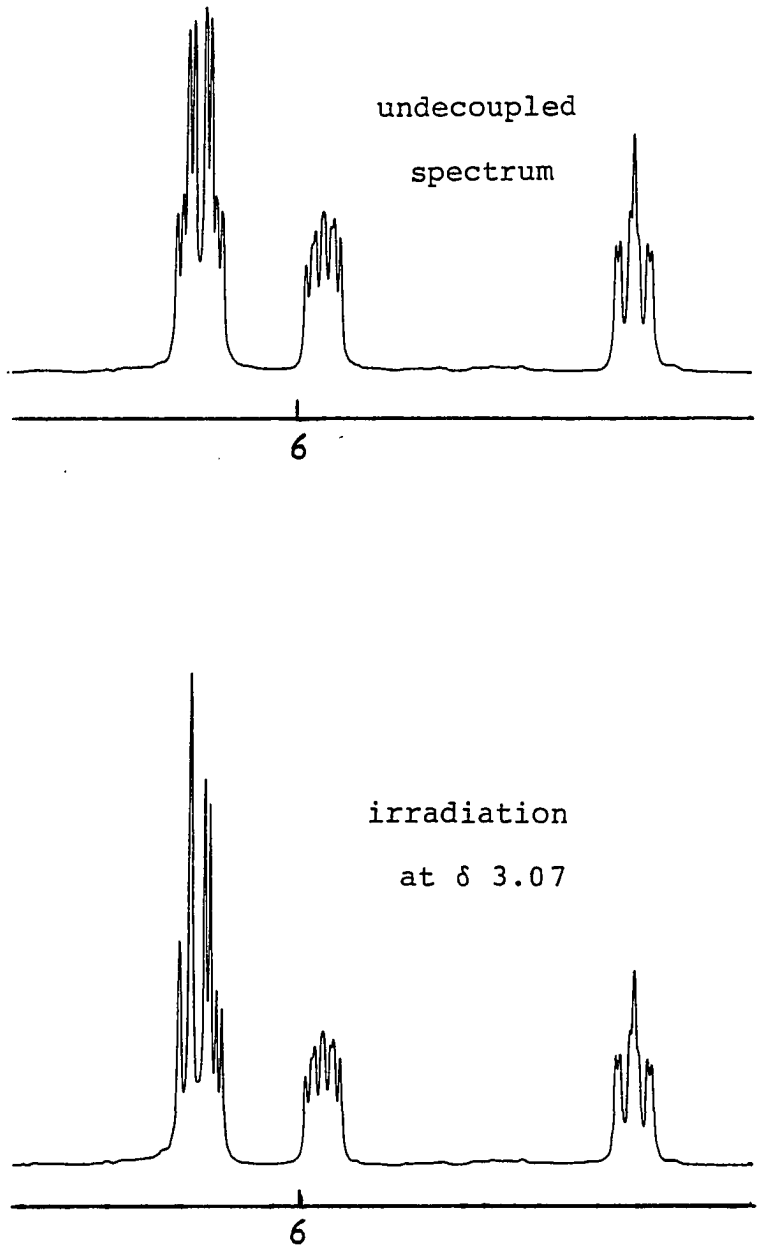


Figure 6. 300 MHz ^{1}H NMR decoupling study of 42-syn

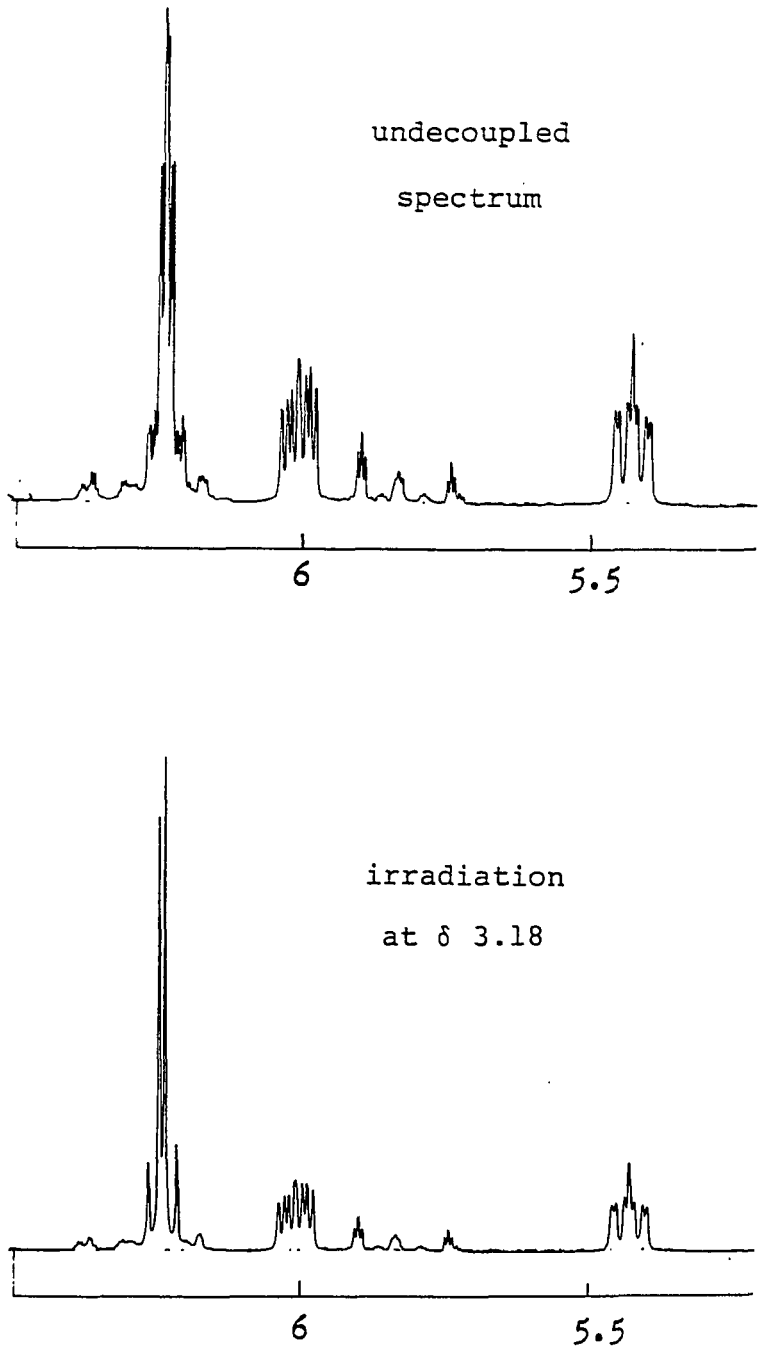
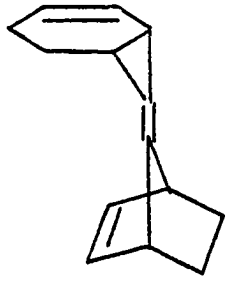


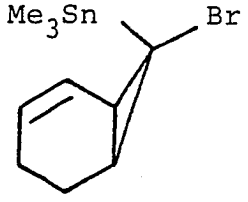
Figure 7. 300 MHz ^{1}H NMR decoupling study of 42-anti

9. Serendipitous preparation of 42-syn from 7,7-dibromobicyclo [4.1.0] hept-2-ene (7)

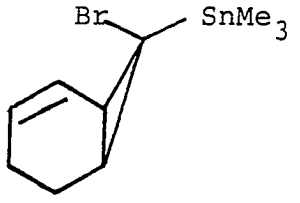
In an attempt to prepare a sample of 35-anti and 35-syn on a large scale, 42-syn was accidently generated instead, evidently because of insufficient cooling. This turned out to be the most convenient large scale preparation of 42-syn.



42-syn



35-anti



35-syn

A 250 ml 3-neck round-bottom flask was equipped with a magnetic stirrer, an addition funnel, and a nitrogen inlet, and was nitrogen-flushed and dried. A solution of 5.02 g (19.9 mmol) of 7,7-dibromobicyclo [4.1.0] hept-2-ene (7) in 50 ml of dry (freshly distilled from LAH) THF was then placed in the flask, and the addition funnel was charged with 4.23 g (21.2 mmol) of trimethylstannyl chloride in 50 ml of dry THF. The flask was cooled to -95° with a "Skelly B" hexane slush bath prior to the slow addition (via syringe,

over a period of 3 to 4 minutes) down the side of the flask of 10 ml (21.9 mmol) of a 2.19 M n-butyllithium/hexane solution. After the solution had been stirred for 40 minutes under nitrogen, while the flask was cooled with the -95° bath, the solution in the addition funnel was added dropwise over a 20 minute period. The resulting solution was stirred under nitrogen, while being allowed to warm to room temperature over a 3.5 hour period. After concentration on a rotary evaporator, the mixture was partitioned between 150 ml of ether and 20 ml of water. The organic layer was washed sequentially with 20 ml of water and 20 ml of saturated sodium chloride solution, dried over anhydrous magnesium sulfate, filtered, and concentrated with a rotary evaporator to afford 5.12 g of yellow oil. Analysis by GC indicated no products other than 42-syn. Isolation by TLC on silica gel (hexane, 2 developments) gave a 35% yield of 42-syn, in 95% purity. (The impurities were not 42-anti.) The 42-syn prepared by this method was identical by GC, GC-MS, ^{1}H NMR, and ^{13}C NMR with that prepared from 35-anti and 35-syn, as described above under entry 8.

10. Deliberate preparation of 42-syn and 42-anti from 7

Both 42-syn and 42-anti could be obtained by treating 7 with 1.16 to 1.5 equivalent of n-butyllithium. Purer products resulted when 1.16 equivalents of n-butyllithium

were used. Also, purer products were obtained when prepared from 80 mg of 7 than from 160 mg (even when the reactions were run at the same concentration). The 42-syn (rf=0.38) and 42-anti (rf=0.30) were isolated by preparative TLC on silica gel (2 developments with hexane).

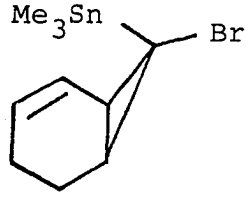
The following is a typical procedure: A 50 ml 3-neck round-bottom flask, equipped with a magnetic stirring bar and an argon inlet, was argon-flushed and dried. It was then charged with a solution of 82.1 mg (0.326 mmol) of 7 in 15 ml of dry (freshly distilled from LAH) THF, and cooled to -78° with a "Skelly B" hexane-dry ice bath prior to the slow (1.5 minute period) addition, down the side of the flask (via syringe) of 0.285 ml (0.419 mmol) of a 1.47 M n-butyllithium/hexane solution. After the solution had been stirred under argon for 60 minutes at -78°, it was allowed to slowly warm to -30° over a 50 minute period. The cooling bath was removed, and stirring under argon was continued for 10 more minutes. The product mixture was next quenched with ca. 0.2 ml of saturated aqueous ammonium chloride, concentrated cautiously (to avoid volatilization of the product) on a rotary evaporator, and partitioned between 2 ml of water, 2 ml of saturated sodium chloride solution and 35 ml of ether. The organic layer was washed with 2 ml of saturated sodium chloride solution, dried over anhydrous magnesium sulfate, filtered, and concentrated cautiously

on a rotary evaporator. The presence of both 42-syn and 42-anti could be detected in the crude mixture by the NMR spectrum in chloroform-d solution. In this solvent, the chemical shift difference between the olefinic protons of the two isomers is ca. δ 0.05. Preparative TLC on silica gel (2 developments with hexane) resulted in a 20% isolated yield of 78% pure 42-syn (with olefinic contaminants other than 42-anti) and an 8% isolated yield of 84% pure 42-anti (with olefinic contaminants other than 42-syn). The 42-syn and 42-anti obtained by this method were, except for the impurities, identical by GC, GC-MS, and NMR with those obtained from 35-anti and 35-syn in entry 8 above.

11. n-Butyllithium treatment of 35-anti (under conditions C) in the presence of traps

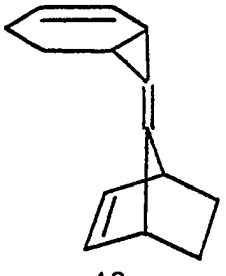
a. 1,3-Diphenylisobenzofuran (DPIBF), 2 equivalents

A 25 ml 3-neck round-bottom flask, equipped with a magnetic stirring bar and an argon inlet, was argon-flushed and dried, and then charged with a solution of 43.1 mg (0.128 mmol) of 35-anti and 69 mg (0.256 mmol) of DPIBF

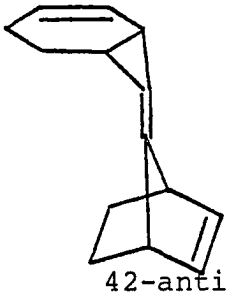


35-anti

in 6 ml of dry (freshly distilled from LAH) THF. The flask was cooled with a -78° bath ("Skelly B" hexane-dry ice) for 15 minutes prior to the slow (1 minute period) addition down the side of the flask of 80 µl (0.20 mmol) of a 2.46 M n-butyllithium/hexane solution via syringe. After 5 minutes of stirring at -78° under argon, 0.30 ml (7.4 mmol) of methanol-O-d (99.5+ atom %D) was syringed in over an 18 second period. After 10 more minutes of stirring at -78°, under argon, the cooling bath was removed, and the stirring was continued for 10 more minutes. Then, 10 drops of water were added as a final quench, followed by cautious concentration (avoiding volatilization of the products) of the mixture on a rotary evaporator. The residue was partitioned between 35 ml of ether, 2 ml of water, and 2 ml of saturated sodium chloride solution. The organic layer was washed with 2 ml of saturated sodium chloride solution, dried over anhydrous magnesium sulfate, filtered, and cautiously concentrated on a rotary evaporator, leaving a bright yellow oily solid. GC and NMR analysis showed 42-syn and 42-anti



42-syn



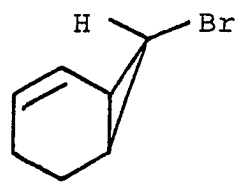
42-anti

as the major products. Only a trace (ca. 2% yield) of a product with a GC retention time longer than that of DPIBF was observed. This product was not investigated any further.

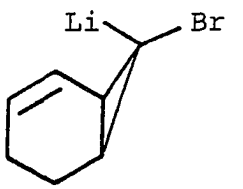
b. Cyclohexene (180 equivalents) The reaction of 0.139 mmol of 35-anti with 1.5 equivalents of n-butyllithium was conducted as in part a, but without DPIBF, and in a solution of 4 ml of dry THF plus 2.5 ml of cyclohexene (previously purified by distillation from phosphorous pentoxide and refrigerator-stored over potassium carbonate). Also, the solution was stirred at -78° for 60 minutes, instead of 5 minutes, prior to the methanol-0-d addition. The product mixture contained 42-syn and 42-anti (ratio ca. 5 to 1 by GC-MS analysis) in ca. 67% combined yield (by NMR measurement). GC-MS analysis showed none of the expected olefin-carbene trapping products.

c. Isobutylene (210 equivalents) The reaction of 0.122 mmol of 35-anti with 1.5 equivalents of n-butyllithium was conducted as in part a, but without DPIBF, and in a solution of 4 ml of dry THF plus 2.5 ml of isobutylene (distilled into the THF solution after having been condensed into a graduated tube). Also, the solution was stirred at -78° for 60 minutes, instead of 5 minutes, prior to the methanol-0-d addition. The % conversion of 35-anti was only 88%, probably due to moisture being introduced during the

condensation of the isobutylene. There was a substantial yield (17% corrected GC yield, based on unrecovered starting material) of 38-anti. Curiously, it had only a ca. 6% incorporation of deuterium according to MS analysis. This result implies a slow proton abstraction from isobutylene by the carbenoid intermediate 34-anti. The coupling products



38-anti



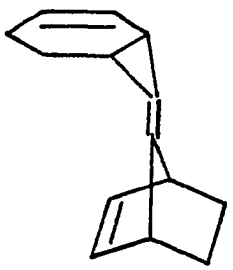
34-anti

42-syn and 42-anti (ratio ca. 10 to 1 by GC-MS) were formed in a combined yield of ca. 61% (by NMR). GC-MS analysis showed none of the expected olefin-carbene trapping products.

d. Triethylsilane (12.4 equivalents) The reaction of 0.124 mmol of 35-anti with 1.5 equivalents of n-butyllithium was carried out according to the procedure of part a, but without DPIBF, and in a solution of 0.25 ml (1.57 mmol) of triethylsilane and 5.5 ml of dry THF. A mixture of 42-syn and 42-anti (ca. 58% combined NMR yield) was obtained as the major product. According to GC-MS analysis, there was no product corresponding to the insertion of a carbene intermediate into the Si-H bond of triethylsilane.

12. Reaction of 42-syn with DPIBF

A solution of 7.2 mg (0.039 mmol) of 42-syn and 38.6 mg



42-syn

(0.143 mmol) of DPIBF in 0.3 ml of benzene-d_6 was sealed in an NMR tube. Heating at 70° for 60 minutes gave no reaction. After 3 hours of heating at 120°, however, NMR analysis indicated that a DPIBF adduct(s) might have been formed in good yield. 60 MHz ^{1}H NMR (C_6D_6): in addition to aromatic absorbances, δ 6.1-5.5 (complex m), 5.2-4.7 (complex m), 2.7-2.35 (complex m), 2.2 (m, possibly a triplet, J = 2Hz), 1.8-0.7 (complex m). GC-MS analysis on Column B showed two isomers in a ca. 1:1 ratio with the expected molecular weight of 454. Their mass spectra are listed below in the order of the isomers' elution from Column B. Isomer 1, 70eV MS (Finnegan GC-MS), m/e (%RIC): 454 (P, 0.57), 426 (0), 270 (P-184, 26.98), 184 (0), 93 (0.79), 92 (1.28), 90 (0.13). Isomer 2, 70eV MS (Finnegan GC-MS), m/e (%RIC): 454 (P, 0.22), 426 (P-28, 0.21) 270 (P-184, 27.47), 184 (P-270, 0.05), 93 (0.29), 92 (0.75), 91 (3.70), 90 (0.46).

13. Preparation of 7-bromo-7-diphenylphosphinoxy-bicyclo [4.1.0] hept-2-ene (57)

A 25 ml 3-neck round-bottom flask, equipped with an addition funnel, a magnetic stirring bar, and an argon inlet, was argon-flushed and dried. It was then charged with a solution of 0.24 g (0.95 mmol) of 7 (7,7-dibromobicyclo-[4.1.0] hept-2-ene) in 12 ml of dry (freshly distilled from LAH) THF. A solution of 0.19 ml (1.1 mmol) of diphenyl-chlorophosphine in 6 ml of dry THF was then placed in the addition funnel. The flask was cooled to -95° to -100° ("Skelly B" hexane slush bath) for 15 minutes prior to the slow addition over a 3 minute period, down the side of the flask, via syringe, of 0.74 ml (1.1 mmol) of a 1.47 M n-butyllithium/hexane solution. After the solution had then been stirred under argon for 12 minutes at -95° to -100° (while care was taken not to let the solution freeze), the solution in the addition funnel was added dropwise over a 90 second period. The solution was stirred for 5 more minutes at -95° to -100°, and then allowed to warm to 0° over a 55 minute period. The cooling bath was removed, and the stirring was continued for 15 minutes. Next, the solution was quenched with 7 drops of saturated aqueous ammonium chloride, concentrated on a rotary evaporator, and partitioned between 35 ml of ether and 2 ml of water plus 2 ml of saturated sodium

chloride solution. The organic layer was then washed with 2 ml of saturated sodium chloride solution, dried over anhydrous sodium sulfate, filtered, and concentrated on a rotary evaporator to give 0.37 g of a yellow oil.

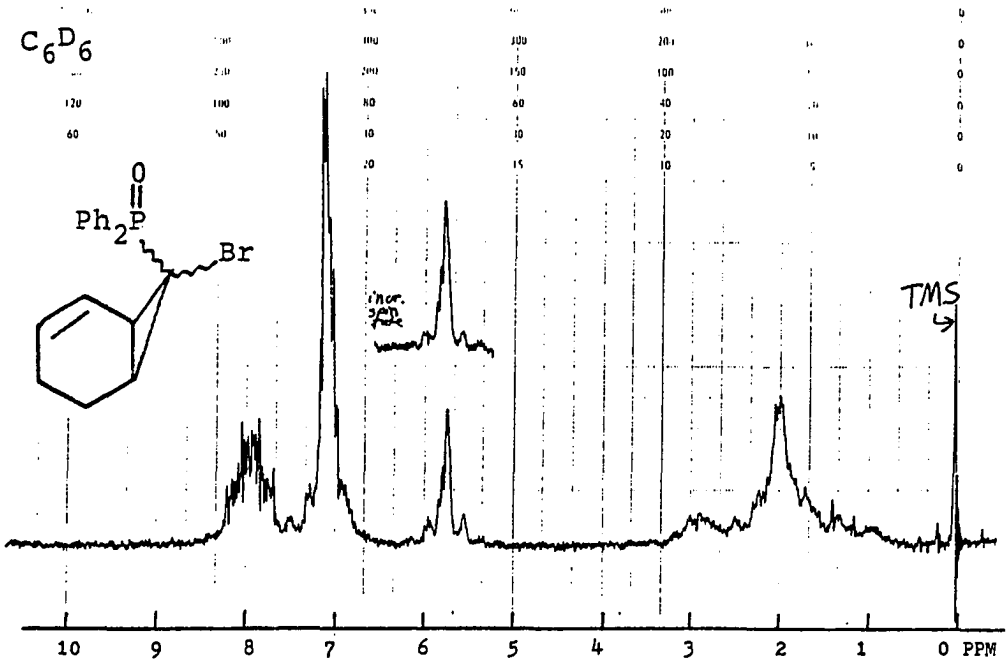
Preparative TLC of 2/3 of the product mixture on silica gel (2 developments with ether) gave 2 major bands (Bands 1 and 3), which may have corresponded to the two epimers of 57. Several other minor bands contained unidentified by-products. Band 1 (one epimer of 57), rf=0.25, 28 mg of oily white solid, 60 MHz ^{1}H NMR (C_6D_6): δ 8.25-7.58 (complex m, relative integr. 4.9), 7.30-6.75 (complex m, including solvent abs.), 5.70 (complex m, relative integr. 2.0), 3.22-0.83 (complex m, relative integr. 8.7); (CCl_4): δ 7.98-7.57 plus 7.54-7.13 (complex multiplets, combined relative integr. 13.0), 5.64 (complex m, relative integr. 2.0), 3.0-0.66 (complex m, relative integr. 9.2). IR (CCl_4): 3090 (sh), 3075 (m), 3050 (m), 3020 (sh), 2975 (sh), 2945 (m), 2895 (sh), 2850 (w), 1965 (br w), 1895 (br, w), 1810 (br w), 1745 (br w), 1640 (br w), 1483 (w), 1440 (s), 1375 (w), 1310 (w), 1243 (w), 1205 (s), 1120 (s), 1104 (m), 1082 (w), 1055 (w), 1030 (w), 945 (w), 862 (w), 710 (m), 688 (s) cm^{-1}. 70eV MS (Finnegan GC-MS, Column B), m/e (%RIC): 374 (P+2, 0.10), 372 (P, 0.10), 297 (0.01), 296 (0.13), 295 (0.16), 294 (0.45), 293 (P-79, 1.50), 292 (0), 291 (0), 202 (4.87),

201 (P-171, 5.62), 92 (1.00), 91 (10.95), 79 (14.98), 78 (3.49), 77 (10.22), 65 (2.47), 51 (5.69), 47 (4.06).

Band 3 (the other epimer of 57), rf=0.15, 12 mg of a colorless oil, 60 MHz ^{1}H NMR (C_6D_6): δ 8.15-7.63 (complex m, relative integr. 4.6), 7.18-6.82 (complex m, includes solvent absorption), 5.58 (complex m, relative integration 2.0), 2.68-0.72 (complex m, relative integration 9.8); (CCl_4): 7.95-7.45 plus 7.45-7.11 (complex multiplets, combined relative integration 11.0), 5.74 (complex m, relative integration 11.9). IR (CCl_4): 3100 (sh), 3080 (m), 3050 (m), 2970 (sh), 2935 (m), 2830 (sh), 1480 (w), 1438 (s), 1220 (sh), 1192 (s), 1122 (s), 1105 (m), 1025 (w), 972 (w), 950 (w), 875 (w), 850 (w), 770 (sh), 695 (s) cm^{-1}. 70eV MS (Finnegan GC-MS, Column B), m/e (%RIC): 374 (P+2, 0.14), 372 (P, 0.15), 356 (P+2-16, 0.01), 297 (0.04), 296 (0.37), 295 (0.20), 294 (0.55), 293 (P-79, 1.01), 292 (1.91), 291 (1.56), 277 (0.36), 262 (1.52), 202 (1.76), 201 (P-171, 7.64), 92 (0.79), 91 (8.95), 79 (0.97), 78 (2.04), 77 (9.88), 65 (4.18), 51 (5.39), 47 (5.78).

14. Treatment of 57 with methyl iodide

Stirring a 4 ml benzene solution of 28 mg (0.078 mmol) of one epimer of 57 (Band 1 above) with 25 µl (0.40 mmol) of methyl iodide in a 25 ml 3-neck round-bottom flask under



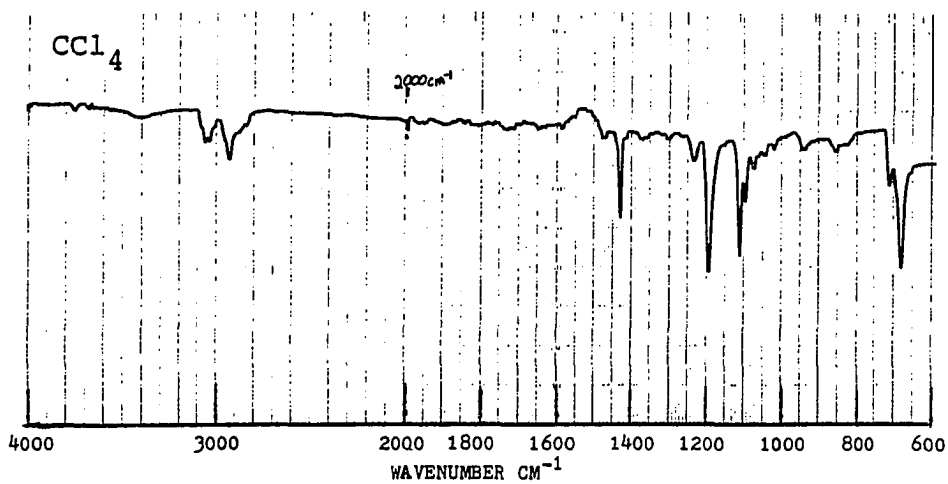


Figure 8. 60 MHz ^1H NMR and IR spectra of 57, TLC Band 1 (7-bromo-7-diphenylphosphinoxybicyclo [4.1.0] - hept-2-ene)

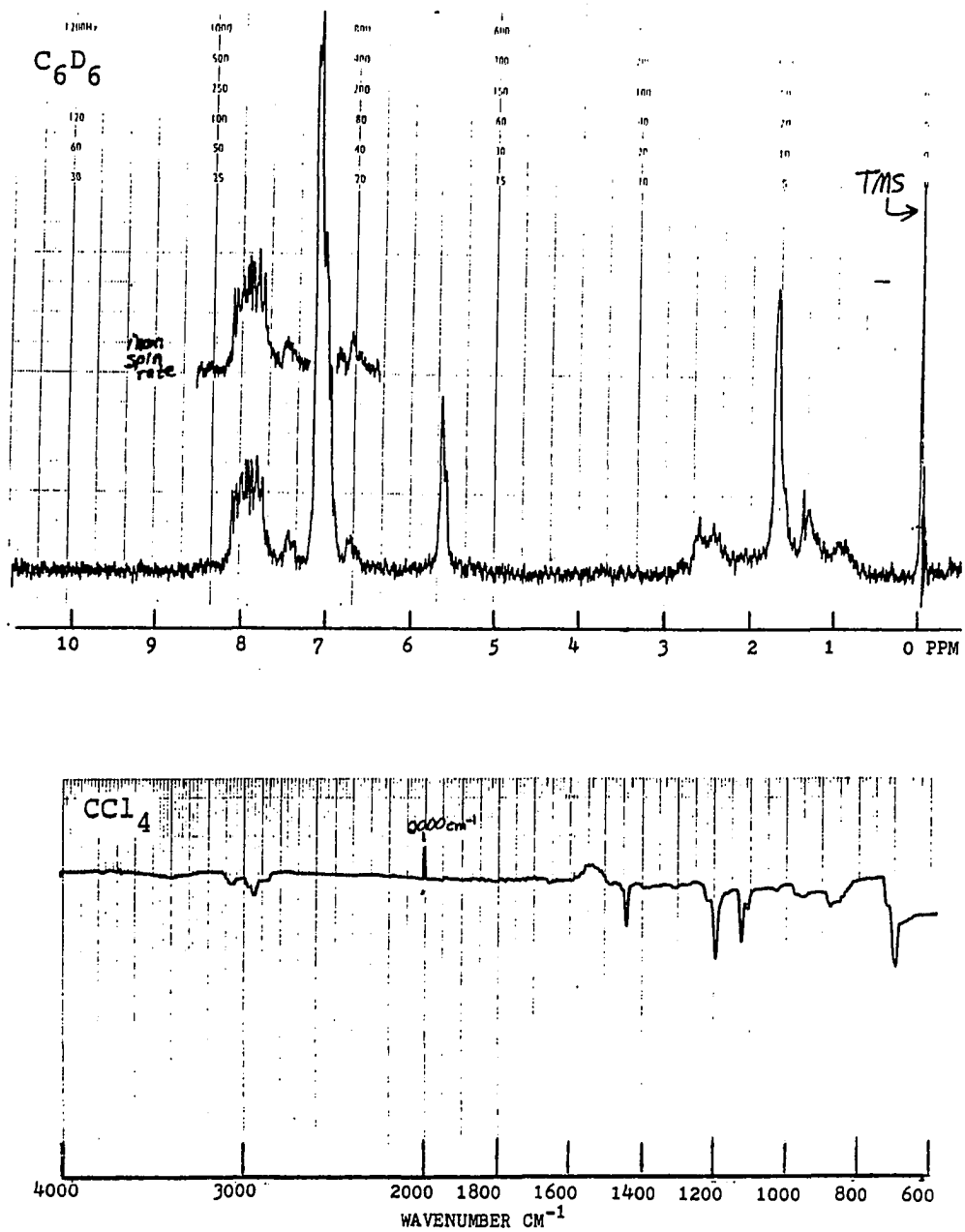


Figure 9. 60 MHz ^1H NMR and IR spectra of 57, TLC Band 3 (7-bromo-7-diphenylphosphinoxybicyclo [4.1.0] hept-2-ene)

nitrogen for 24 hours at room temperature resulted in no reaction. Similarly, treatment with 0.5 ml of pure methyl iodide in an NMR tube at room temperature for 24 hours gave no reaction.

Treatment of 12 mg of the other epimer of 57 (Band 3 above) with 0.5 ml of pure methyl iodide in an NMR tube at room temperature for 28 hours also resulted in no reaction.

15. Preparation of P,P,P-diphenylmethoxy-7-bromo-bicyclo [4.1.0] hept-2-enylphosphonium triflate (58)

A 110 mg (ca. 0.31 mmol) sample of one epimer of 57 (Band 1 above), dissolved in 7 ml of dry (stored over 4A molecular sieves) benzene, was placed in a dried, argon-flushed 25 ml 3-neck round-bottom flask (equipped with a magnetic stirrer and an argon inlet). Then 100 µl (0.88 mmol) of methyl triflate was syringed in under argon. The resulting solution was stirred at room temperature under argon for 2.5 hours. A white paste gradually precipitated out. An argon flush was used to concentrate the solution to ca. 4 to 5 ml. The benzene solution was next withdrawn via pipet, and the residue was rinsed with 1 ml of dry benzene. The excess benzene was flushed off with argon, leaving a very viscous white oil. The product was very sensitive to water and/or acetone, causing the NMR spectrum in acetone-d_6 to change

within 1 or 2 hours. 58, Isomer I, 60 MHz ^{1}H NMR (acetone-d_6), immediately after dissolving the sample: δ 8.57-7.40 (complex m, relative integr. 20.4), 6.14 (br s, relative integr. 2.0), 5.89 (m, relative integr. 0.4), 5.77 (br s, relative integr. 1.7, probably water, since the chemical shift was concn. dependent), 3.95 (s, relative integr. 1.6), 3.74 (s, relative integr. 1.7), 3.07-0.64 (complex m, including solvent absorption).

A 12 mg (ca. 0.034 mmol) sample of the other epimer of 57 (Band 3 above) was dissolved in 0.5 ml of benzene-d_6, placed in an NMR tube, and flushed briefly with argon prior to the addition of 17 μl (0.15 mmol) of methyl triflate. After another brief argon flushing, the solution was allowed to stand at room temperature for 30 hours, after which time a small amount of brown oil had gradually settled to the bottom of the tube. The tube was cut, so that the benzene-d_6 layer could be withdrawn via pipet. The oil was dissolved in acetone-d_6. The NMR spectrum had to be run immediately, because the spectrum of the product changed within 1 or 2 hours when dissolved in acetone-d_6. Compound 58, Isomer II, 60 MHz ^{1}H NMR (acetone-d_6), immediately after dissolving the sample: δ 8.23-7.65 (complex m, relative integr. 6.3), 7.65-7.45 (m, relative inegr. 3.5), 5.75 (m, relative integr. 2.0), 4.22 (large br s, probably water, since its chemical shift was concn. dependent), 4.15 (s, relative integr. 1.4), 3.98

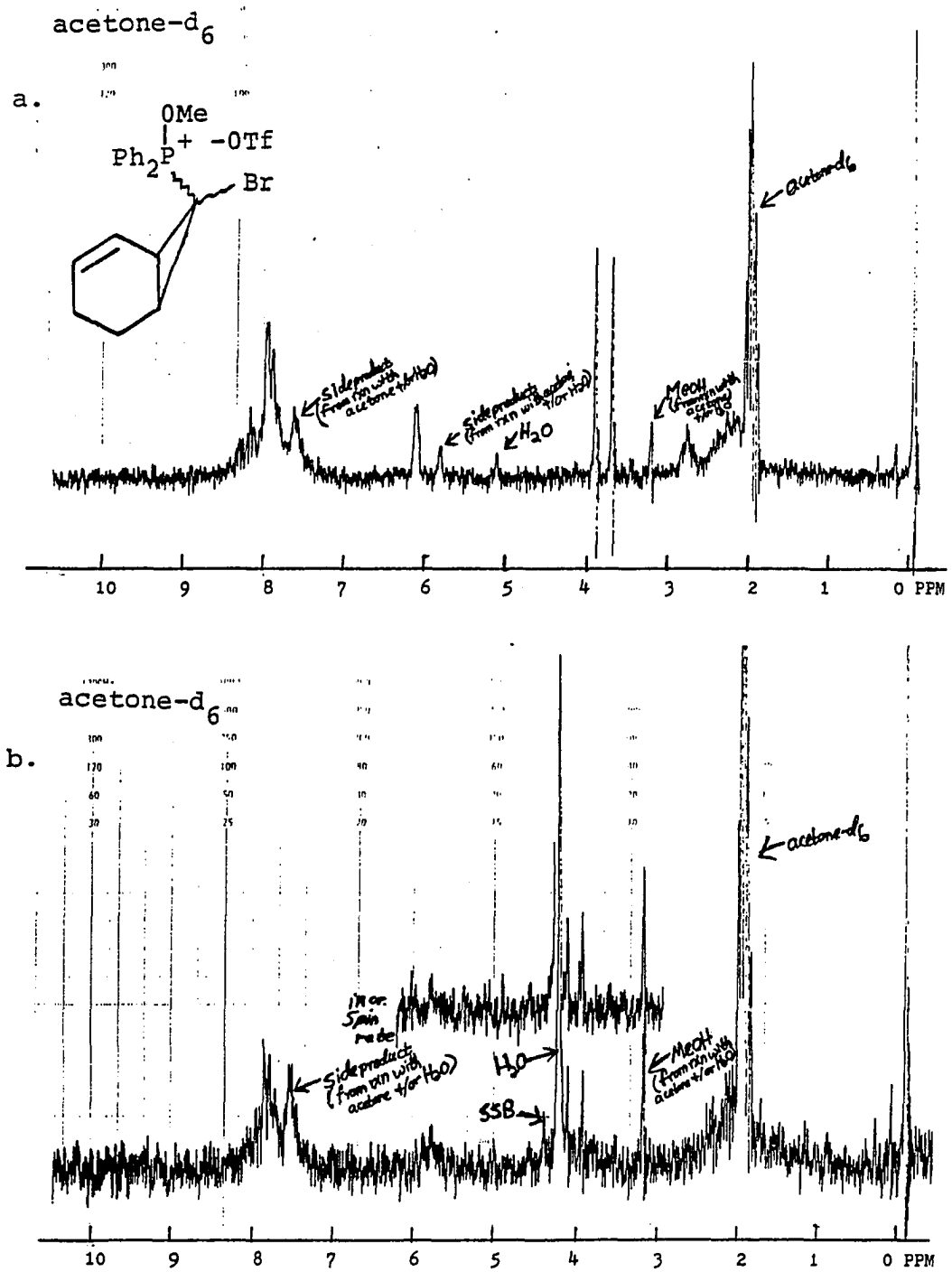


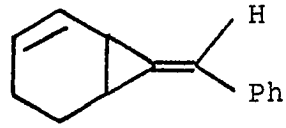
Figure 10. 60 MHz ^{1}H NMR spectra of 58: a. Isomer I, b. Isomer II (P,P,P-diphenylmethoxy-7-bromo-bicyclo[4.1.0]hept-2-enylphosphonium triflate)

(s, relative integr. 1.4), 3.22 (s, relative integr. 0.88, probably methanol), 2.8-1 (m, including solvent absorption).

16. Treatment of 58 with n-butyllithium and benzaldehyde

To the sample of 58 (Isomer I) prepared above (ca. 0.31 mmol) in a 25 ml 3-neck round-bottom flask was added 6 ml of dry (freshly distilled from LAH) THF. The resulting solution (under nitrogen) was cooled to -106° ("Skelly B" hexane slush bath) for 15 minutes. The solution became cloudy during the cooling. Then, 0.25 ml (0.37 mmol) of a 1.47 M n-butyllithium/hexane solution was slowly syringed in down the side of the flask over a 3 minute period. After 15 minutes of stirring at -104° to -107° under nitrogen, a solution of 34 µl (0.34 mmol) of benzaldehyde (previously distilled from zinc powder) dissolved in 0.5 ml of hexane was slowly syringed in down the side of the flask over a 1 minute period. The yellow color of the solution immediately became lighter during the benzaldehyde addition. After having been stirred at -103° to -106° for 5 minutes, the solution was allowed to warm to ca. + 10° over a 1 hour period. The bath was then removed, and the stirring under nitrogen was continued for another hour. Next, the solution was quenched with 10 drops of saturated ammonium chloride solution, concentrated on a rotary evaporator, and, finally, worked up with ether, water, and saturated sodium chloride

solution. Drying with anhydrous sodium sulfate, filtration, and concentration on a rotary evaporator resulted in 93 mg of yellow oil. Preparative TLC on silica gel (15% ether/ 85% hexane) gave a 24% yield of phenylbutylcarbinol (tentatively identified by NMR and GC-MS). Material extracted from the baseline of the TLC plate showed aromatic absorptions (possibly diphenylphosphine and diphenylphosphine oxide groups) as well as some absorption that resembled a tetrahydrofuranyl group. There was no evidence for the presence of the desired Wittig product 62.

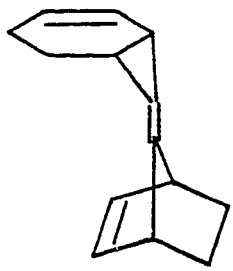


62

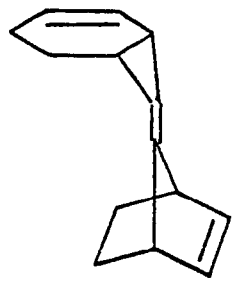
17. Preparation of 7-bromo-7-diphenylphosphinobicyclo-[4.1.0]hept-2-ene (55)

A 100 ml 3-neck round-bottom flask, equipped with an addition funnel, a magnetic stirrer, and an argon inlet, was argon-flushed and dried, and then charged with a solution of 0.504 g (2.00 mmol) of 7 (7,7-dibromobicyclo [4.1.0] hept-2-ene) in 30 ml of dry (freshly distilled from LAH) THF. A solution of 0.39 ml (2.2 mmol) of diphenylchlorophosphine in 4 ml of dry THF was then placed in the addition funnel.

The flask was next cooled to -101° for 15 minutes prior to the addition via syringe of 1.65 ml (2.43 mmol) of a 1.47 M n-butyllithium/hexane solution down the side of the flask over a 3 minute period. After 12 minutes of stirring at -101° to -104°, the solution in the addition funnel was added over a 2.5 minute period. The solution was next stirred for an additional 10 minutes at -101° to -107°, and then allowed to slowly warm to 10° over a 1 hour period. The cooling bath was removed, and stirring under nitrogen was continued for 15 more minutes. Quenching with 10 drops of saturated ammonium chloride solution was followed by concentration on a rotary evaporator, and a workup with benzene, water, and saturated aqueous sodium chloride. Drying over anhydrous sodium sulfate, filtration, and concentration in vacuo yielded 0.86 g of yellow oil. Preparative TLC of 1/2 of the crude product mixture on silica gel (20% ethyl acetate/80% hexane) gave 4 bands. They were extracted from the silica gel with benzene. Band 1 (rf=0.89) consisted of a very small amount of 42-syn plus 42-anti. Band 2 (rf=0.83)



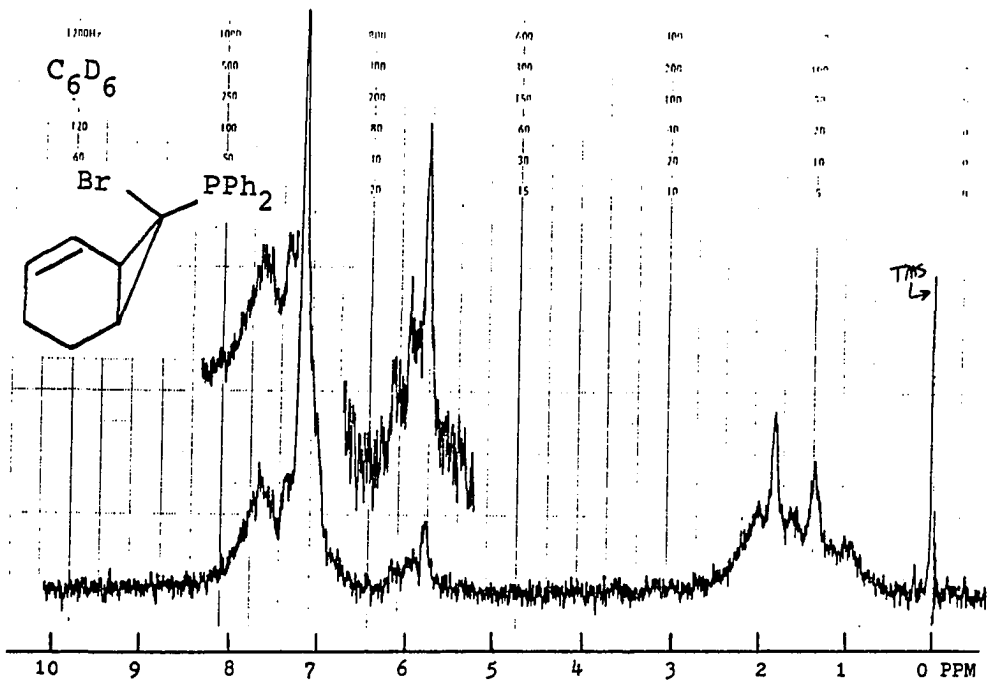
42-syn



42-anti

contained 19 mg of material whose identity is uncertain. Band 2, 60 MHz ^{1}H NMR (CCl_4): 7.15 (m, relative integr. 10.0), 5.9 (v. small br m), 2.1-0.7 (complex m, relative integr. 14.6); (C_6D_6): 7.6-7.2 (complex m, relative integr. 3.2), 7.05 (m, relative integr. 6.8), 6.0-5.4 (br m, relative integr. 0.5), 2.2-0.6 (complex m, relative integr. 7.0). IR (CCl_4): 3085 (m), 3070 (m), 2975 (m), 2940 (s), 2885 (sh), 2858 (m), 1480 (m), 1434 (s), 1378 (w), 1122 (w), 1090 (br w), 1070 (very w), 1025 (m), 690 (s) cm^{-1}.

Band 3 (rf=0.77) contained 24 mg (6.7% yield) of the major isolable product, 60. Its stereochemistry was assigned on the basis of the results of the reaction of its methylphosphonium iodide with n-butyllithium and benzaldehyde (vide infra). Syn-7-bromo-anti-7-diphenylphosphinbicyclo-[4.1.0]hept-2-ene (60), 60 MHz ^{1}H NMR (CCl_4): δ 7.3 (complex m, relative integr. 8.7), 5.82 (m, relative integr. 2.0), 2.35-0.8 (complex m, relative integr. 7.2); (C_6D_6): δ 7.9-7.4 (complex m, relative integr. 3.8), 7.11 (m, incl. solvent abs.), 6.14-5.64 (complex m, relative integr. 2.0), 2.4-0.7 (complex m, relative integr. 7.2). IR (CCl_4): 3085 (m), 3065 (m), 3040 (m), 3010 (sh), 2970 (sh), 2935 (m), 2860 (w), 1955 (br w), 1880 (br w), 1810 (w), 1645 (br w), 1585 (w), 1480 (m), 1448 (sh), 1432 (s), 1395 (w), 1375 (w), 1350



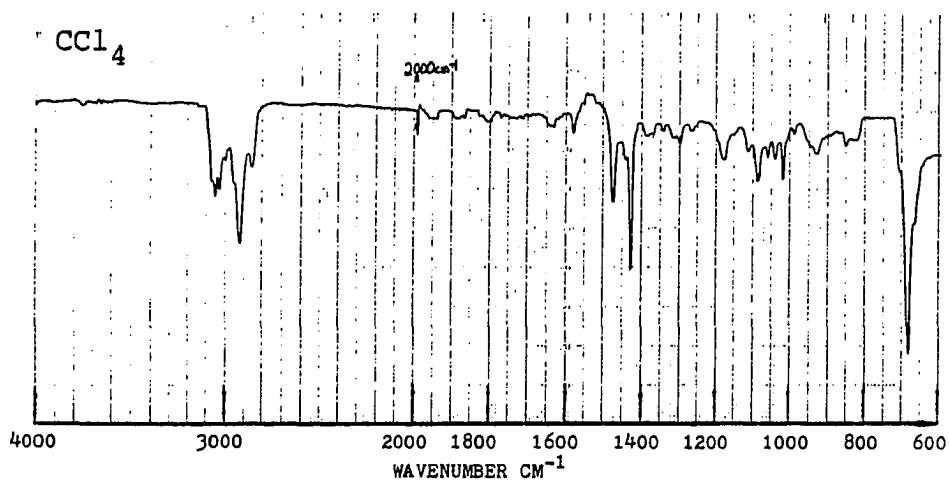


Figure 11. 60 MHz ^1H NMR and IR spectra of 60. (syn-7-bromo-anti-7-diphenylphosphino-bicyclo [4.1.0] hept-2-ene)

(w), 1325 (w), 1305 (w), 1270 (w), 1185 (br m), 1120 (w), 1092 (m), 1065 (w), 1045 (w), 1024 (m), 935 (br w), 855 (w), 830 (br sh), 685 (s) cm^{-1}.

Band 4 (rf=0.71) contained 15 mg (4.2% yield) of a compound tentatively identified as the C^7 epimer of 60, i.e., anti-bromo-55. 60 MHz ^1H NMR (CCl_4): δ 7.68-6.8 (complex m, relative integr. 24.3), 5.8 (m, relative integr. 2.0), 2.65-0.8 (complex m, relative integr. 8.9); (C_6D_6): 7.9-7.57 (m, relative integr. 5.1), 6.91 (m, very close to solvent absorption, relative integr. 21.4), 5.85 (apparent dd, rel. integr. 2.0, J = 8 Hz, with further fine splitting), 2.47-1.2 (complex m, relative integr. 8.4). IR (CCl_4): 3080 (m), 3062 (m), 3040 (m), 3005 (sh), 2965 (sh), 2930 (m), 2860 (br sh), 1955 (br w), 1885 (br w), 1810 (br w), 1725 (br w), 1643 (br w), 1585 (m), 1560 (sh), 1480 (m), 1450 (sh), 1432 (s), 1380 (br w), 1325 (w), 1303 (w), 1270 (w), 1192 (sh), 1180 (w), 1085 (m), 1065 (w), 1045 (w), 1023 (m), 1010 (sh), 992 (w), 955 (sh), 932 (m), 855 (w), 825 (w), 685 (s) cm^{-1}. GC-MS analysis of the above products was not useful because they decomposed and/or rearranged extensively on GC columns.

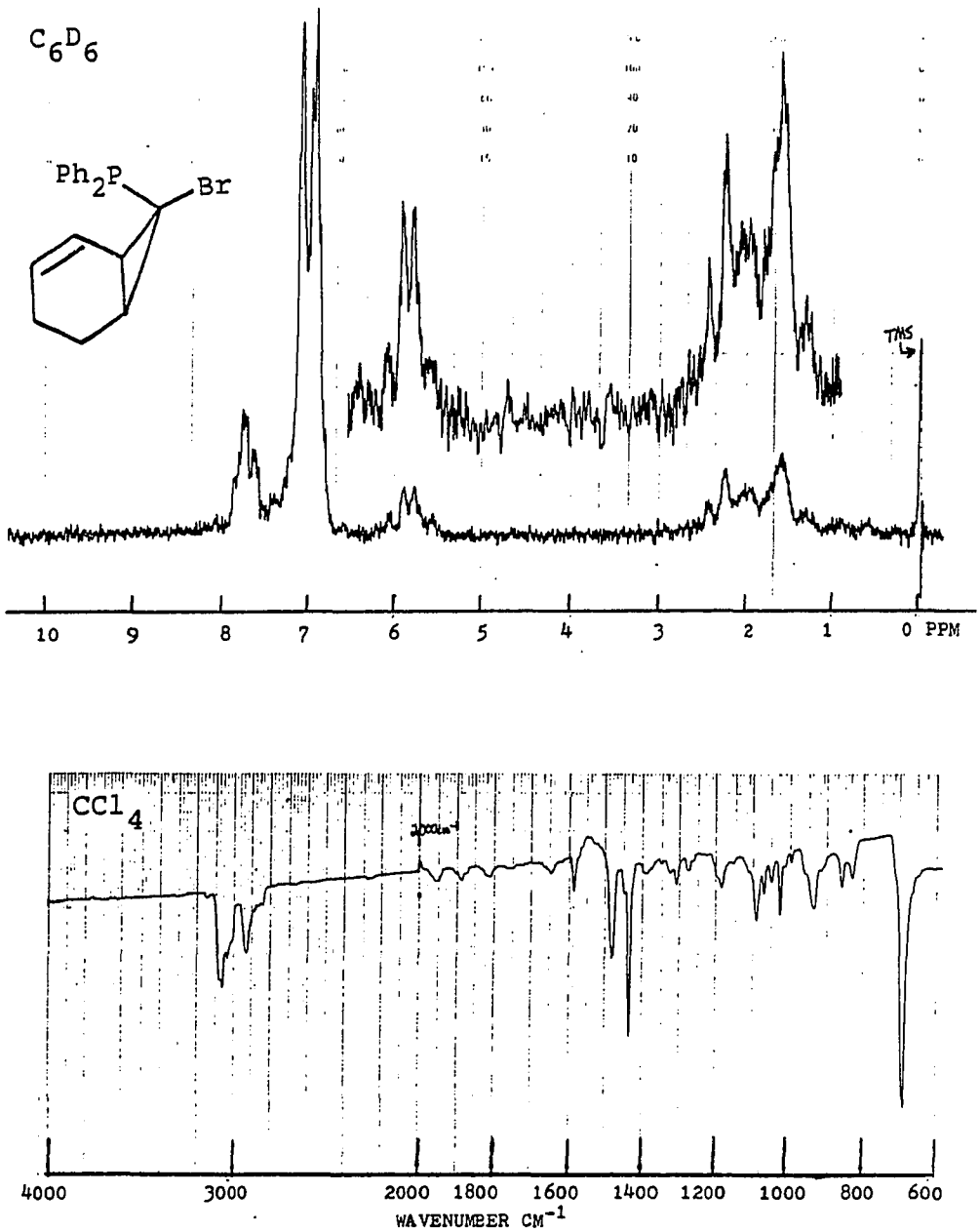


Figure 12. 60 MHz ^1H NMR and IR spectra of anti-bromo-55 (anti-7-bromo-syn-diphenylphosphinobicyclo [4.1.0] hept-2-ene)

18. Preparation of P,P,P-diphenylmethyl-anti-7-bromobicyclo[4.1.0]hept-2-enylphosphonium iodide (61)

A 20 mg (0.056 mmol) sample of 60 (Band 3 under entry 17 above) was dissolved in 1 ml of benzene-d_6 (previously dried over potassium carbonate), then treated with 30.5 µl (0.49 mmol) of methyl iodide (previously dried over 4A molecular sieves), and, finally, allowed to stand at room temperature with exclusion of light. After 20 hours, a large amount of white oily solid had formed. The benzene solution was removed via pipet, and the solid was rinsed with a small amount of dry benzene. The solid was almost insoluble in either benzene or acetone, but was quite soluble in chloroform. 61, 60 MHz ^{1}H NMR ($CDCl_3$): δ 8.2-7.6 (complex m, relative integr. 14.7), 6.03 (m, relative integr. 2.0), 3.12 (d, J = 13 Hz, relative integr. 2.5), 2.4-2 (complex m, relative integr. 8.1). IR ($CHCl_3$): 2990 (sh), 2945 (s), 2882 (sh), 1587 (m), 1575 (br sh), 1540 (w), 1480 (w), 1436 (s), 1390 (br w), 1345 (br w), 1312 (w), 1215 (br m, probably an impurity), 1112 (s), 992 (w), 960 (br m), 940 (sh), 898 (s), 855 (w), 678 (w), 650 (w) cm^{-1}.

19. Treatment of 61 with n-butylithium and benzaldehyde

A sample of 63 mg (0.13 mmol) of 61 prepared as described in the preceding entry was suspended in 4 ml of dry

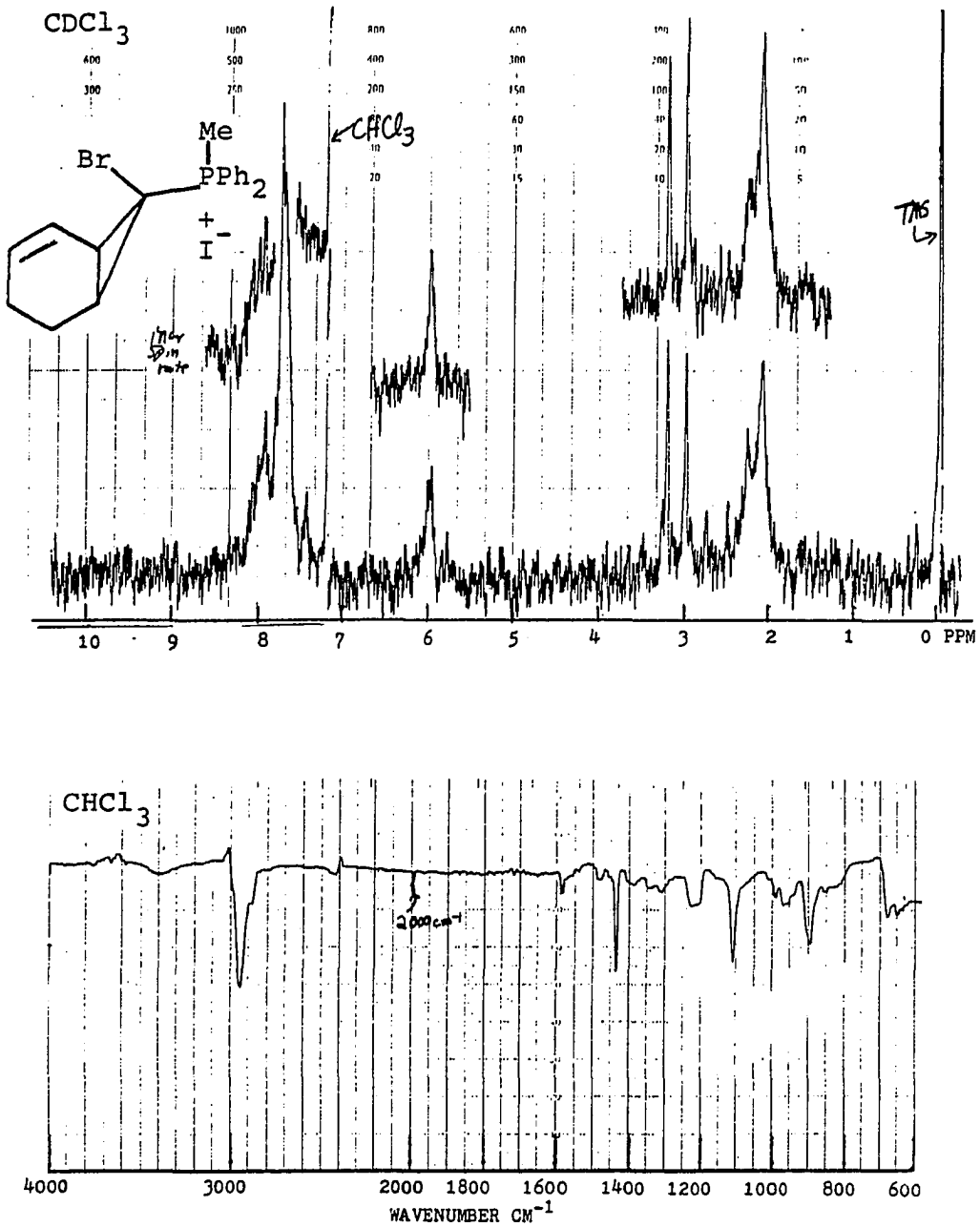
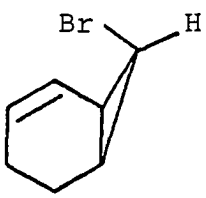


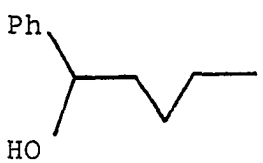
Figure 13. 60 MHz ^{1}H NMR and IR spectra of 61 (P,P,P-diphenylmethyl-anti-7-bromo-bicyclo [4.1.0] hept-2-enylphosphonium iodide)

(freshly distilled from LAH) THF in an argon-flushed 25 ml 3-neck round-bottom flask which had been equipped with a magnetic stirring bar and an argon inlet. The stirred suspension was cooled to -103° to -106° ("Skelly B" hexane slush bath) for 15 minutes prior to the slow addition via syringe of 0.12 ml (0.18 mmol) of a 1.47 M n-butyllithium/ hexane solution down the side of the flask over a 50 second period. The solution quickly turned deep yellow. After 15 minutes of stirring at -103° to -106° under argon, a solution of 17 µl (0.17 mmol) of benzaldehyde (previously distilled from zinc powder) in 0.5 ml of hexane was slowly syringed in through the center neck of the flask. The reaction solution became cloudy, pale yellow. After 5 more minutes of stirring at -101° to -106°, the cooling bath was allowed to slowly warm. Within one hour, the temperature had reached -10°, after which time the bath was removed, and the solution was then stirred under argon for 2 more hours. A white precipitate remained suspended at that time. Upon the addition of a quench (consisting of 11 drops of water), said precipitate slowly disappeared. The solution was next concentrated on a rotary evaporator, and partitioned between 30 ml of benzene and 2 ml of water, plus 2 ml of saturated sodium chloride solution. The organic layer was washed with 2 ml of saturated sodium chloride

solution, dried over anhydrous sodium sulfate, filtered, and concentrated on a rotary evaporator to yield 55 mg of an orange oil. NMR analysis showed a 14% yield of 38-syn, and an 8% recovery of unreacted benzaldehyde. GC-MS analysis (Finnegan, Column B) indicated the presence of 38-syn, 59, and 62 in the following uncorrected relative molar amounts--0.40:0.50:0.09. There were also major amounts of several unidentified products with high retention times.



38-syn



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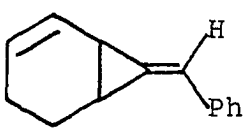


62

20. One-pot modified Wittig reaction of 7,7-dibromobicyclo[4.1.0]hept-2-ene (7)

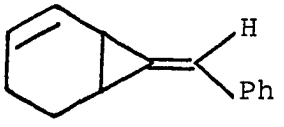
A solution of 0.113 g (0.448 mmol) of 7 in 6 ml of dry (freshly distilled from LAH) THF was placed in a 25 ml 3-neck round-bottom flask which had been equipped with a magnetic stirring bar, an addition funnel, and an argon inlet. Next, a solution of 90 µl (0.50 mmol) of diphenylchlorophosphine in 2.5 ml of dry THF was placed in the addition funnel, and the flask was cooled to -95° to -100° ("Skelly

B" hexane slush bath). After the solution had been allowed to equilibrate at -95° to -100° for 15 minutes, 0.35 ml (0.52 mmol) of a 1.47 M n-butyllithium/hexane solution was syringed in down the side of the flask over a 2 minute period. After 15 more minutes of stirring at -95° to -100° (care had to be taken not to let the solution freeze), the solution in the addition funnel was added dropwise over a 1 minute period. A deep yellow color immediately formed. After another 10 minutes of stirring at -95° to -98°, the solution was allowed to slowly warm to -55°.

Then a solution of 100 µl (1.60 mmol) of methyl iodide in 0.5 ml of hexane was syringed in down the side of the flask over a 30 second period. The solution was stirred at -45° for 5 more minutes, prior to the removal of the cooling bath. The color of the solution slowly lightened during 1.5 more hours of stirring under argon. A small amount of white precipitate had collected in the bottom of the flask. After the mixture had been stirred at room temperature under argon for 17 more hours, a large amount of solid had collected.

Then the solvent was evaporated with an argon flush, and the oily solid residue was suspended in 8 ml of dry (freshly distilled from LAH) THF. The flask was next cooled to dry ice-acetone temperature for 15 minutes prior

to the syringing-in down the side of the flask of 0.35 ml (0.52 mmol) of a 1.47 M n-butyllithium/hexane solution over a 2 minute period. A brown color quickly developed. After the solution had been stirred for 10 more minutes at -78° under argon, a solution of 46 µl (0.45 mmol) of benzaldehyde (previously distilled from zinc powder) in 0.5 ml of hexane was syringed in down the side of the flask. The color of the solution immediately faded from brown to yellow. After another 10 minutes of stirring at -78° under argon, the bath was allowed to warm to room temperature over a 2.5 hour period. There was almost no precipitate at that time. The solution was quenched with a few drops of water, concentrated on a rotary evaporator, and partitioned between ether and water. The organic layer was washed with saturated sodium chloride solution, dried over anhydrous sodium sulfate, filtered, and concentrated on a rotary evaporator. GC-MS analysis showed a very complex mixture. A trace amount of a compound tentatively identified as the desired product, 62, was observed. Preparative TLC on silica gel (2 developments with hexane) gave 5 bands, none of which was recognizable as 62.

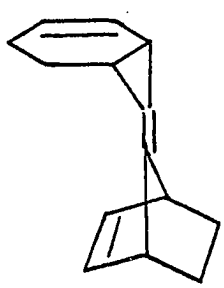


62

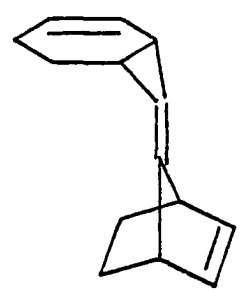
21. Peterson olefination reaction between syn-7-trimethylsilyl-anti-7-bromobicyclo [4.1.0] hept-2-ene (63) and bicyclo [2.2.1] hept-2-en-7-one (52)

A 25 ml 3-neck round-bottom flask was equipped with a magnetic stirring bar and an argon inlet, and was dried and argon-flushed. It was next charged with a solution of 35.0 mg (0.143 mmol) of 63[34] in 0.5 ml of benzene-d_6, plus 4.5 ml of dry (freshly distilled from LAH) THF. The flask was cooled to -78° under argon for 10 minutes before 0.10 ml (0.19 mmol) of a 1.87 M n-butyllithium/hexane solution was syringed in down the side of the flask over a 1 minute period. This addition resulted in a slightly yellowish solution. After an additional 10 minutes of stirring under argon at -78°, a solution of 17.8 µl (21.0 mg) of 88% pure 52 (0.171 mmol), which was contaminated with 7,7-dimethoxybicyclo [2.2.1] hept-2-ene, in 1 ml of hexane was syringed in through the center neck of the flask over a 1 minute period. The yellow color immediately faded. After 30 more minutes of stirring under argon at -78°, the cooling bath was removed, and stirring under argon was continued for 1.5 more hours. The solution turned back to yellow during that time. Then 12 drops of water were syringed in, followed by 1 ml of saturated ammonium chloride solution, resulting in a colorless solution. Concentration on a rotary evaporator was followed

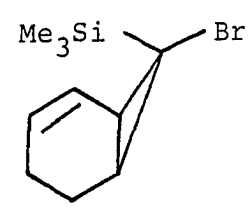
by the addition of 1 ml of water, and extraction with 30 ml of ether. (The aqueous layer had a neutral pH.) The organic layer was washed with saturated sodium chloride solution, dried over anhydrous magnesium sulfate, filtered, and concentrated on a rotary evaporator to yield 34 mg of a colorless oil. The 60 MHz ^{1}H NMR spectrum (benzene-d_6) showed a trace of 7,7-dimethoxybicyclo [2.2.1] hept-2-ene, plus at least two triplets centered at ca. δ 5.8. There was a very complex aliphatic absorption, as well as 4 trimethylsilyl peaks (2 large singlets and 2 smaller singlets) from δ 0 to δ 0.25. By comparison with authentic samples, it could be seen that 42-syn and 42-anti, and 63 were not present in the mixture. The mixture was assumed to consist mostly of 64.



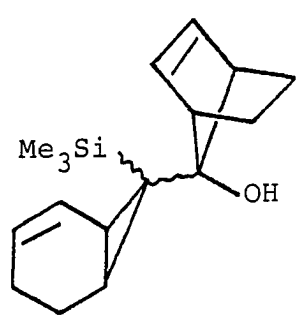
42-syn



42-anti



63



64

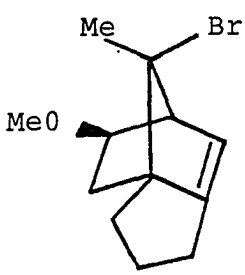
A 25 ml 3-neck round-bottom flask was equipped with a magnetic stirring bar and an argon inlet, and was dried and argon-flushed. It was then charged with 0.314 g (1.88 mmol) of 24% potassium hydride-mineral oil dispersion, and then flushed with argon for 10 minutes. The potassium hydride was washed with 4 x 2 ml of dry (stored over 4A molecular sieves) hexane, and then flushed dry with argon. A solution of 34 mg (0.125 mmol) of the crude 64, just prepared above, in 4 ml of dry (freshly distilled from LAH) THF was then added to the flask. The solution immediately turned yellow. It was stirred under argon at room temperature for 25 hours, during which time the solution turned brown. The flask was cooled to 0°, and the solution was quenched cautiously with 12 drops of water, followed by 5 ml of saturated ammonium chloride solution. The mixture was next warmed to room temperature, concentrated on a rotary evaporator, and extracted with 30 ml of ether. (The water layer had a neutral pH.) The organic layer was washed with 2 ml of saturated sodium chloride solution, dried over anhydrous magnesium sulfate, filtered, and concentrated on a rotary evaporator. The crude 60 MHz NMR spectrum showed, in addition to the 7,7-dimethoxybicyclo [2.2.1] hept-2-ene impurity, traces of 42-syn and 42-anti (identified by comparison with authentic samples), along with much larger amounts of other olefinic material.

GC-MS analysis showed trace amounts (ca. 10% yield) of 42-syn and 42-anti (0.4 to 1 isomeric ratio), along with larger amounts of bicyclo[4.1.0]hept-2-ene and/or bicyclo[2.2.1]hept-2-ene derivatives containing trimethylsilyl and/or n-butyl groups, as well as several other unidentified compounds.

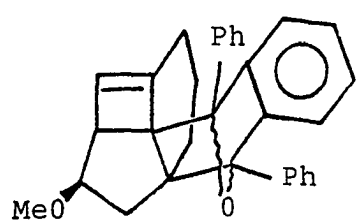
22. Methyllithium treatment of 10,10-dibromo-exo-4-methoxytricyclo[4.3.1.$0^{1,6}$]dec-2-ene (18) in the presence of triethylsilane

a. 1 M triethylsilane A 25 ml 3-neck round-bottom flask, equipped with a magnetic stirring bar and an argon inlet, was argon-flushed and dried prior to being charged with a solution of 48.7 mg (0.151 mmol) of 18 (prepared by the known procedure[20]), 1.00 ml (6.28 mmol) of triethylsilane, and 49.1 mg (0.182 mmol) of DPIBF in 4 ml of dry (freshly distilled from LAH) ether. The solution was stirred briefly at room temperature under argon, and then 1.30 ml (1.66 mmol) of 1.28 M methyllithium/ether solution (Alfa, "Low Halide") was syringed in during a 2 minute period. The resulting solution was stirred at room temperature under argon for 20 minutes, and then quenched by the slow addition of 1 ml of water (Caution: frothing!), while the flask was being cooled with a room temperature water bath. After the solution had been stirred for a few more minutes, it was diluted

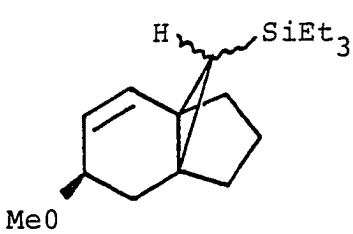
with 30 ml of ether, and washed successively with two 5 ml protions of water (until the washing were neutral), and 2 ml of saturated sodium chloride solution, and dried over anhydrous magnesium sulfate overnight (open to the room to allow as much as possible of the DPIBF to air-oxidize). Filtration and concentration in vacuo resulted in 0.119 g of a viscous yellow oil which was analyzed by NMR (using benzaldehyde, previously distilled from zinc powder under argon, as the internal standard). Products 19 and 24 were identified by comparison with authentic spectra. The expected triethylsilane insertion products (69 and, possibly, 70) could not be detected by NMR analysis.



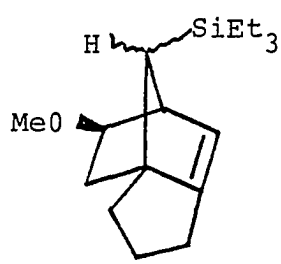
19



24



69



70

b. 3 M triethylsilane This experiment was performed in the same way as the above 1 M triethylsilane experiment, except with the following amounts of reagents: 48.7 mg of 18, 3.09 ml of triethylsilane, 49.6 mg of DPIBF, and 1.20 ml of methyllithium/ether solution. Note: the DPIBF did not completely dissolve until the methyllithium addition was begun.

23. Preparation of 3-methylcyclohex-2-enone (83) and 3-methylcyclohex-2-enol (82)

Compound 83 was prepared according to the procedure of Smith and Rouault[35], with some slight modifications. Ethyl acetoacetate (52.3 ml, 411 mmol) and paraformaldehyde (6.16 g, equivalent to 205 mmol of formaldehyde) were mixed in a 250 ml round-bottom flask. Then 2 ml of piperidine were added, and the flask was allowed to stand with occasional swirling. Within 10 minutes, an exothermic reaction ensued, and it was necessary to occasionally dip the flask in an ice bath. After 40 minutes, the exothermicity had subsided, and the reaction mixture consisted of a yellow solution mixed with a small amount of white amorphous solid. It was then heated on a steam bath for 4 hours with occasional swirling. The crude 4,6-dicarboethoxy-3-methylcyclohex-2-enone thus prepared was mixed with a solution consisting of 115 ml of glacial acetic acid, 12 ml of concentrated sulfuric acid, and 77 ml of water,

and was then heated to reflux for 5 hours. The resulting brown solution was diluted with 50 ml of ether, cooled to 0°, and then made just slightly alkaline by gradually adding the required amount of a solution of 89 g of sodium hydroxide in 250 ml of water (while monitoring with pH paper). The layers were then separated, and the aqueous layer was re-extracted with two 50 ml portions of ether. The ether layers were combined and washed with 10 ml of water, 10 ml of saturated sodium bicarbonate solution, 10 ml of water, and 10 ml of saturated sodium chloride solution, and then dried (anhydrous sodium sulfate), filtered, and concentrated *in vacuo* to give a brown oil (57% crude yield). The product was purified by distillation through a short vigreaux column at aspirator pressure, resulting in a 44% yield (based on ethyl acetoacetate) of *83*. *60 MHz ^{1}H NMR* (CCl_4): δ 5.69 (m, 1H), 2.45-1.67 (complex m, 9H, with a singlet at δ 1.93).

Compound *82* was prepared, with small modifications, according to the procedure described by Bowman *et al.*[36] A 500 ml 3-neck round-bottom flask, equipped with a magnetic stirring bar, an addition funnel, a nitrogen inlet, and a reflux condenser, was nitrogen-flushed and dried, and then charged with 1.50 g (39.5 mmol) of LAH and 100 ml of anhydrous ether (a fresh can). A solution of 6.98 g (63.5 mmol) of *83* in 50 ml of anhydrous ether was placed in the

addition funnel. The suspension in the flask was cooled to 0°, and stirred under nitrogen while the solution in the addition funnel was added dropwise over a 30 minute period. The mixture was next allowed to warm to room temperature, and then heated to reflux, with stirring, under nitogen, for 2.5 hours. It was then cooled to 0°, and quenched with 35 ml of 20% Rochelle's salt, followed by 20 ml of water and 20 ml of saturated ammonium chloride solution. The resulting mixture was separated, and the aqueous layer was back-extracted with three 75 ml portions of ether. The combined ether layers were washed with 10 ml of saturated ammonium chloride solution, 10 ml of saturated sodium chloride solution, dried (anhydrous magnesium sulfate), filtered, and concentrated on a rotary evaporator to give 6.3 g (89% crude yield) of 82. It was suitable for use without further purification. 60 MHz ^{1}H NMR (CCl_4): δ 5.42 (m, 1H), 4.04 (m, 1H), 2.30 (s, 1H, exchangeable with D_2O), 2.05-1.15 (m, 9H).

24. Preparation of 3-methylcyclohex-2-enone tosylhydrazone (80)

Birch and Subba Rao[37] published a procedure for making 80 which involved heating p-toluenesulfonylhydrazine with an excess of 82 in a THF/benzene solution, with a trace of p-toluenesulfonic acid. However, the following procedure

was found to be more convenient. (The procedure used was that described by Billups, et al.[38] for the synthesis of 2-methylcyclohex-2-enone tosylhydrazone.) A 50 ml 3-neck round-bottom flask, equipped with a magnetic stirring bar, an addition funnel, and a reflux condenser, was charged with 5.18 g (27.8 mmol) of p-toluenesulfonylhydrazine and 9 ml of 60% methanol/40% water. (Heating was required to dissolve the p-toluenesulfonylhydrazine.) The addition funnel was charged with 3.06 g (27.8 mmol) of enone 83. The solution in the flask was heated to reflux, and the enone was then added all at once, followed by another 1 ml of 60% methanol/40% water. After the resulting solution had been heated to reflux for a few minutes, it was allowed to stop boiling, and the stirring bar was removed (causing a precipitate to begin forming). The flask was stoppered, and immediately placed in a refrigerator. After 4 hours, a viscous oil had separated out, so the bottom of the flask was scratched, the solution was seeded with a few crystals of a crude sample of 80, and refrigeration was then continued for 5 days. Filtration left a solid which was washed with 20 ml of ice-cold 40% methanol/60% water, and recrystallized from absolute ethanol (15 ml). The first and second crops had almost identical NMR spectra, and were combined (2.3 g of yellowish powder). The remaining mother liquor was concentrated, and

recrystallized from ethanol (25 ml), to afford another 2.5 g of product, which had an NMR spectrum the same as those of the first and second crops. The total yield of 80 was 61%. 60 MHz ^{1}H NMR (acetone-d_6): δ 8.94 (br s, ca. 1 H, probably NH), 7.91-7.17 (AB q, spacings = 9, 18.5 Hz, ca. 4 H), 5.75 (m, ca. 1 H) 2.5-1.5 (complex m, incl. solv. absorption).

25. Preparation of 1-methylcyclohexa-1,3-diene (79)

The method of Birch and Subba Rao[37] gave only a trace amount of 79, in the form of a dilute benzene solution. The following procedure was found to work much better. (The procedure used was a combination of that described by Shapiro and Duncan[39] for the synthesis of 1,7,7-trimethybicyclo-[2.2.1] hept-2-ene with that described by Billups et al.[38] for 2-methylcyclohexa-1,3-diene.) A 250 ml 3-neck round-bottom flask was fitted with a magnetic stirring bar, an addition funnel, and a nitrogen inlet, and was nitrogen-flushed and dried. It was next charged with 2.40 g (8.63 mmol) of 80 and 40 ml of dry (freshly distilled from LAH) ether. Then 5 ml of dry ether were placed in the addition funnel. The mixture in the flask was stirred at ambient temperature for 15 minutes, and the resulting suspension was then cooled to 0°. The dropwise addition of the ether in the addition funnel was started right before 17.0 ml (22.1 mmol) of a 1.3 M methyllithium/ether solution was syringed

into the addition funnel. (This procedure was carried out in order to prevent clogging of the addition funnel.) The dropwise addition of the methyllithium/ether solution was continued over a 30 minute period. The stirred mixture in the flask gradually turned deep orange. It was then stirred under nitrogen at room temperature for 2 hours. (Gas evolution was quite evident during the first 0.5 hour, and then gradually subsided.) The resulting mixture was cooled to 0° and quenched with 25 ml of water. The orange color almost immediately gave way to a yellowish tint. The ice bath was removed and the stirring was continued for a few more minutes. Then the mixture was transferred to a separatory funnel, and the organic layer was removed, washed sequentially with two 10 ml portions of saturated ammonium chloride solution, two 10 ml portions of water, and one 10 ml portion of saturated sodium chloride solution, and then dried (anhydrous sodium sulfate). After being filtered, the solution was concentrated on a rotary evaporator at 0°, affording 0.998 g of a brown oil mixed with a small amount of solid. NMR analysis showed it to be a mixture of toluene and 79. The NMR spectrum agreed very well with that published by Babad et al.[40] and by Skattebol[41]. (The NMR spectrum reported by Birch and Subba Rao[37] was evidently in error.) Compound 79, 60 MHz ^{1}H NMR (CCl_4): δ 5.83-5.18 (m, 3H), 1.96 (br s, ca. 4H), 1.66 (br s, ca. 3H).

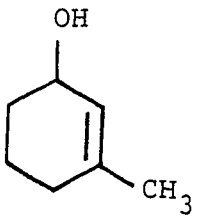
26. Preparation of a mixture of 6-methyl-7,7-dibromobicyclo[4.1.0]hept-2-ene (78) and 3-methyl-7,7-dibromobicyclo[4.1.0]hept-2-ene (81)

A 100 ml 3-neck round-bottom flask, fitted with a magnetic stirring bar, an addition funnel, and a nitrogen inlet, was nitrogen-flushed and dried, and charged with 0.655 g (5.84 mmol) of commercial potassium tert-butoxide powder, along with 10 ml of hexane. A crude 0.988 g sample of 79 (prepared above in entry 25) was dissolved in 4 ml of hexane, filtered through glass wool, mixed with 0.450 ml (5.14 mmol) of bromoform, and then placed in the addition funnel. The stirred solution in the flask was cooled to -78° (dry ice-acetone bath), and the solution in the addition funnel was then added dropwise over a 15 minute period. Stirring under nitrogen at -78° was continued for 2 more hours, and the stirred mixture was then allowed to slowly warm to 10° over a 3.5 hour period. It was then poured into 20 ml of ice-cold water, and the resulting mixture was transferred to a separatory funnel. The organic layer was removed, and the aqueous layer was re-extracted with 20 ml of ether. The organic layers were combined, and were sequentially washed with two 5 ml portions of saturated ammonium chloride solution, 5 ml of water, and 5 ml of saturated sodium chloride solution, and then dried (anhydrous sodium sulfate), filtered, and concentrated in vacuo to provide a dark red oil. Purifi-

cation by preparative TLC on silica gel (hexane) gave a ca. 1.6 to 1 mixture of 78 and 81, respectively (rf=0.65), which was inseparable by TLC (15% yield based on 80). The spectral and analytical data for 78 will be presented later. The data for 81 are: 60 MHz ^{1}H NMR (CCl_4): δ 5.62 (br m), 2.25-1.85 (m, mixed with absorptions due to 78), 1.71 (br s). 70eV MS (Finnegan GC-MS, Column C), m/e (%RIC): 268 (P+4, 0.09), 266 (P+2, 0.24), 264 (P, 0.07), 253 (P+4-15, 0.02), 251 (P+2-15, 0.10), 249 (P-15, 0.02), 187 (P+2-79, 2.08), 185 (P-79, 2.20), 159 (0.61), 157 (0.62), 106 (P-2x79, 8.20), 105 (13.64), 93 (2.74), 91 (11.88), 79 (5.42), 78 (4.55), 77 (8.23), 65 (3.58), 63 (2.79), 53 (2.64), 52 (2.50), 51 (7.68), 50 (3.70).

27. Preparation of 6-methyl-2-hydroxy-7,7-dibromo-bicyclo [4.1.0] heptane (85)

A 250 ml 3-neck round-bottom flask was equipped with a magnetic stirring bar, an addition funnel, and a nitrogen inlet, and was nitrogen-flushed and dried. The addition funnel was charged with a solution of 3.13 g (28.0 mmol) of 82 and 5.7 ml (65 mmol) of bromoform in 15 ml of hexane. Then



82

11.2 g (100 mmol) of commercial potassium tert-butoxide was placed in the flask, followed by 75 ml of hexane. The flask was cooled to -78° (acetone-dry ice bath), and the solution in the addition funnel was then added dropwise over a 45 minute period to the stirred potassium tert-butoxide suspension. The cooling bath was next allowed to warm to -55°, and was then maintained at -50° to -55°, by the addition of small pieces of dry ice, for 75 minutes. The resulting mixture was warmed to room temperature, and then partitioned between 50 ml each of saturated ammonium chloride solution, water, and ether. The separation was made difficult by the presence of polymeric material. The organic layer was washed sequentially with three 10 ml portions of water and 10 ml of saturated sodium chloride solution, and then dried (anhydrous magnesium sulfate). Filtration and concentration in vacuo left 8.66 g of brown oil. Purification by preparative TLC (silica gel, 60% ether/40% hexane) resulted in 2 bands. Band 1 (rf=0.88, 32% yield) was tentatively identified as 6-methyl-2-oxa-7,7-dibromobicyclo [4.1.0] heptane (84). 60 MHz ^{1}H NMR (CCl_4): δ 2.4-1.1 (complex m). IR (CCl_4): 1730 cm^{-1} (br s).

Band 2 (rf=0.61, 20% yield) was identified as the desired product 85. 60 MHz ^{1}H NMR (CCl_4): δ 3.77 (br t, 1H, J = 5 Hz), 2.35 (br s, 1H), 1.15-1.95 (m, 10H, with br s at δ 1.45). IR (CCl_4): 3635 (m), 3005 (w), 2960 (s), 2940

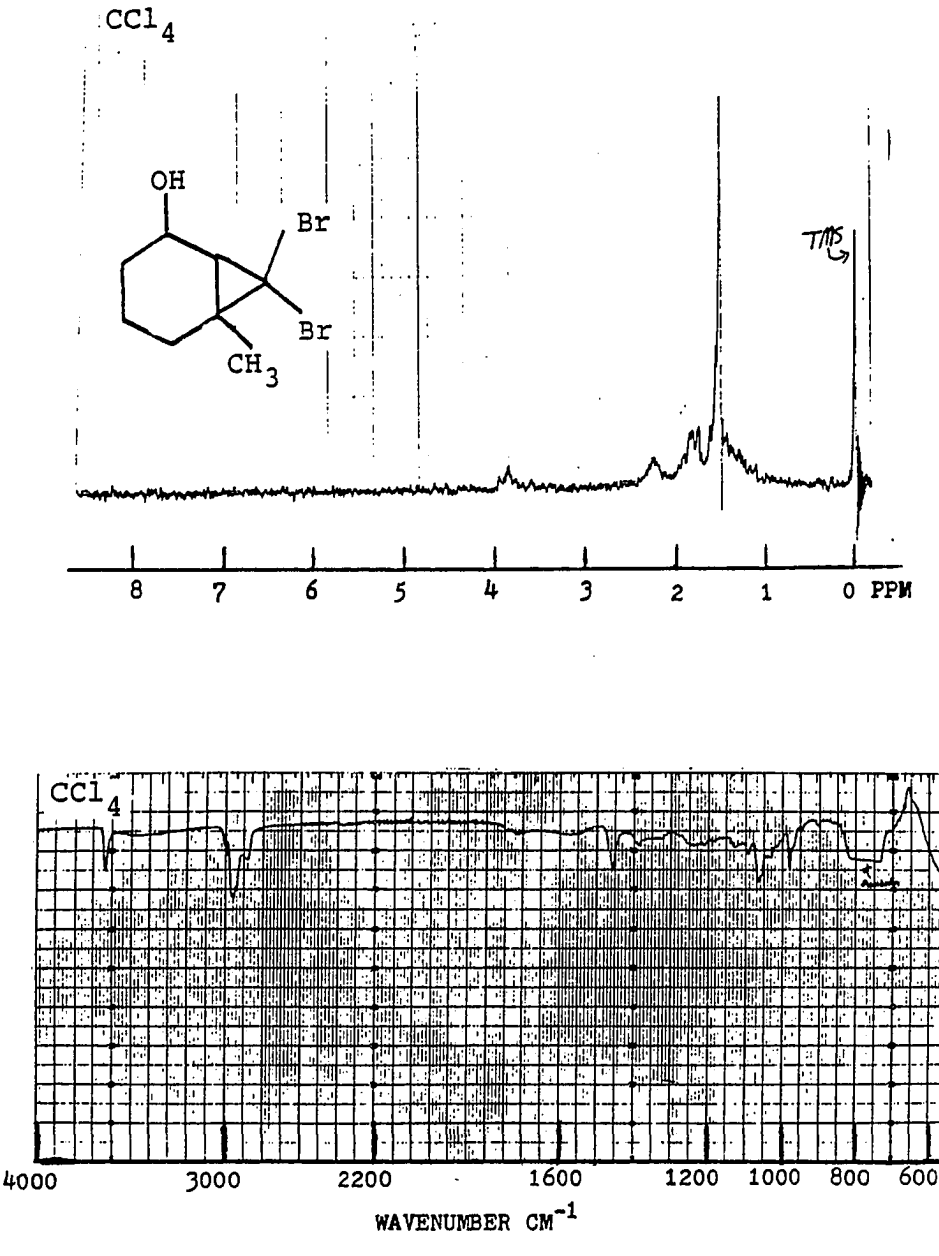


Figure 14. 60 MHz ^{1}H NMR and IR spectra of 85 (6-methyl-2-hydroxy-7,7-dibromobicyclo-[4.1.0]heptane)

(sh), 2880 (m), 1457 (m), 1387 (w), 1240 (br w), 1212 (w), 1190 (w), 1130 (w), 1093 (w), 1067 (m), 1055 (sh), 1042 (w), 1030 (w), 1015 (w), 1000 (w), 980 (m), 968 (sh), 947 (w), 905 (w), 703 (w) cm^{-1}. ^{13}C NMR, Jeol FX-90Q (CCl_4): δ 67.795 (rel. intens. 1770), 44.792 (894), 41.213 (1785), 30.291 (1784), 28.535 (2196), 28.340 (2249), 27.625 (1677), 18.521 (1967). The product did not travel through a GC column very well, and the GC-MS data did not appear to be very useful. Analysis: Calcd. for $C_8H_{10}Br_2$ (P-18): m/e 265.9129. Found: m/e 265.9134. Calcd. for $C_8H_{12}Br_2O$: 33.83% C, 4.26% H, 56.27% Br. Found: 33.95% C, 4.19% H, 56.16% Br.

Running the reaction in the same way as described above, but, after the addition of the bromoform solution, either a) allowing the dry ice-acetone bath to warm gradually to room temperature, or b) stirring the solution at -78° for 3 hours, and then replacing the dry ice-acetone bath with an ice water bath, both resulted in a ca. 2 to 1 mixture of 85 plus starting material, respectively, along with some 84, and a large amount of polymer. Evidently, at temperatures much greater than -40° to -50°, dibromocarbene polymerizes faster than it reacts with enol 82 (actually the anion of 82 under the strongly basic reaction conditions).

28. Preparation of 6-methyl-2-mesyloxy-7,7-dibromo-bicyclo[4.1.0]heptane (86)

A 100 ml 3-neck round-bottom flask was equipped with a magnetic stirring bar, an addition funnel, and a nitrogen inlet, and was nitrogen-flushed and dried. A solution of 2.30 ml (29.7 mmol) of methanesulfonyl chloride in 10 ml of dry (stored over 4A molecular sieves) pyridine was then placed in the flask, and a solution of 5.45 g (19.2 mmol) of 85 in 2 ml of dry pyridine was added to the addition funnel. While the solution in the flask was being stirred under nitrogen, and cooled with a room temperature water bath, the solution in the addition funnel was added dropwise over a 3 to 4 minute period. The resulting solution was stirred under nitrogen for 18 hours, after which time it was partitioned between an ice-cold mixture of 50 ml each of water and ether. The organic layer was washed sequentially with three 10 ml portions of water, and 10 ml of saturated sodium chloride solution, and was then dried (anhydrous magnesium sulfate), filtered, and concentrated on a rotary evaporator to give 3.95 g of brown oily solid. Purification by preparative TLC (silica gel, 50% ether/hexane)

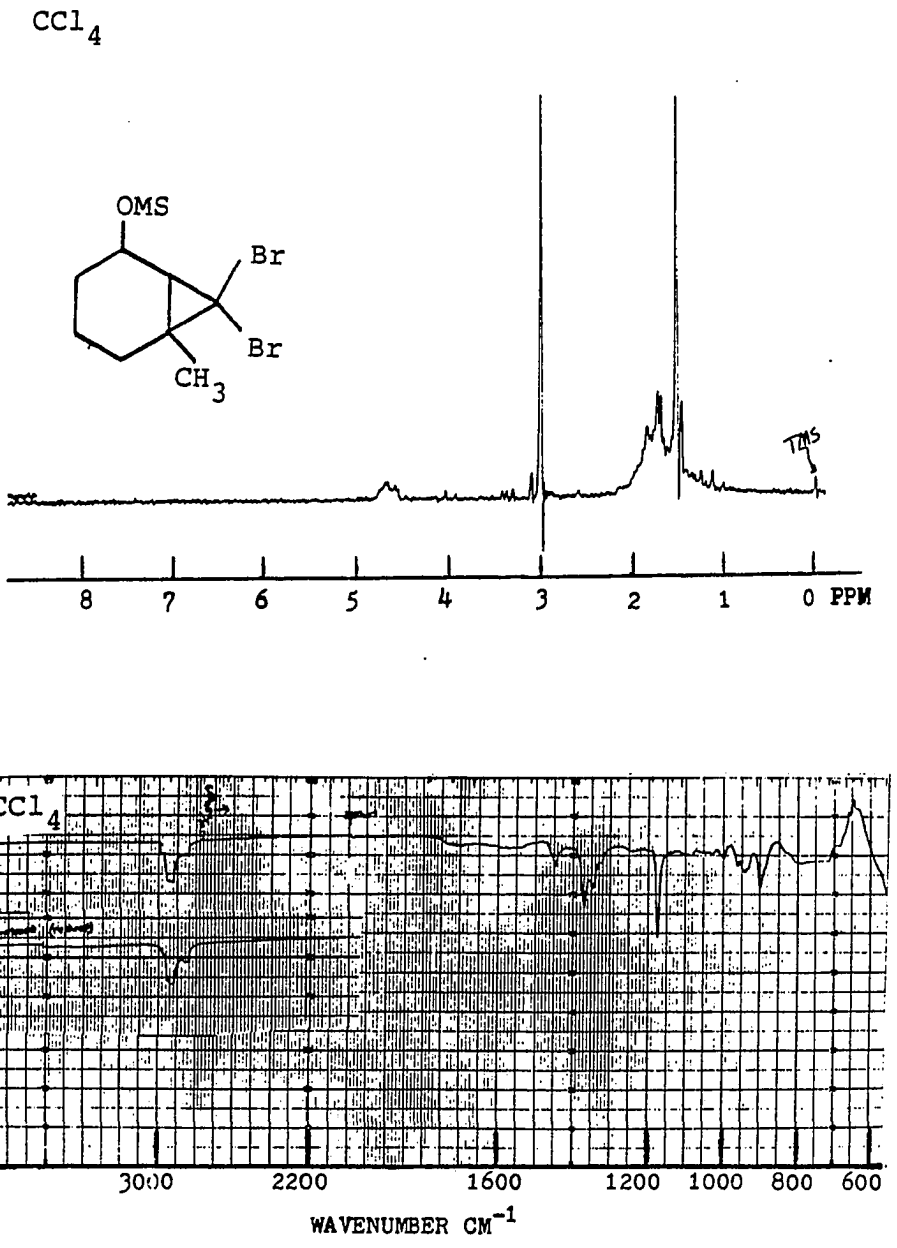
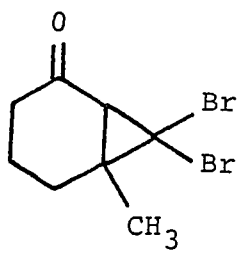


Figure 15. 60 MHz ^{1}H NMR and IR spectra of 86 (6-methyl-2-mesyloxy-7,7-dibromo-bicyclo [4.1.0] heptane)

resulted in 2 bands. Band 1 (rf=0.84) consisted of 84. Band



84

2 (rf=0.47, 22% yield) was identified as the desired product 86. 60 MHz ^{1}H NMR (CCl_4): δ 4.82-4.55 (m, 1 H), 3.12 (small s, probably a second epimer of 86, ca. 0.24 H), 3.01 (s, 3 H), 2.19-1.02 (complex m, 10 H, with a sharp s at δ 1.53). IR (CCl_4): 2990 (sh), 2940 (br s), 2860 (br w), 1449 (br m), 1371 (s), 1348 (m), 1325 (sh), 1176 (s), 1088 (br w), 1032 (w), 1002 (br w), 964 (w), 951 (sh), 944 (m), 935 (sh), 901 (br m).

29. Treatment of 86 with DBU

A 25 ml 3-neck round-bottom flask, equipped with a magnetic stirring bar, a reflux condenser, and a nitrogen inlet, was nitrogen-flushed and dried prior to being charged with a solution of 44.2 mg (0.122 mmol) of 86 in 5 ml of dry (freshly distilled from LAH) THF. A solution of 50.0 µl (0.334 mmol) of DBU (1,8-diazabicyclo[5.4.0]undec-7-ene) in 3 ml of dry THF was then added. The resulting stirred solution was heated to reflux, stirred for 2 hours under a nitrogen atmosphere, after which it was cooled to room temperature, and then poured into 10 ml of water. The residue resulting from concentration in vacuo was extracted with three 15 ml portions of ether. The organic layers were combined and washed sequentially with two 5 ml portions of water and one 5 ml portion of saturated sodium chloride solution, and dried (anhydrous magnesium sulfate). Filtration and concentration on a rotary evaporator left 36 mg of an oil which was identified by NMR analysis as starting material.

30. Treatment of 86 with sodium hydride

a. At 0° in THF A 25 ml 3-neck round-bottom flask was equipped with an addition funnel, a magnetic stirring bar, and a nitrogen inlet, and was nitrogen-flushed and dried. Then, 0.126 g (2.63 mmol) of a 50% sodium hydride-mineral oil dispersion was placed in the flask, flushed with

nitrogen, and washed with three 5 ml portions of hexane. A solution of 28.0 mg (0.0774 mmol) of 86 in 3 ml of dry (freshly distilled from LAH) THF was placed in the addition funnel, and 2 ml of dry THF were added to the flask. The suspension in the flask was cooled to 0°, and stirred under nitrogen during the dropwise addition of the 86/THF solution over a 10 minute period. The solution was then stirred, with a nitrogen balloon attached, for 11 hours in a cold room (0° to 5°). While the solution was still at ca. 0°, the excess sodium hydride was cautiously quenched with a mixture of 5 ml of saturated ammonium chloride solution and 5 ml of water. Then, the solution was concentrated at $\geq$100 mm pressure on a rotary evaporator, and the residue was extracted with two 20 ml portions of ether. The aqueous layer was reconcentrated on a rotary evaporator at full aspirator vacuum, and re-extracted with 20 ml of ether. The combined ether layers were washed with three 5 ml portions of saturated ammonium chloride solution, dried (anhydrous magnesium sulfate), filtered, and concentrated at $\geq$200 mm pressure on a rotary evaporator to yield 67 mg of a liquid. NMR analysis showed only starting material plus solvents.

b. At room temperature in DMF A 25 ml 3-neck round-bottom flask, equipped with a magnetic stirring bar, an addition funnel, and a nitrogen inlet, was nitrogen-flushed and dried prior to being charged with 69.4 mg (1.45 mmol)

of a 50% sodium hydride-mineral oil dispersion, which was then washed with three 3 ml portions of hexane. Then 3 ml of dry (stored over 4A molecular sieves) DMF was added to the flask, and a solution of 47.9 mg (0.132 mmol) of 86 in 3 ml of dry DMF was placed in the addition funnel. The 86/DMF solution was next added dropwise over a 2 minute period to the stirred sodium hydride suspension under nitrogen. The resulting solution was stirred at ambient temperature under nitrogen for 23 hours, after which time it was poured into an ice-cold mixture of 5 ml of water, 5 ml of saturated ammonium chloride solution, and 10 ml of ether, and then partitioned. The aqueous layer was re-extracted with three 15 ml portions of ether. The organic layers were combined and washed with two 5 ml portions of water and one 5 ml portion of saturated sodium chloride solution, dried (anhydrous magnesium sulfate), filtered, and concentrated on a rotary evaporator to give 12 mg of an oil. NMR analysis showed unidentified products containing no olefinic protons. Back-extraction of the combined aqueous layers gave back 27 mg of DMF.

31. Treatment of 86 with potassium tert-butoxide

a. At 0° A 50 ml 3-neck round-bottom flask was equipped with a magnetic stirring bar, an addition funnel, and a nitrogen inlet, and was nitrogen-flushed and dried prior to being charged with 33.5 mg (0.300 mmol) of commercial

potassium tert-butoxide powder, along with 4 ml of hexane. A solution of 46.1 mg (0.127 mmol) of 86 in 3 ml of dry (freshly distilled from LAH) ether was then placed in the addition funnel. The stirred solution in the flask was cooled to 0° under nitrogen, and the solution in the addition funnel was added dropwise over a 15 minute period. The joints in the apparatus were sealed with parafilm, and the solution was stirred in a cold room at 0° to 5° for 14 hours. A solution of 5 ml of water plus 5 ml of saturated ammonium chloride solution was then added at 0°. The resulting mixture was diluted with 20 ml of ether, and then separated. The organic layer was washed sequentially with two 5 ml portions of water and one 5 ml portion of saturated sodium chloride solution, dried (anhydrous magnesium sulfate), filtered, and concentrated on a rotary evaporator at $\geq$100 mm pressure, resulting in 33 mg of an oil. NMR analysis showed solvents and starting material, with no evidence of any olefinic material.

b. At room temperature A 25 ml 3-neck round-bottom flask was fitted with an addition funnel and a nitrogen inlet, equipped with a magnetic stirring bar, and then nitrogen-flushed and dried. The flask was next charged with 81.0 mg (0.723 mmol) of commercial potassium tert-butoxide, followed by 3 ml of hexane, and then a solution of 83.0 mg (0.230 mmol)

of 86 in 2 ml of dry (freshly distilled from LAH) THF was placed in the addition funnel. The potassium tert-butoxide/hexane suspension was stirred at 0° under nitrogen while the 86/THF solution was added dropwise over a 10 minute period. After the resulting mixture had been stirred under nitrogen at 0° for 15 more minutes, it was allowed to warm to room temperature, stirred for an additional 2 hours, and then extracted with three 25 ml portions of ether. The ether layers were combined and washed with 10 ml of saturated ammonium chloride solution, two 10 ml portions of water, and one 10 ml portion of saturated sodium chloride solution, dried (anhydrous magnesium sulfate), filtered, and concentrated in vacuo to yield 17 mg of a yellow oil. NMR analysis showed unidentified compounds which contained no olefinic protons. Back extraction of the combined aqueous layer gave negligible material.

32. Attempted preparation of 6-methyl-2-chloro-7,7-dibromobicyclo [4.1.0] heptane from 86 plus thionyl chloride

a. 1 Hour at 55° A 50 ml 3-neck round-bottom flask, equipped with a magnetic stirring bar, a reflux condenser, and a nitrogen inlet, was nitrogen-flushed and dried. A solution of 0.230 g (0.810 mmol) of crude 86 in 10 ml of dry (freshly distilled from LAH) THF was added, followed by 0.200 ml

(0.840 mmol) of dry (stored over 4A molecular sieves) tri-n-butylamine. The resulting solution was cooled to 0°, and 0.180 ml (2.43 mmol) of thionyl chloride was then added via syringe. After the solution had been allowed to warm briefly, it was heated to reflux under nitrogen for 50 minutes. (The solution turned greenish brown.) It was then cooled to room temperature, concentrated in vacuo, and partitioned between 30 ml of ether and 10 ml of saturated sodium bicarbonate solution. The aqueous layer was back-extracted with two 20 ml portions of ether. The ether layers were combined and washed successively with three 5 ml portions of saturated ammonium chloride solution, and then 5 ml each of saturated sodium bicarbonate solution, water, and saturated sodium chloride solution. Drying (anhydrous magnesium sulfate), filtration, and concentration on a rotary evaporator left 0.36 g of brown oil mixed with amorphous solid. The product was analyzed by NMR, and separated by preparative TLC on silica gel (10% ether /90% hexane).

b. 15 Minutes at 50° This experiment was run similarly to the way experiment a was, except that a purified sample of 86 was used, and triethylamine was used instead of tri-n-butylamine. After the addition of the thionyl chloride at 0°, the reaction mixture was stirred for 3 hours under nitrogen at ambient temperature, followed by 15 minutes

at 50°. The workup was conducted as in experiment a. The product was analyzed by NMR, and separated (see end of entry 32) by preparative TLC on silica gel (10% ether/90% hexane).

c. 3 hours at room temperature This experiment was done similarly to the way experiment a was, except that triethylamine was used instead of tri-n-butylamine. After the 0° addition of the thionyl chloride, the mixture was stirred for 3 hours under nitrogen at room temperature. It was then cooled to 0° prior to the addition of 5 ml of saturated aqueous sodium chloride, followed by concentration in vacuo, and extraction with 50 ml of ether. (The aqueous layer was strongly acidic at this point!) The organic layer was washed with two 5 ml portions of saturated sodium bicarbonate solution, 5 ml of water, and 5 ml of saturated sodium chloride solution, and was dried (anhydrous magnesium sulfate), filtered, and concentrated in vacuo to afford 0.116 g of an oil. The crude product was analyzed by NMR, and was separated by preparative TLC on silica gel (10% ether/90% hexane).

TLC and GC analysis of all three of the reaction mixtures (a, b, and c) showed that they were complex (at least 6 components). The NMR spectrum of the major component of each mixture (rf on silica gel, 10% ether/90% hexane, was 0.5) was complex, and showed a multiplet at δ 3.6, which integrated to 1.3 to 2 protons. The GC-MS analyses were indecipherable.

33. Preparation of 6-methyl-2,7,7-tribromobicyclo-[4.1.0]heptane (87)

To a solution of 0.269 g (0.744 mmol) of 86 in 60 ml of acetone was added 0.32 g (3.7 mmol) of anhydrous lithium bromide. The resulting mixture was heated to reflux for 44 hours, cooled, concentrated in vacuo, and partitioned between 70 ml of ether and 20 ml of water. The ether layer was washed with 10 ml of saturated sodium chloride solution, dried (anhydrous magnesium sulfate), filtered, and concentrated on a rotary evaporator to yield 0.21 g of brown oil. The product did not travel through GC columns well, and the GC-MS analysis did not show a parent ion, but did indicate that the two epimers of 87 were probably present. The following mass spectrum is representative of the two isomers. 70 eV MS (Finnegan GC-MS, Column A), m/e (%RIC): 269 (P+4-79, 0.23), 267 (P+2-79, 0.52), 265 (P-79, 0.27), 212 (0.15), 188 (1.12), 187 (1.16), 186 (1.67), 185 (1.21), 184 (0.48), 173 (0.41), 171 (0.68), 169 (0.31), 159 (0.51), 158 (0.56), 157 (0.48), 107 (4.70), 106 (P-3 x 79, 3.67), 105 (10.01), 103 (1.58), 95 (6.80), 92 (2.34), 91 (7.91), 79 (7.66), 77 (6.49), 67 (1.84), 65 (3.42), 63 (1.65), 55 (3.08), 53 (2.37), 52 (2.61), 51 (6.18), 50 (2.22).

Purification on silica gel (10% ether/90% hexane) resulted in two major bands. Band 1 (rf = 0.76, 16% yield) was

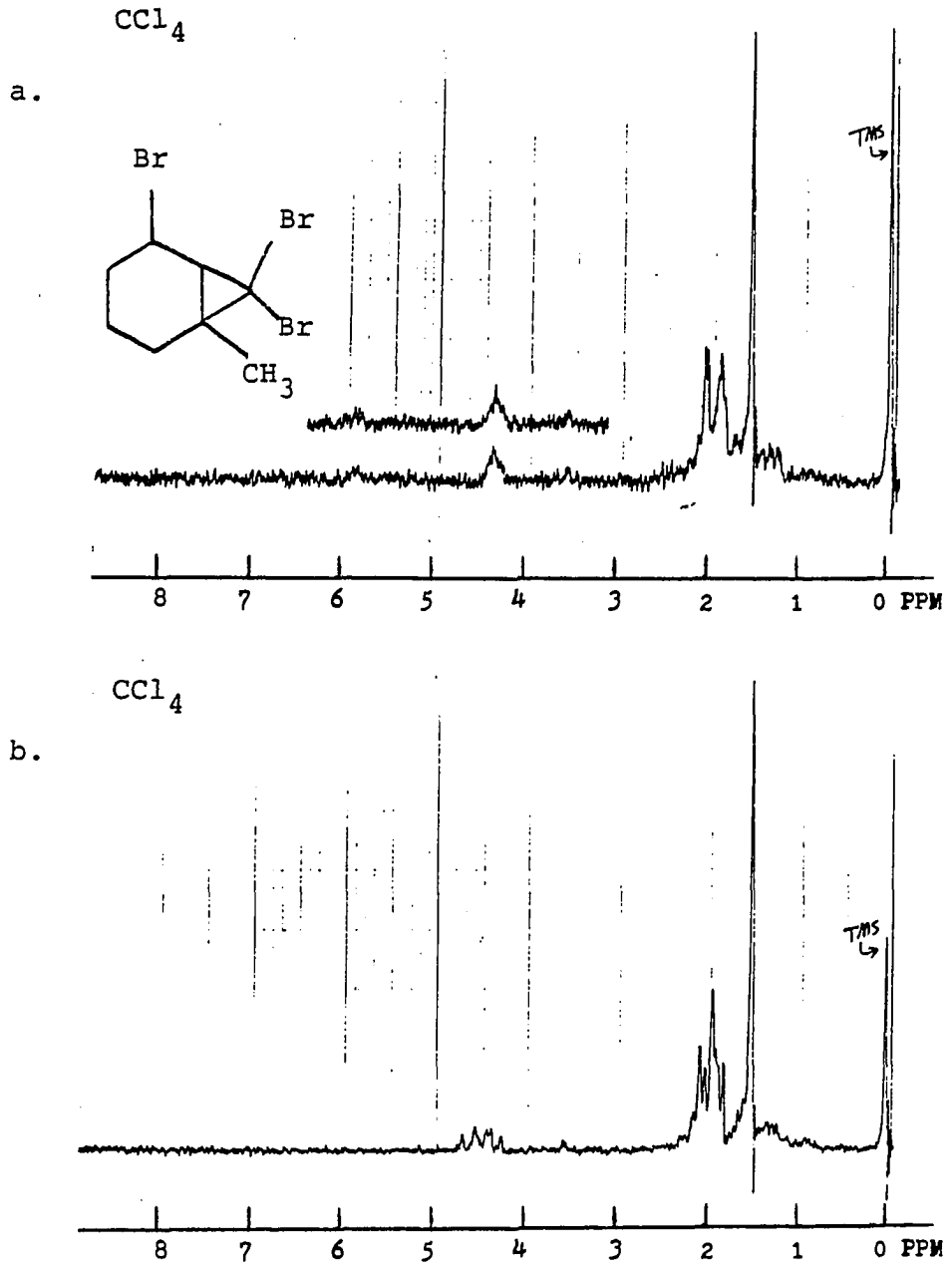


Figure 16. 60 MHz ^{1}H NMR spectra of the two epimers of 87: a. TLC Band 1, b. TLC Band 2 (6-methyl-2,7,7-tribromobicyclo [4.1.0] heptane)

tentatively identified as one epimer of 87. 60 MHz ^{1}H NMR (CCl_4): δ 4.48-4.23 (m, 1H), 2.5-1.2 (complex m, 10H, with a singlet at δ 1.53).

Band 2 (rf = 0.56, 20% yield) was tentatively identified as the other epimer of 87. 60 MHz ^{1}H NMR (CCl_4): δ 4.71-4.20 (broadened dd, 1H, spacings = 8, 9 Hz), 2.3-1.1 (complex m, 10H, with a singlet at δ 1.48).

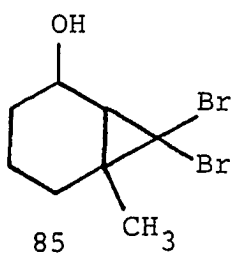
34. Treatment of 87 with potassium tert-butoxide

A 25 ml 3-neck indented flask, equipped with a magnetic stirring bar, an addition funnel, and a nitrogen inlet, was nitrogen-flushed and dried, and then charged with 51.0 mg (0.455 mmol) of commercial potassium tert-butoxide powder plus 2.5 ml of dry (freshly distilled from LAH) ether. A solution of 31.0 mg (0.0893 mmol) of 87 in 3 ml of dry ether was then placed in the addition funnel. The flask was cooled to 0°, and the solution in the addition funnel was added dropwise over a 5 minute period. The solution was allowed to slowly warm to room temperature, and stirred under nitrogen for 3 hours. Then, the solution was cooled back down to 0°, quenched with 5 ml of saturated ammonium chloride solution, diluted with 20 ml of ether plus 5 ml of water, and separated. The organic layer was washed with 5 ml of water and 5 ml of saturated sodium chloride solution, dried (anhydrous sodium sulfate) filtered, and concentrated in vacuo to give 40 mg

of an oil. NMR analysis showed a complex mixture, whose major components had retention times shorter than that of 7,7-dibromobicyclo- 4.1.0 hept-2-ene (7). They obviously could not have been the desired dehydrobromination product.

35. Preparation of 6-methyl-7,7-dibromobicyclo [4.1.0]-hept-2-ene (78) by treating 85 with "Burgess reagent" (88)

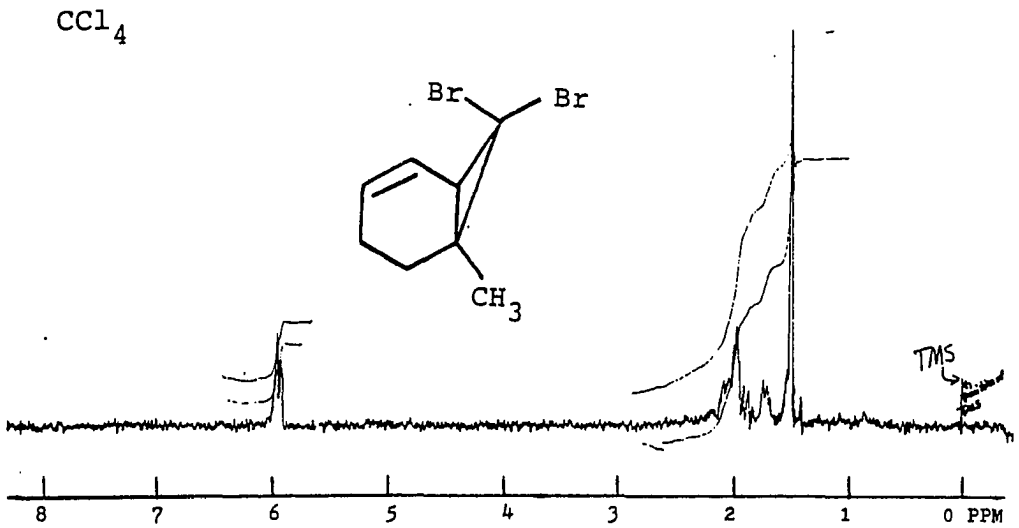
A 25 ml 3-neck round-bottom flask was equipped with a magnetic stirring bar, an addition funnel, and a reflux condenser, and was then nitrogen-flushed and dried. A solution of 48.1 mg (0.169 mmol) of 85 in 4 ml of dry (stored over 4A



85

molecular sieves) benzene was placed in the flask, and then 61.7 mg (0.259 mmol) of Burgess reagent, methyl-[carboxysulfamoyl] triethylammonium hydroxide inner salt (88),[42] along with 4 ml of dry benzene, was added to the flask. The 85/benzene solution was added dropwise, under nitrogen, over a 20 minute period to the stirred solution in the flask. The resulting solution was stirred under nitrogen at 50° for 67 minutes, and then heated to reflux for 90 minutes. After the

solution had been cooled to room temperature, it was quenched with 10 ml of water, diluted with 8 ml of benzene, and transferred to a separatory funnel. The organic layer was removed, and washed with 5 ml of saturated sodium chloride solution, dried (anhydrous sodium sulfate), filtered, and concentrated in vacuo to yield 48 mg of an oil. Purification by preparative TLC on silica gel (hexane) afforded a 28% yield of 78 (rf = 0.59). 60 MHz ^{1}H NMR (CCl_4): δ 5.88 (m, 2H), 1.65-2.2 (m, 5H), 1.48 (s, 3H). IR (CCl_4): 3045 (m), 2995 (w), 2960 (m), 2933 (s), 2872 (w), 2845 (w), 1647 (w), 1453 (m), 1430 (br w), 1213 (w), 1085 (br w), 1075 (sh), 1010 (w), 995 (w), 825 (br w), 692 (s), 645 (m) cm^{-1}. ^{13}C NMR, Jeol FX-90Q, of a very dilute sample (CCl_4): δ 124.108 (rel. intens. 279), 118.744 (267), 44.417 (285), 39.596 (175), 38.350 (499), 34.398 (311). 20 eV MS (Finnegan GC-MS, Column A), m/e (%RIC): 268 (P+4, 0.03), 266 (P+2, 0.09), 264 (P, 0.03), 253 (P+4-15, 0.32), 251 (P+2-15, 0.71), 249 (P-15, 0.35), 187 (P+2-79, 10.43), 185 (P-79, 10.89), 159 (1.44), 157 (1.50), 106 (P-2 x 79, 17.19), 105 (38.76), 93 (3.86), 91 (2.17), 79 (1.55), 66 (0.19). (Note that the parent peak was extremely weak at 70 eV.) Analysis Calcd. for $C_7H_7Br_2$ (P-15): m/e 248.8914. Found: m/e 248.8917. (The parent peak was visible, but too weak to be measured accurately.)



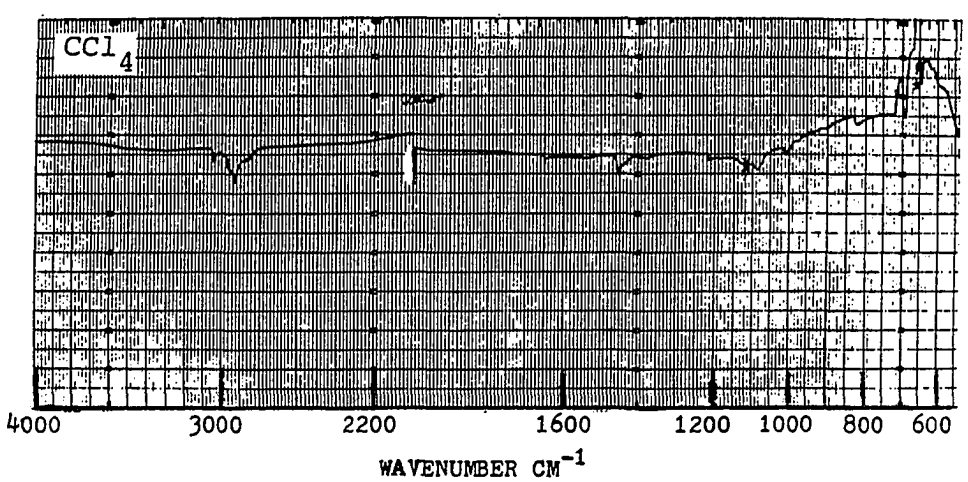


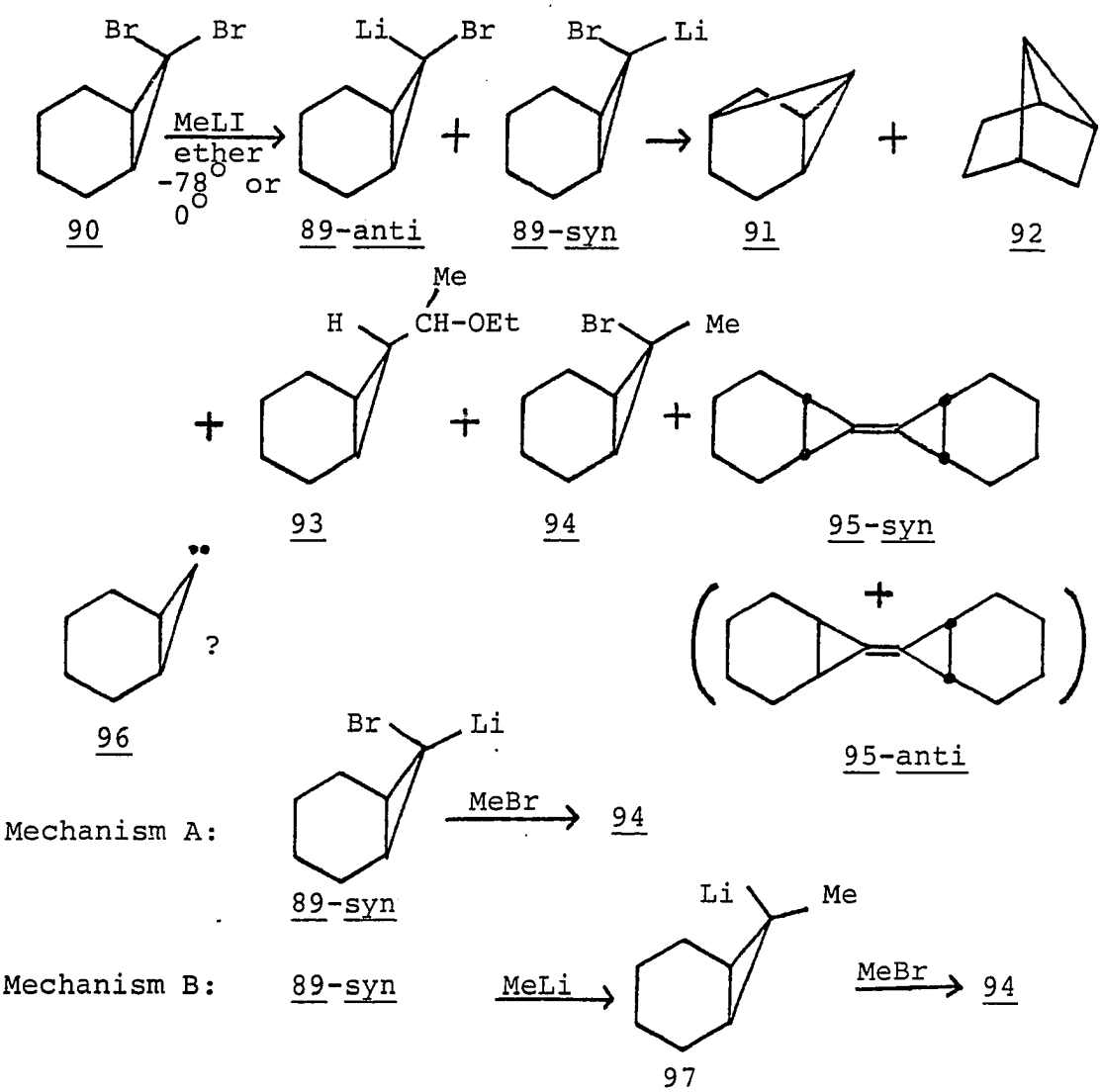
Figure 17. 60 MHz ^{1}H NMR and IR spectra of 78 (6-methyl-7,7-dibromobicyclo [4.1.0] hept-2-ene)

II. 7-BROMO-7-LITHIOBICYCLO[4.1.0]HEPTANE

A. Introduction

As is shown in Scheme XIX, in ether solution, carbenoids 89-anti and 89-syn (generated by methyllithium treatment of dibromide 90) are known to produce compounds 91 through 94, and 95-syn.[43-46] In the early work,[43,45] only one stereo-

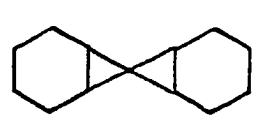
Scheme XIX:



isomer of the dimer (with unspecified stereochemistry) was isolated. Later, Köbrich and Goyert[46a] found that a trace of the other stereoisomer was formed as well. On the basis of ^{1}H NMR data, they assigned the major isomer to 95-anti, and the minor isomer to 95-syn. More recently, however, Fukuda et al.[46b] discovered (through ^{13}C NMR analysis of the corresponding cyclopropanated derivatives) that a 1:10 mixture of 95-anti and 95-syn, respectively is formed. Products 91 and 92 are obviously derived from an intramolecular C-H insertion reaction of either carbenoids 89-anti and 89-syn, or carbene 96. Insertion of 89-anti and 89-syn, or of 96, into a C-H bond of solvent could result in insertion product 93. (The author of this dissertation has taken the liberty of assuming the anti stereochemistry of 93, by analogy with the corresponding THF-insertion product, to be discussed shortly.) Products 95-syn and 95-anti must result from the dimerization of 89-anti and 89-syn, or of 96. The formation of bromide 94 was explained by Marquis and Gardner[44] as resulting from a reaction between carbenoid 89-syn and methyl bromide (Mechanism A of Scheme XIX). However, many precedents now exist[18-20,47,48] for an alternative explanation, i.e., Mechanism B of Scheme XIX. Mechanism B entails a displacement of the bromine of 89-anti by methyllithium, resulting in alkyllithium 97, followed by a lithium-halogen exchange reac-

tion between 97 and methyl bromide. (The electrophilicity of α-halocyclopropyllithiums will be made more apparent during the course of this section. As was already discussed in the Introduction to Chapter I, ^{13}C NMR evidence[5,6] demonstrates the polarized nature of the C-Br bond of α-bromocyclopropyllithium derivatives, which explains their electrophilic properties.) The effects of various salts upon the product distribution, shown in Table X, have been interpreted as implicating probable carbenoid (89-anti plus 89-syn) intermediacy rather than carbene (96) intermediacy for most of the products.[45] Closer scrutiny of the data reveals, however, that such a conclusion might not be warranted because of some ambiguity concerning the actual reaction temperature used for experiment 1 of Table X.

Moore and Ward[45] have reported cyclopropanation product 98 (10% isolated yield) from the methyllithium reaction of 90 in ether/cyclohexene solution (unspecified solvent concentrations) at -80°. It was suggested that 98 might have arisen



98

from the addition of carbene 96 to the double bond of cyclohexene. They reported a similar olefin trapping product (unspecified yield) from a reaction of 90 with methyllithium

Table X. Salt effects upon the product distribution obtained from 89-anti and 89-syn and/or 96 in ether solution

Expt.	MeLi Reagent	Temp.	%Yield (91+92)
1	MeLi·LiI	-80 to 0°	39
2	MeLi·LiCl	-78°	14
3	MeLi·LiCl	0°	33
4	MeLi·LiCl (inv. add.)	0°	27

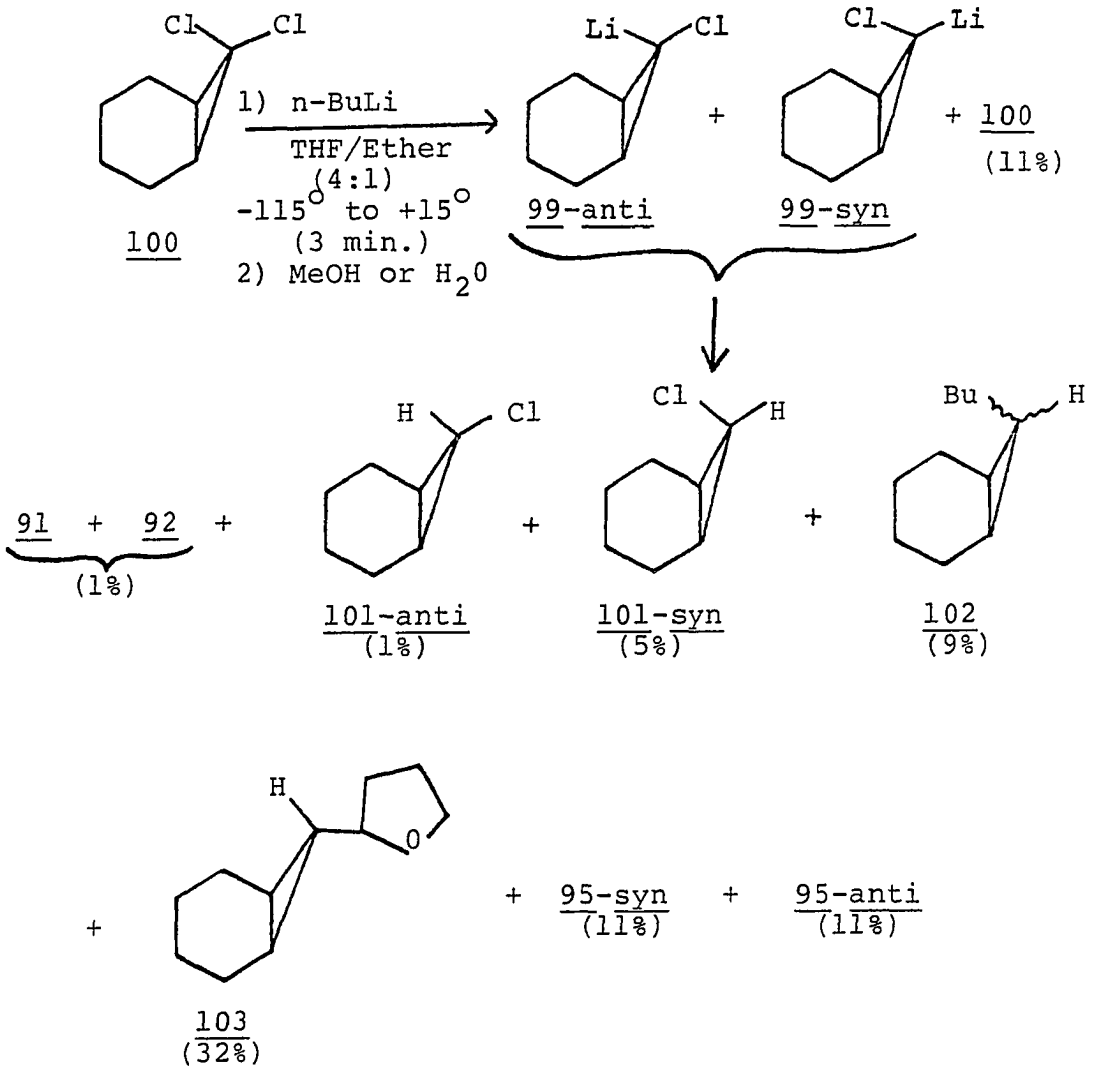
[a]Stereochemistry assigned by consideration of the results reported in reference 46b.

[b]Not reported among the products.

%Yield 93	%Yield 94	%Yield 95-syn[a]	Ref.
20	ca. 0[b]	30	43,45
64	10	7	44
35	32	tr.	44
17	55	tr.	44

in ether/isobutylene solution. However, because α-halo-alkyllithium compounds can react directly with olefins,[49a] these olefin trapping results could also be explained by the intermediacy of carbenoids 89-anti and 89-syn. (Jones and

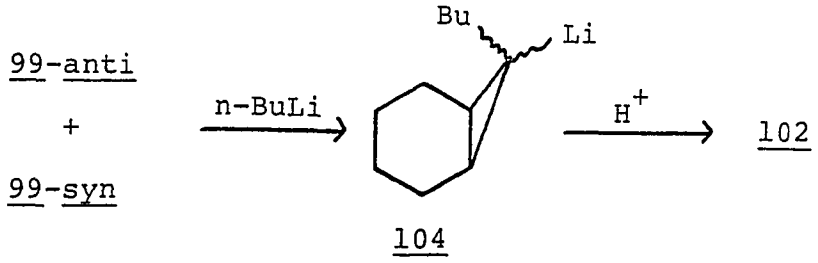
Scheme XX:



Petrillo[49b] more recently found that methyllithium treatment of 7,7-dibromobicyclo[4.1.0]hept-3-ene in the presence of cis- or trans-2-butene resulted in the stereospecific generation of the corresponding cyclopropanation product in 30% yield. These reactions may also have proceeded through carbenoid intermediates.)

Köbrich and Goyert[46a] studied the chemistry of chlorocarbenoids 99-anti and 99-syn (generated from dichloride 100, as shown in Scheme XX) in THF/ether solution. Products 91, 92, 101-anti, 101-syn, 102, 103, 95-syn, and 95-anti were observed, in the yields indicated in Scheme XX.

Product 102 might be formed by the mechanism shown below.[46a] As was already mentioned earlier in connection



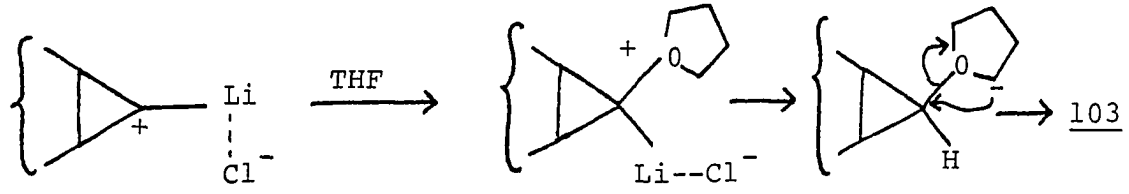
with product 94, this proposed alkyllithium displacement of the halogen atom of carbenoid 99-anti and 99-syn is well precedented.[18-20,47,48] The resulting alkyllithium, 104, can then be protonated either by solvent, or by the quenching

agent, to give product 102. A 4-fold increase in the amount of n-butyllithium actually raised the yield of 102 from 9% to 21%.[46a]

Products 101-anti and 101-syn result from protonation of carbenoids 99-anti and 99-syn, respectively.

Were the other products derived from a carbene or from carbenoids? Köbrich and Goyert[46a] contended that they arose from carbenoid intermediates for the following reasons. When they studied the reaction in a THF solution containing a 10-fold excess of cyclohexene, they obtained only a 3% yield of cyclopropanation product 98. It could therefore be concluded that the cyclopropanation reaction does not compete effectively with the "normal" processes, which result in compounds 91, 92, 101-anti, 101-syn, 102, 103, 95-syn, and 95-anti. The second reason why they disfavored the intermediacy of any free carbene under their reaction conditions was the extremely low yield (1%) of the intramolecular C-H insertion products 91 and 92. They reasoned that a free carbene, a highly reactive intermediate, should prefer intramolecular reactions over intermolecular reactions, especially in the absence of efficient carbene traps.

Köbrich and Goyert[46a] proposed the following carbenoid mechanism for the THF insertion product 103:

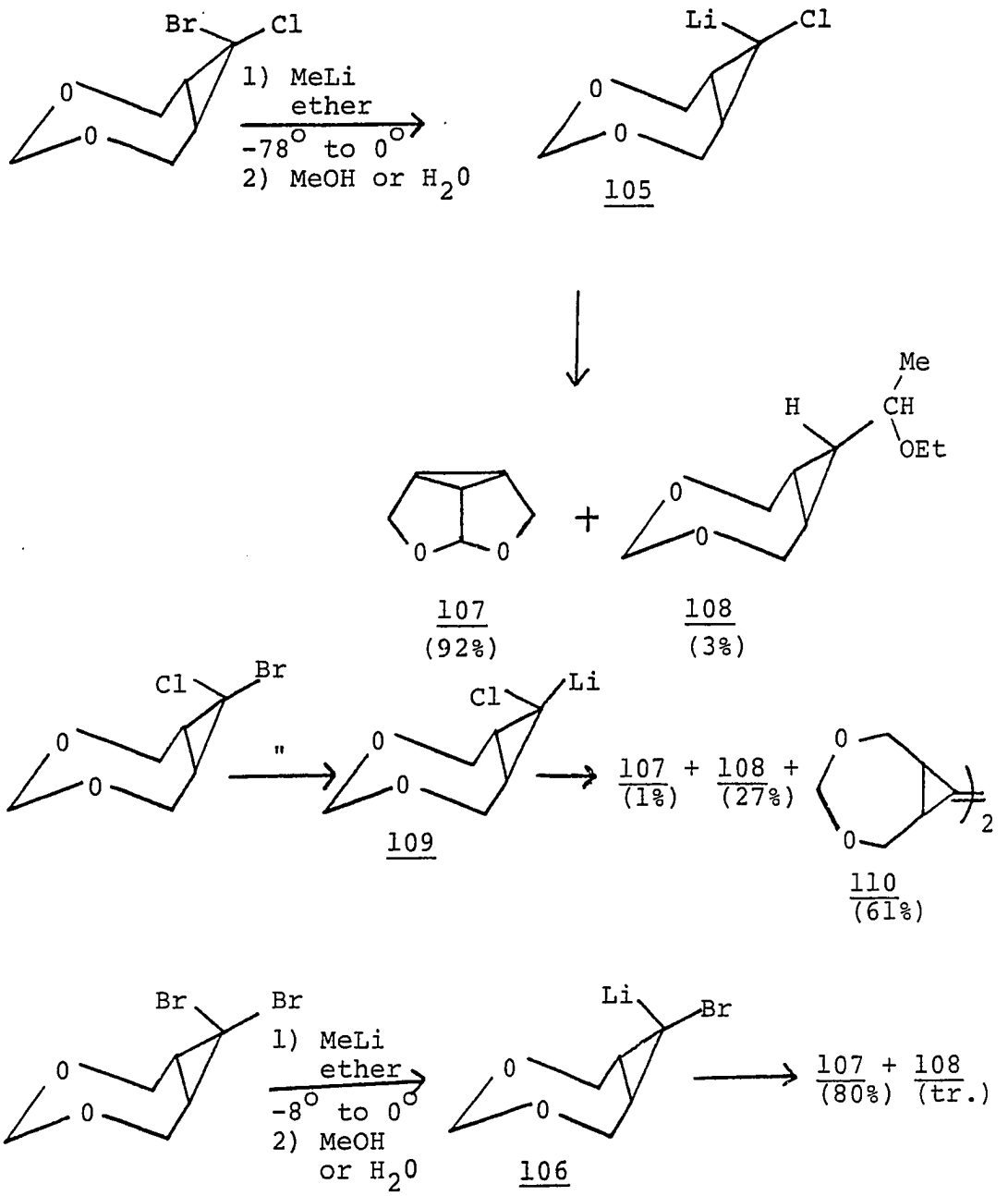


Due to the work of Taylor and Chaney,[50] it can now be stated with certainty that the solvent insertion products 103 and 93 must be derived from carbenoids, and not from carbenes. As is shown in Scheme XXI, carbenoids 105 and 106 gave almost exclusively the intramolecular C-H insertion product 107, and only trace amounts of the solvent C-H insertion product 108. Carbenoid 109, on the other hand, gave mainly solvent insertion product 108 and dimer 110. This very dramatic dependence of product distribution upon the stereochemistry of the 1-halo-1-lithiocyclopropane derivatives requires a carbenoid mechanism.

For dimers 95-syn and 95-anti, Köbrich and Goyert[46a] suggested a mechanism involving an association of two carbenoid molecules, in the form of a dimeric aggregate.

An important distinction can be made between the "cyclopropylidene" intermediate obtained by alkyllithium treatment of gem-dihalocylopropanes, and that obtained from diazocyclopropanes. As shown in Scheme XXII, Jones[51] found that 2,2-diphenylcyclopropylidene (111), generated from the corresponding diazo compound (112) could be trapped by cis-2-butene and trans-2-butene, to give the corresponding

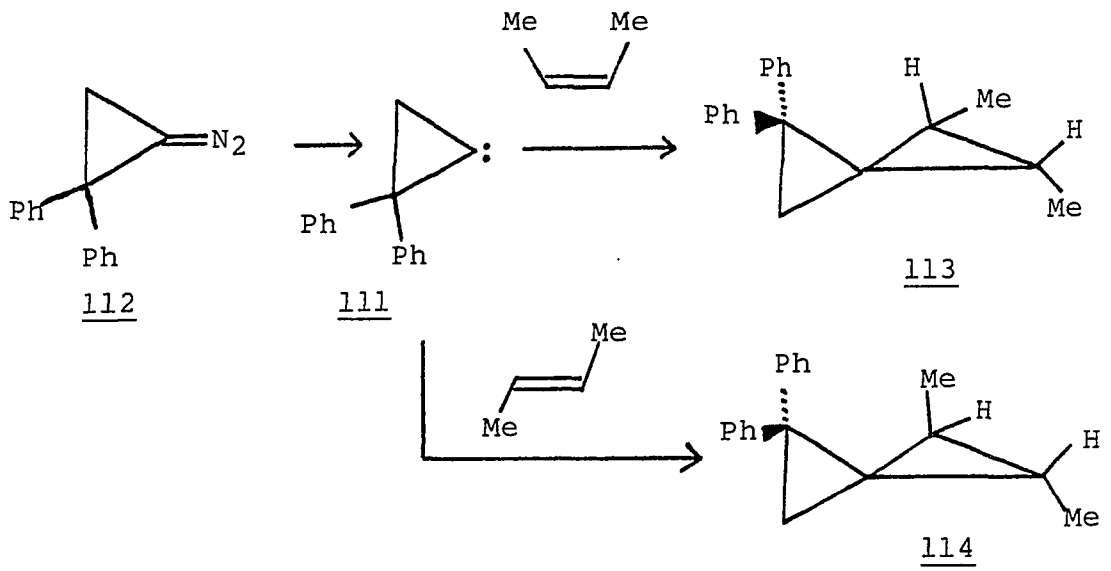
Scheme XXI:

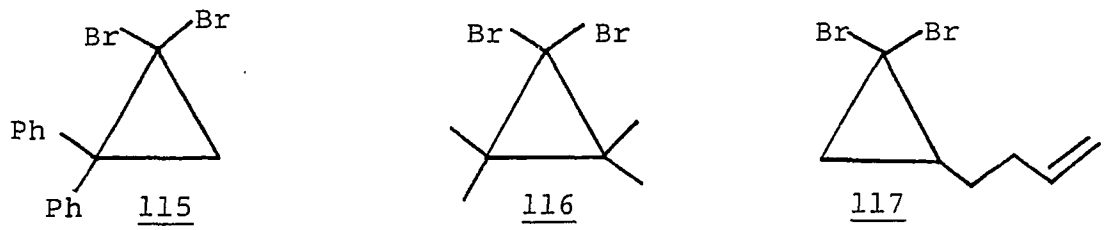

Br
Cl
1) MeLi
ether
-78° to 0°
2) MeOH or H2O
Li
Cl
105
Me
H
CH
OEt
107
(92%)
108
(3%)
"
109
107 + 108 +
(1%) (27%)
110
(61%)
Br
Br
1) MeLi
ether
-8° to 0°
2) MeOH
or H2O
106
107 + 108
(80%) (tr.)

spiropentanes, 113 and 114, respectively. Although Skattebol[52] obtained high yields of allene products from the methyllithium or n-butyllithium treatment of dibromides 115 through 119, he could not detect any carbene trapping products when he ran the reaction in the presence of isobutylene, tetramethylethylene, or triphenylphosphine. These results make very obvious the difference between the reactive intermediates obtained by the two methods. It is possible, though not demanded by the data, that the diazocyclopropane gives a free carbene, whereas the 1-halo-1-lithiocyclopropanes do not.

Thus, there exists in the literature no definitive answer to the question: What conditions are necessary for 1-halo-1-lithiocyclopropanes to generate the corresponding cyclopropylidenes? This question is of paramount importance in relation to the study of the Skattebol rearrangement of 1-bromo-1-lithio-2-vinylcyclopropanes discussed in Chapter I. The use of olefin trapping as a criterion for free carbene intermediacy is, by itself, inadequate, because, as was already mentioned in this section, α-haloalkyllithiums can undergo direct bimolecular addition reactions with olefins.[49a] This situation led Kirmse,[53a] in a 1965 review article, to state: "Olefin addition has become completely useless as a means of detecting carbenes. At present, the only reliable

Scheme XXII:





criterion for the occurrence of carbenes is the (intramolecular) insertion into C-H bonds, which has permitted detection of alkyl- and dialkyl-carbenes." Unfortunately, the more recent results obtained by Goldstein and Dolbier[53b], and by

Taylor and Chaney[50] (see Scheme XXI) on the mechanism of C-H insertion reactions also tend to invalidate the use of intramolecular C-H insertion products as a criterion for free carbene intermediacy.[53c]

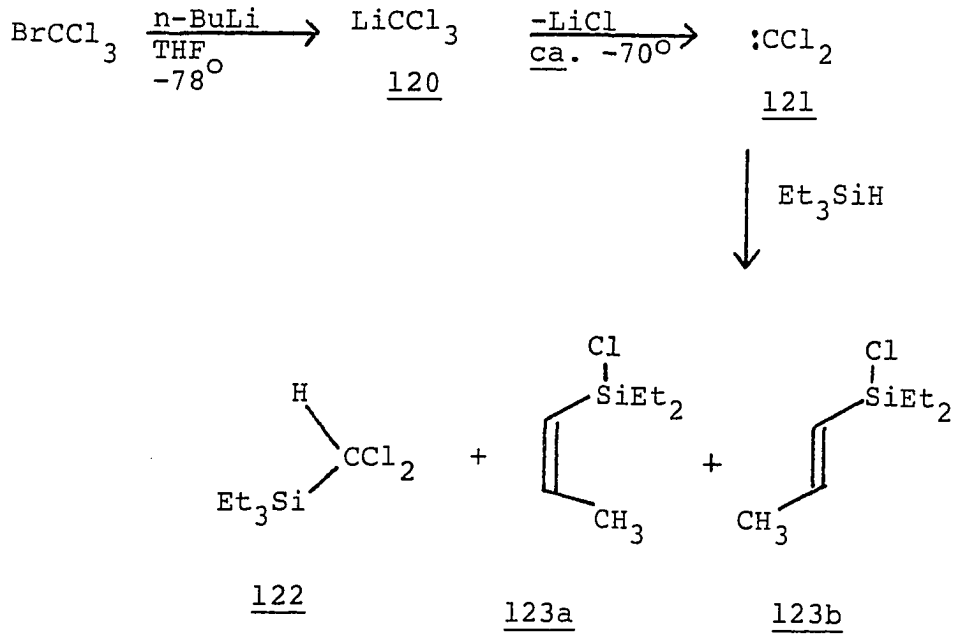
Triethylsilane, which traps carbenes via Si-H insertion,[54] might, a priori, be expected to be a less ambiguous carbene trap than olefins. It was therefore decided to undertake a mechanistic study of the reactions of 7-bromo-7-lithiobicyclo [4.1.0] heptane (89-anti and 89-syn) with the following objectives: a) to determine what conditions are necessary to generate a free carbene, and b) to study the viability of triethylsilane as a complement to olefinic carbene traps at low temperatures.

B. Results and Discussion

1. Triethylsilane trapping of dichlorocarbene at low temperature

The first order of business was to determine whether triethylsilane would be suitable for use as a carbene trap under the low temperature conditions typically used for reactions of carbenoids like 89-anti and 89-syn. The model carbenoid/carbene system chosen was trichloromethyllithium (120)/dichlorocarbene (121), shown in Scheme XXIII. Strong literature evidence shows that, in THF solution, carbenoid 120 generates carbene 121 at ca. -70°. (This has been veri-

Scheme XXIII:



fied by potentiometric measurement of the lithium chloride produced at temperatures between -100° and -65°,[55] trapping studies with carbon dioxide before and after warming to -65°, [56] and trapping studies with olefins at -100° and -65°.[56] The selectivity of the dichlorocarbene for different olefins was found to be identical with that of dichlorocarbene generated from other precursors.[57,58]) Triethylsilane was already known to efficiently trap dichlorocarbene at high temperatures,[59-62] but nothing was known about the feasibility of low temperature trapping.

The major product of the low temperature trapping of dichlorocarbene was indeed Si-H insertion product 122 (Scheme

XXIII). Also observed were smaller amounts (as described in the Experimental) of products tentatively identified as olefins 123a and 123b (presumably formed via the diatropic rearrange-

Table XI. Triethylsilane trapping of dichlorocarbene

Expt.	Temp. n-BuLi addn.	Max. rxn. temp.[a]	Temp. of quench[b]	$BrCCl_3$ M	THF M	Et_3SiH M	%Yield 122 before workup[c]	%Yield 122 after workup[d]
1	-78°	-78°	-78°	0.041	11.3	0.26	6	5
2	-78°	-62°	-78°	0.042	11.5	0.13	15	12
3	-78°	-62°	-78°	0.041	11.4	0.26	43	28
4	-78°	-62°	-78°	0.039	10.9	0.51	56	40
5	-78°	-62°	-78°	0.039	9.8	1.0	63	44
6	-78°	r.t.	r.t.	0.041	11.4	0.26		32
7	-78°	r.t.	r.t.	0.041	11.4	0.26		30

[a]The maximum temperature was held for 30 minutes prior to the quench.

[b]For the quench, a water/THF solution was added.

[c]Yield measured by GC integration vs. internal standard, with correction factors.

[d]Yield measured by NMR integration vs. internal standard.

ment of a chlorine and an ethyl group of 122, followed by dehydrohalogenation). The rearrangement of 122 to 123a and 123b is precedented.[62b] As can be seen from the data in Table XI, triethylsilane functions very well as a selective trap for dichlorocarbene at low temperatures. At -78°, at which temperature carbenoid 120 should not generate dichlorocarbene (121), almost no trapping occurred (experiment 1 of Table XI). The small amount of 122 that did form (5% yield) was probably the result of some local heating during the n-butyllithium addition. From -62° to room temperature (experiments 2 through 7 of Table XI), reasonably good yields of trapping product 122 were obtained. Some of the data of Table XI are plotted in Figure 18.

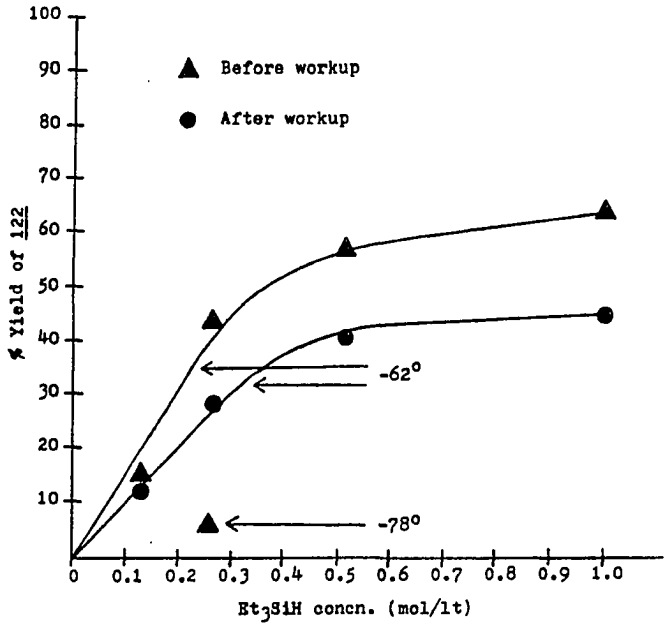
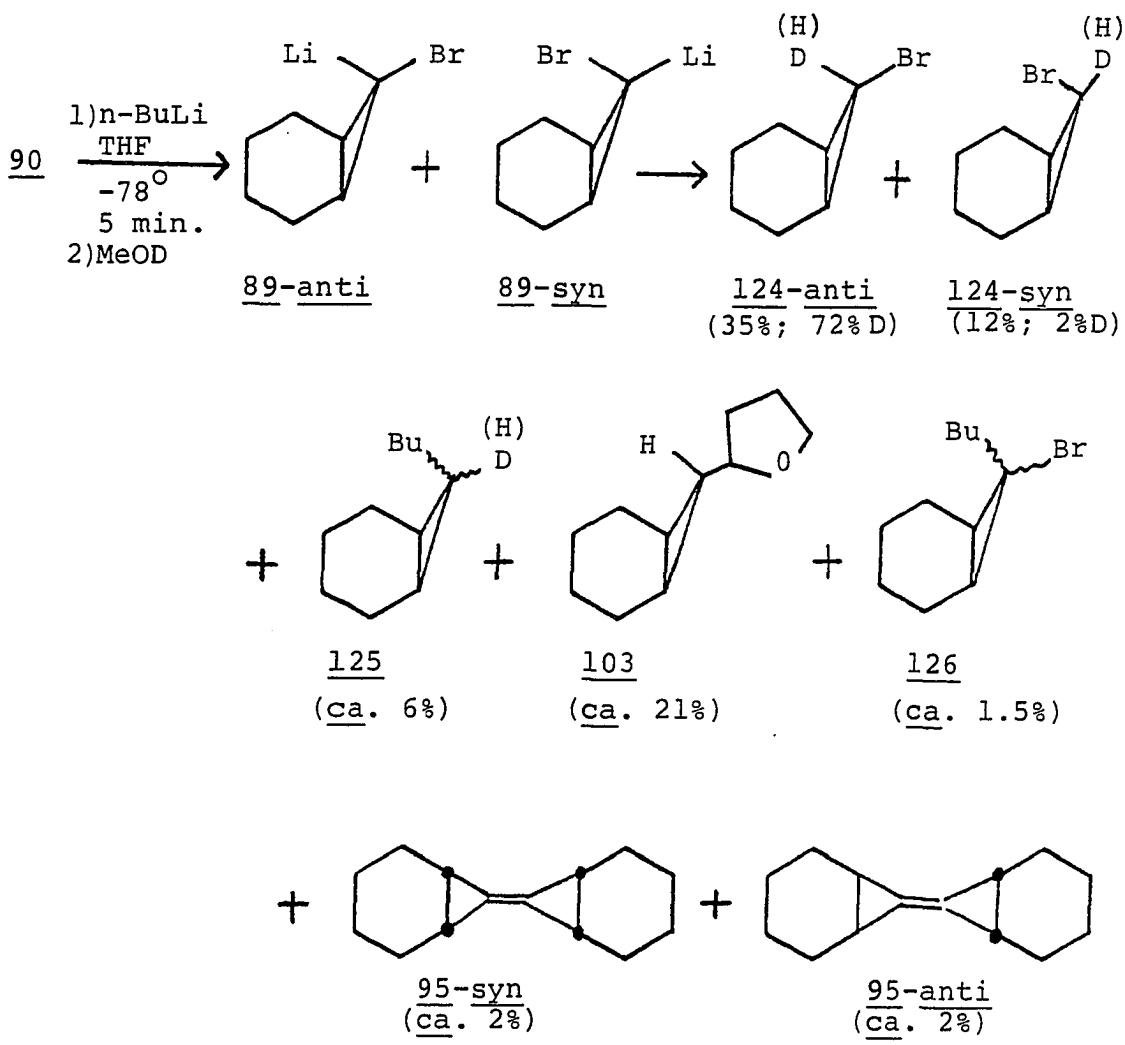


Figure 18. Triethylsilane trapping of dichlorocarbene at -78° and -62°

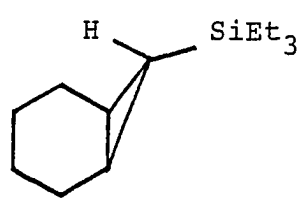
2. Reactions of 7-bromo-7-lithiobicyclo [4.1.0] heptane

When carbenoids 89-anti and 89-syn (generated by treating dibromide 90 with n-butyllithium) were reacted in THF at -78° for 5 minutes, followed by a methanol-0-d quench (Scheme XXIV),

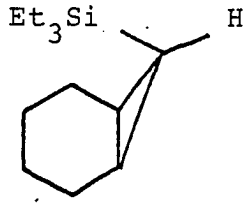
Scheme XXIV:



products 124-anti, 124-syn, 125, 103, 126, 95-syn, and 95-anti resulted. (No attempts were made to search for intramolecular C-H insertion products 91 and 92.) This product mixture is quite similar to that obtained by Köbrich and Goyert[46a] from the corresponding chlorocarbenoid (Scheme XX). When excess triethylsilane was included in the reaction mixture, traces of 127-anti and 127-syn, apparent carbene insertion products, were also formed.



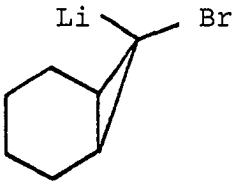
127-anti



127-syn

Reaction of 89-anti and 89-syn in ether, instead of in THF, resulted in a product mixture similar to that reported by other workers (Scheme XIX and Table X). It consisted of products 124-anti (9%), 124-syn (3.5%), 125 (ca. 10%), 93 (ca. 1%), 126 (ca. 3%), 95-anti (ca. 0.7%), and 95-syn (ca. 11%). (The stereochemistries of 95-syn and 95-anti were assigned on the basis of their relative yields, by considering the results of Fukuda et al.,[46b] already discussed earlier, in connection with the results shown in Scheme XIX and Table X.) The presence of excess triethylsilane again resulted in traces of Si-H insertion products 127-anti and 127-syn.

The data in Table XII show that, in THF solution, an appreciable amount of carbenoid 89-anti remained unreacted unless the reaction mixture was allowed to warm to at least



89-anti

-44° (experiment 4, Table XII). In ether solution, however, most of the carbenoid reacted even at temperatures as low as -78° (experiment 6, Table XII). This observed lower stability of an α-haloalkyllithium in ether than in THF is well precedented.[7,56] Recent theoretical calculations[63] suggest that this effect might originate from different aggregation states in the two solvents.

Next, the effect of triethylsilane concentration, and of the reaction temperature, on the yield of carbene trapping products 127-anti and 127-syn were explored. Tables XIIIa, XIIIb, and XIIIc detail the results.

Note that for experiments 9, 10, and 11 of Tables XIIIa, XIIIb, and XIIIc, large quantities of n-butyltriethylsilane (presumably from n-butyllithium displacement of a hydride from triethylsilane) were also observed. The uncorrected GC yields (see footnote a, Table XIIIc) for experiments 9, 10, and 11 were 7.5%, 43%, 46%, respectively.

Table XII. Effects of temperature and solvent on the reaction of carbenoids 89-anti and 89-syn[a]

Expt.	Eq. of n-BuLi	Solv.	Temp. n-BuLi addn.	Max. temp.	Time[b] (min.)	Temp. of quench[c]
1(IX-6)[f]	1.3	THF	-78°	-78°	5	-78°
2(VIII-63)[f]	1.2	THF	-78°	-78°	60	-78°
3(VIII-68)[f]	1.3	THF	-78°	-62°	15	-78°
4(VIII-70)[f]	1.3	THF	-78°	-43.5°	15	-78°
5(VIII-71)[f]	1.3	THF	-78°	r.t.	15	-78°
6(VIII-74)[f]	1.3	ether	-78°	-78°	60	-78°

[a]Conditions D (described in Experimental) were used.

[b]Time at the maximum temperature, prior to the quench.

[c]Methanol-0-d quench.

[d]Yield measured by GC integration vs. an internal standard, with correction factors.

[e]%D incorporation calculated from mass spectral data:

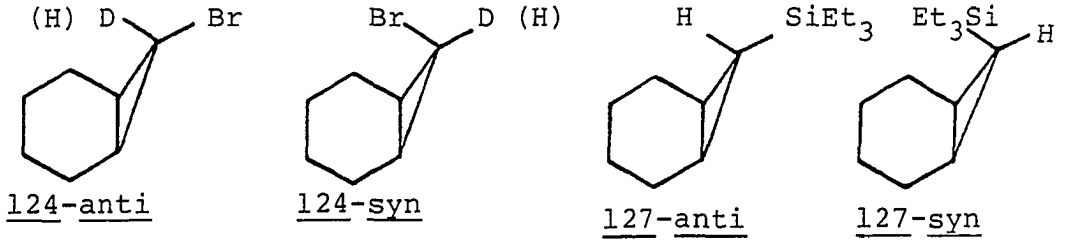
$$\%D = \frac{177_{\text{intens.}} - \left[\left(\frac{P+1}{P}\right)^{*} \times 174 \text{ intens.}\right] + 178 \text{ intens.}}{174 \text{ intens.} + 177 \text{ intens.} + 178 \text{ intens.}}$$

*Experimental natural $\left(\frac{P+1}{P}\right)$ ratio

[f]Notebook number, followed by page number.

%Yield[d] 124-anti	%D[e] in 124-anti	%Yield[d] 124-syn	%D[e] in 124-syn
35	72	12	2
31	59	14	0
32	58	15	0
25	3	18	0
21	0	15	1
9	48	3.5	0.5

Table XIIIb shows that triethylsilane trapping products 127-anti and 127-syn were formed in substantial quantity only in experiments 9, 10, and 11 (with combined yields of 3%, 9%, and 8%, respectively). These results lead one to conclude that carbenoids 89-anti and 89-syn do generate small amounts of the corresponding free carbene (96) if the n-butyllithium is added at or above room temperature. (In view of the formation of n-butyltriethylsilane, however, it is also possible that 89-anti and 89-syn react directly with triethylsilane.) At all the temperatures explored, increased triethylsilane concentration did result in increased yields of 127-anti and 127-syn.



124-anti 124-syn 127-anti 127-syn

The final question to be explored was: What effect does the solvent have on the yield of carbene trapping products 127-anti and 127-syn? The results are in Tables XIVa, XIVb, and XIV c.

It has already been mentioned that using ether solvent (experiment 6, Table XII) instead of THF (experiment 2, Table XII) resulted in a lower recovery of unreacted carbenoid.

Table XIIIa. Effects of triethylsilane concentration and temperature on the yields of 124-anti, 124-syn, 127-anti, and 127-syn: conditions

Expt.	Eq. of n-BuLi	Temp. n-BuLi addn.	Max. temp.	Time[a] (min.)
1[b](IX-6)[c]	1.3	-78°	-78°	5
2[b](VIII-63)[c]	1.2	-78°	-78°	60
3[b](IX-42)[c]	1.4	-78°	-78°	60
4[b](IX-2)[c]	1.3	-78°	-78°	60
5[b](VIII-68)[c]	1.3	-78°	-62°	15
6[b](VIII-70)[c]	1.3	-78°	-43.5°	15
7[b](VIII-71)[c]	1.3	-78°	r.t.	15
8[e](IX-20)[c]	1.3	r.t.	r.t.	60
9[e](IX-34)[c]	1.3	r.t.	r.t.	60
10[g](IX-40)[c]	1.4	+53°	+53°	60
11[g](IX-41)[c]	1.4	+53°	+53°	60

[a]Reaction time at the max. temp., prior to the quench.

[b]Conditions D (described in Experimental) were used.

[c]Notebook number, followed by page number.

[d]Methanol- -d quench.

[e]Conditions E (described in Experimental) were used.

[f]Water quench.

[g]Conditions F (described in Experimental) were used.

Temp. of quench	SM M	THF M	Et_3SiH M
-78[od]	0.021	12	0
-78[od]	0.021	12	0.27
-78[od]	0.021	10	1.0
-78[od]	0.021	7.2	2.6
-78[od]	0.022	12	0.27
-78[od]	0.022	12	0.27
-78[od]	0.021	12	0.27
r.t.[f]	0.022	12	0.27
r.t.[f]	0.022	10	1.0
r.t.[f]	0.023	10	1.0
r.t.[f]	0.023	6.0	3.1

Table XIIIb. Effects of triethylsilane concentration and temperature on the yields of 124-anti, 124-syn, 124-anti, and 127-syn: product yields

Expt.	%Yield[a] 124-anti	%Yield[a] 124-syn	%Yield[b] 127-syn+ 127-anti	NMR yield (%)[c] 127-anti	NMR yield (%)[c] 127-syn
1	35(72%D)[d]	12(2%D)[d]	N/A	N/A	N/A
2	31(59%D)[d]	14(0%D)[d]	0.3, 0.2		
3	32(70%D)[d]	13(8%D)[d]	0.9, 0.6	ca. 0	ca. 0
4	18(59%D)[d]	10(.5%D)[d]	0.8, 0.7	ca. 0	ca. 0
5	32(58%D)[d]	15(0%D)[d]	0.3, 0.1		
6	25(3%D)[d]	18(0%D)[d]	0.6, 0.4		
7	21(0%D)[d]	15(1%D)[d]	0.8, 0.6		
8	15	2.5	6.2[e], 1.1	ca. 0	ca. 0
9	21	3.1	11[e], 3.1	3.2	trace
10	12	5.5	17, 4.2	7.0	ca. 2
11	12	4.5	14, 6.3	5.7	ca. 2

[a]Yield measured by GC integration vs. an internal std. with correction factors. (Structures precede Table XIIIa.)

[b]Uncorrected GC yield, measured by GC-MS quantitation (Column C) vs. 124-anti, assuming 1:1 GC correction factors.

[c]Yield measured by NMR (FT ^{1}H NMR, 90 MHz) integration relative to 124-anti.

[d]%D incorporation calcd. as in footnote e, Table XII.

[e]Uncorrected GC yield (inaccurate because of overlap with one epimer of 126).

Table XIIIc. Effects of triethylsilane concentration and temperature on the yields of 95-anti, 95-syn, 103, 125, and 126.

Expt.	%Yield[a] 125[b] (or 102)[d]	%Yield[a] 103	%Yield[a,c] 126	%Yield[a] 95-anti, and 95-syn
1	5.5, 0.8	21	1.5	1.5, 2.3
2	0.2, 0.05	19	1.9	1.2, 1.7
3	5.0, 0.6	9.5	2.0	1.3, 1.7
4	0.2(<.2)	6.0	1.6	1.0, 1.5
5	0.8, 0.2	18	1.6	1.1, 1.6
6	0.5, 0.04	32	1.6	1.7, 2.3
7	1.4, 0.2	42	1.6	1.8, 2.2
8	0.9, 0.9	38	12	1.2, 0.9
9	1.1, 1.0	31	12	1.0, 0.7
10	0.9, 0.9	28	7.1	0
11	0.8, 0.8	13	6.6	0

[a] Uncorrected GC yield, measured by GC-MS quantitation (Column C) vs. 124-anti, assuming the relative GC correction factors to be 1:1. (Structures in Scheme XXIV.)

[b] Two stereoisomers.

[c] Only one epimer (unspecified stereochemistry) could be detected separately, because the other one was obscured by either 127-anti or 127-syn.

[d] The protonated analog of 125.

Table XIVa. Effect of solvent on the yields of 124-anti, 124-syn, 127-anti, and 127-syn: conditions

Expt.	Eq. of n-BuLi	Temp. n-BuLi addn.	Max. temp.	Time[a] (min.)	Quench (Temp.)
1[b](VIII-63)[c]	1.2	-78°	-78°	60	MeOD (-78°)
2[b](VIII-74)[c]	1.3	-78°	-78°	60	MeOD (-78°)
3[d](IX-5)[c]	1.3	-100°	-78°	60	MeOD (-78°)
4[b](VIII-68)[c]	1.3	-78°	-62°	15	MeOD (-78°)
5[b](IX-12)[c]	1.4	-78°	-62°	15	MeOD (-78°)
6[b](IX-23)[c]	1.9	-78°	-62°	20	MeOD (-78°)
7[g](IX-20)[c]	1.3	r.t.	r.t.	60	H_2O (r.t.)
8[g](IX-30)[c]	1.3	r.t.	r.t.	60	H_2O (r.t.)
9[g](IX-34)[c]	1.3	r.t.	r.t.	60	H_2O (r.t.)
10[g](IX-45)[c]	1.3	r.t.	r.t.	60	H_2O (r.t.)
11[h](IX-40)[c]	1.4	+53°	+53°	60	H20 (r.t.)
12[h](IX-35)[c]	1.4	+53°	+53°	30	H20 (+53°)

[a]Time at the max. temp., prior to the quench.

[b]Conditions D (described in Experimental) were used.

[c]Notebook number, followed by page number.

[d]Conditions G (described in Experimental) were used.

[e]12-C-4-ether added 5 to 10 min. after the n-butyllithium, at the same temperature.

[f]12-C-4 present before n-butyllithium addition.

[g]Conditions E (described in Experimental) were used.

[h]Conditions F (described in Experimental) were used.

SM M	Solv., M	12-C-4 M	Et_3SiH M
0.021	THF, 12	0	0.27
0.021	ether, 9.1	0	0.27
0.021	THF, 12	0.09[e]	0.27
0.022	THF, 12	0	0.27
0.020	THF, 11	0.21[e]	0.27
0.020	THF, 11	0.20[f]	0.26
0.022	THF, 12	0	0.27
0.020	THF, 11	0.20[f]	0.26
0.022	THF, 10	0	1.0
0.022	ether, 7.9	0	1.0
0.023	THF, 10	0	1.0
0.021	THF, 10	0.20[f]	1.0

Table XIVb. Effect of solvent on the yields of 124-anti, 124-syn, 127-anti, and 127-syn: product yields

Expt.	%Recov.[a] SM	%Yield[a] 124-anti	%Yield[a] 124-syn
1	0	31(59%D)[d]	14(0%D)[d]
2	0	9(48%D)[d]	3.5(.5%D)[d]
3	0	22(32%D)[d]	20(.8%D)[d]
4	0	32(58%D)[d]	15(0%D)[d]
5	0	34(0%D)[d]	18(0%D)[d]
6	0	26(21%D)[d]	15(.3%D)[d]
7	0	15	2.5
8	5.3	23	4.1
9	0	21	3.1
10	0	6.4	2.1
11	0	12	5.5
12	15	21	3.2

[a-e]See footnotes a through e, respectively under Table XIIIb. (Structures precede Table XIIIa.)

%Yield[b] 127-anti, 127-syn	NMR Yield (%)[c] 127-anti	NMR Yield (%)[c] 127-syn
0.3, 0.2		
0.3, 0.4		
0, 0		
0.3, 0.1		
0, 0		
0, 0		
6.2[e], 1.1	ca. 0	ca. 0
4.5, 0.6		
11[e], 3.1	3.2	trace
4.0[e], 0.4	trace	ca. 0
17, 4.2	7.0	ca. 2
7.1[e], 2.1		

Table XIVc. Effect of solvent on the yields of 95-anti, 95-syn, 103, 125 and 126

Expt.	%Yield[a] 126[b] (or 102)[d]	%Yield[a] 103	%Yield[a,c] 126	%Yield[a] 95-anti, and 95-syn
1	0.2, 0.05	19	1.9	1.2, 1.7
2	7.7, 1.7	18	2.7	1.4, 22.0
3	0.4, ca. 0	5.5	0.7	1.3, 3.1
4	0.8, 0.2	18	1.6	1.1, 1.6
5	0.7, 0.2	14	1.3	1.1, 1.6
6	4.0, 0.7	16	2.2, 17	1.4, 2.6
7	0.9, 0.9	38	12	1.2, 0.9
8	2.4, 1.1	30	8.6	0.8, 0.6
9	1.1, 1.0	31	12	1.0, 0.7
10	2.8, 1.2	10	11	1.6, 0
11	0.9, 0.9	28	7.1	0, 0
12	2.5, 1.3	20	8.0	0.7, 0.5

[a] Uncorrected GC yield, measured by GC-MS quantitation (Column C) vs. 124-anti, assuming the relative GC correction factors to be 1:1. (Structures in Scheme XXIV.)

[b] Two stereoisomers.

[c] Same as footnote c, under Table XIIIc, except for experiment 6, in which both epimers were detected.

[d] See footnote d, under Table XIIIc.

However, using ether (experiments 2 and 10, Tables XIVa and XIVb) instead of THF (experiments 1 and 9, Tables XIVa and XIVb) did not increase the yields of triethylsilane trapping products 127-anti and 127-syn. Evidently, in ether solution, lower recoveries of unreacted carbenoid resulted because the carbenoid is more reactive toward nucleophilic attack (probably due to aggregation and solvation effects[7,63]) in that medium, and not because carbene generation is facilitated.

The results in Table XIVb show that the presence of 12-crown-4-ether (experiments 3, 5, 6, 8, and 12) actually lowered the yields of carbene trapping products 127-anti and 127-syn. Furthermore, the data for experiments 3, 5, and 6 show that the presence of 12-crown-4-ether substantially reduced the %D incorporation in carbenoid trapping product 124-anti. These effects of 12-crown-4-ether probably arise from an increase in the basicity of carbenoids 89-anti and 89-syn, due to solvation of the lithium cation by the 12-crown-4-ether. Thus, 12-crown-4-ether is apparently not effective in aiding carbene generation from these particular carbenoids.

C. Conclusion

At low temperatures, triethylsilane efficiently trapped dichlorocarbene (at -62°), but did not react substantially with its precursor, trichloromethyllithium (at -78°). Tri-

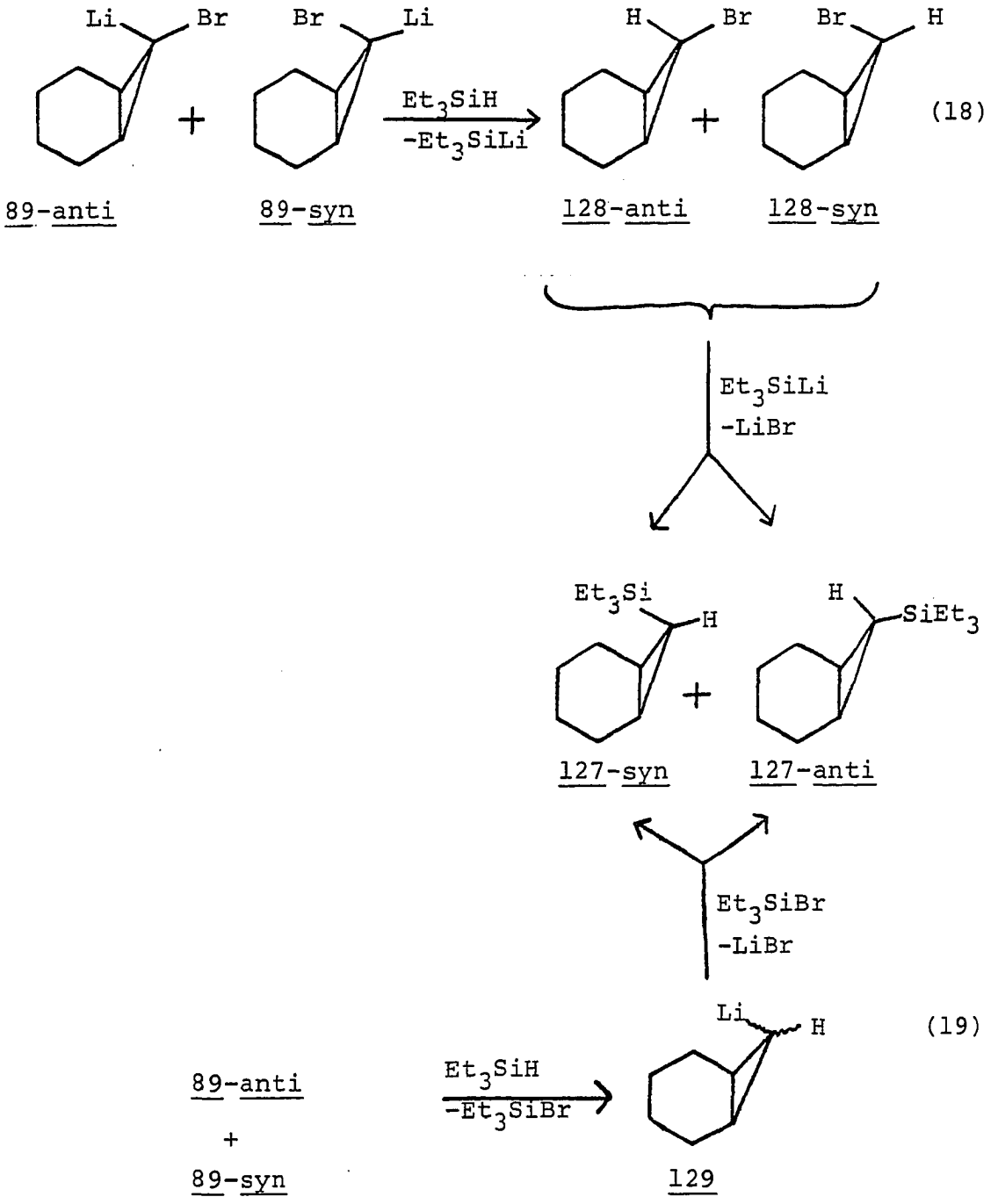
ethylsilane therefore shows promise as a new complement to olefinic carbene traps.

Although less unreacted carbenoid was recovered from reactions of anti-7-bromo-syn-7-lithiobicyclo[4.1.0]heptane (89-anti) and its C^7-epimer (89-syn) in ether solvent than in THF, there was no corresponding increase in the yields of triethylsilane insertion products 127-anti and 127-syn. Ether solvent apparently does not facilitate carbene generation from these carbenoids.

The use of 12-crown-4-ether also did not seem to facilitate carbene generation from these particular carbenoids. It seemed to simply enhance there basicity.

Finally, it was found that substantial quantities of 127-anti and 127-syn were formed only if the n-butyllithium was added at or above room temperature. Because such relatively harsh conditions were required, one is tempted to speculate that products 127-anti and 127-syn might have arisen through a mechanism other than insertion of free carbene 96 into the Si-H bond. Two such mechanistic possibilities are offered in Scheme XXV (equations 18 and 19), and involve the key intermediates 128-anti and 128-syn, and 129, respectively. The control experiments which would be necessary in order to test for these possibilities did not seem worthwhile because of the very low yields (0 to 9%)

Scheme XXV:


Li
Br
Br
Li
Et_3SiH
$-Et_3SiLi$
H
Br
Br
H
(18)
89-anti
89-syn
128-anti
128-syn
Et_3SiLi
-LiBr
Et_3Si
H
H
$SiEt_3$
127-syn
127-anti
Et_3SiBr
-LiBr
Li
H
(19)
89-anti
+
89-syn
Et_3SiH
$-Et_3SiBr$
129

of 127-anti and 127-syn under all of the reaction conditions tested.

A very important consideration is whether the cyclopropanation product 98, obtained by Moore and Ward[45] (10% isolated yield from a -80° reaction in ether solution containing cyclohexene) and by Köbrich and Goyert[46a] (3% GC yield from a -115° to room temperature reaction in 80% THF/20% ether solution containing cyclohexene) resulted from a reaction between cyclohexene and free carbene 96, or between cyclohexene and carbenoids 89-anti and 89-syn. The conditions used by Moore and Ward are closely approximated by experiment 2 (-78°, ether) of Tables XIVa, XIVb, and XIVc. In that experiment, the amounts of products 127-anti and 127-syn were negligible (<<3%). Furthermore, experiment 10 of Tables XIVa, XIVb, and XIVc (room temperature, ether) also resulted in negligible amounts (<<3%) of 127-anti and 127-syn. These data suggest that the substantial amount of cyclopropanation product 98, observed by Moore and Ward,[45] was probably the result of a direct reaction between cyclohexene and carbenoids 89-anti and 89-syn.

Experiment 7 of Tables XIIIa, XIIIb, and XIIIc (-78° to room temperature, THF) approximates the conditions used by Köbrich and Goyert.[46a] Negligible amounts (<<3%) of triethylsilane insertion products 127-anti and 127-syn were

formed. Taking these conditions a step further, to experiments 8 and 9 of Tables XIIIa, XIIIb, and XIIIc (room temperature, THF), one sees that small amounts (ca. 3%) of 127-anti and 127-syn were formed when the n-butyllithium was added at room temperature. It is therefore uncertain, without duplicating their reaction conditions exactly, whether or not Köbrich and Goyert did, in fact, trap free carbene 96 with cyclohexene. Nonetheless, Köbrich and Goyert[46a] have already concluded that free carbene 96 probably does not play a substantial role in the reactions of carbenoids 89-anti and 89-syn under their conditions.

The conclusion that the low temperature chemistry of carbenoids 89-anti and 89-syn probably does not involve the corresponding free carbene intermediate, 96, supports the contention in Chapter I that the 1,3-rearrangements of their unsaturated counterparts (34-anti and 34-syn, respectively) also do not involve a free carbene intermediate.

D. Experimental

1. General considerations

For the general considerations, see the experimental section of Chapter I.

2. n-Butyllithium treatment of bromotrichloromethane in the presence of triethylsilane (preparation of dichloro-triethylsilylmethane, 122)

Bromotrichloromethane (Aldrich spectrophotometric grade) was purified by first washing it with two portions of 40% aqueous sodium hydroxide, then twice with water, and once with saturated sodium chloride solution, drying it over anhydrous potassium carbonate/magnesium sulfate, and, finally distilling it under argon (b.p. 102 to 103°).

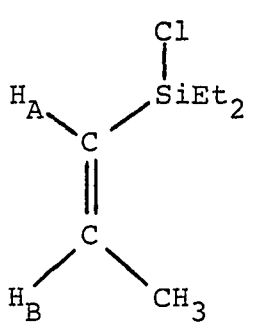
A 25 ml 3-neck round-bottom flask was equipped with a magnetic stirring bar and an argon inlet, and was argon-flushed and dried. It was next charged with a solution of 24 µl (0.244 mmol) of bromotrichloromethane in 5.5 ml of dry (freshly distilled from LAH) THF plus 0.250 ml (1.57 mmol) of triethylsilane, and then cooled to -78° ("Skelly B" hexane-dry ice bath) for 15 minutes. n-Butyllithium (0.220 ml, 0.323 mmol) was then syringed in down the side of the flask over a 2 minute period. A transient yellow color was formed during the n-butyllithium addition. After the solution had been stirred under argon at -78° for three more minutes, one of three things was done: a) the solution was stirred at -78° for 30 minutes, or b) the -78° bath was replaced with a -62° bath (chloroform slush), and the solution was stirred for another 30 minutes at -62°,

or c) the -78° bath was removed, and stirring was continued for another 30 minutes. After performing either option (a) or (b) above, the solution was cooled back down to -78° for 10 minutes, and quenched by syringing in a solution of 5.0 mmol of water dissolved in 1 ml of distilled THF, over a 10 to 20 second period. After 10 more minutes of stirring at -78°, the cold bath was removed, and the solution was stirred under argon for an additional 10 minutes. A measured amount (6 to 7 mg) of p-di-tert-butylbenzene standard was added, and a small aliquot of the solution was saved for GC analysis. The main portion of the solution was carefully concentrated on a rotary evaporator (being careful to avoid volatilization of the product). The residue was partitioned between 35 ml of ether and 3 ml of water, plus 2 ml of saturated sodium chloride solution, and the organic layer was then washed with 3 ml of saturated sodium chloride solution. Drying (anhydrous magnesium sulfate) and filtration were followed by careful concentration in vacuo, leaving a brown oil which was analyzed by NMR.

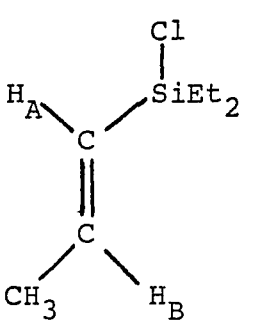
The procedure used after performing option (c) above was the same as that just described for options (a) and (b), except that the solution was quenched with 10 drops of water at room temperature, and then worked up as for options (a) and (b).

The major product identified was dichlorotriethylsilylmethane (122). The crude 60 MHz ^{1}H NMR (CCl_4) included the following peaks: δ 5.32 (s), 2.3-0.35 (complex m). This NMR spectrum compares well with that reported in the literature.[60,62] 70 eV MS (Finnegan GC-MS), m/e (%RIA): 200 (P+2, 0.03), 198 (P, 0.06), 163 (P-35, 0.01), 129 (P+2-71, 9.75), 127 (P-71, 14.50), 115 (P-83, 100.00), 101 (13.74), 99 (19.39), 93 (17.24), 87 (P-83-28, 88.86), 78 (6.76), 65 (15.02), 63 (15.98), 59 (42.39).

The GC trace showed two impurities which might be the two stereoisomers 123a and 123b (shown below), in a ca. 1:1 ratio. Their mass spectra could not be readily understood. The crude NMR spectrum showed two doublets, centered at δ 5.58 (spacings = 4 and 5 Hz), which were tentatively assigned to protons A of 123a and 123b, and a multiplet at δ 4.0 to δ 3.45, which was tentatively assigned to protons B of 123a and 123b. The combined NMR yields of 123a and 123b in experiments 1 through 7 (Table XI) were 8%, 17%, 22%, 15%,



123a



123b

11%, 16%, and 19%, respectively. A possible mechanism for the generation of 123a and 123b was already discussed in the text. GC analysis showed no tetrachloroethylene (minimum detection limit = 3% yield). It is very important to note that in experiments in which methanol instead of water was used as the quench, 122 was only a minor product (0 to 3% yield). Compounds 123a and 123b, however, were still major products (16% combined yield). A second compound, tentatively identified as triethylmethoxysilane (NMR, CCl_4: δ 3.35, s, due to the methoxy group), which was apparently transformed into triethysiloxane on the GC column. (Triethylsiloxane was the major product observed by GC-MS.) A possible mechanism for the formation of triethylmethoxysilane is a displacement of dichloromethane from 122 by methanol.

3. Preparation of 7,7-dibromobicyclo [4.1.0] heptane (90)

Compound 90 has been previously prepared from cyclohexene and dibromocarbene.[31,64] The following is a detailed description of the procedure used in the present work.

A 100 ml 3-neck round-bottom flask was equipped with an addition funnel, a magnetic stirring bar, and a nitrogen inlet, and was nitrogen-flushed and dried, and then charged with 3.831 g (34.2 mmol) of commercial potassium tert-butoxide powder and 25 ml of hexane. A solution of 2.45 ml (28.0 mmol) of bromoform and 2.90 ml (28.6 mmol) of cyclo-

hexene in 9 ml of hexane was placed in the addition funnel. The flask was next cooled to -78° (dry ice-acetone bath), and the solution in the addition funnel was added dropwise over a 35 minute period to the stirred potassium tert-butoxide suspension. It is important to add the bromoform/olefin solution through the center neck of the flask, to avoid freezing of it along the side of the flask. It is sometimes difficult to stir the potassium tert-butoxide suspension, especially if the reaction is run on a larger scale than that described here. The addition of a small amount of extra hexane usually helps in such an event. If the preparation is to be done on much more than double the scale described here, it is better to use an overhead mechanical stirrer, instead of a magnetic stirrer.

The mixture was then allowed to warm slowly while being stirred under nitrogen for 17 hours. It was next partitioned between 30 ml each of water and ether. The aqueous layer was re-extracted with 2 x 20 ml of ether. The organic layers were combined and washed sequentially with 3 x 5 ml of water, and 1 x 5 ml of saturated sodium chloride solution, dried (anhydrous magnesium sulfate), filtered, and concentrated on a rotary evaporator to give 5.7 g of a yellowish oil. Distillation through a short path distillation head at 0.05 to 0.1 mm pressure afforded (after the collection of a brief

forerun) a 65% yield (based on cyclohexene) of 90 as a colorless liquid (b.p. 37.5° to 41° at 0.05 to 0.1 mm). 60 MHz ^{1}H NMR for compound 90[31,64] (CCl_4): δ 2.4-0.9 (complex m).

4. n-Butyllithium treatment of 7,7-dibromobicyclo[4.1.0]-heptane (90) in the presence of triethylsilane

a. Conditions D: n-butyllithium added at -78° A 25 ml 3-neck round-bottom flask, equipped with a magnetic stirring bar and an argon inlet, was argon-flushed and dried. It was then charged with a weighed amount (30 to 40 mg) of 7,7-dibromobicyclo[4.1.0]heptane (90), and the desired amount of triethylsilane, dissolved in enough dry (freshly distilled from LAH) THF or ether to make up a total volume of 6 ml. The flask was next cooled to -78° ("Skelly B" hexane-dry ice bath) for 15 minutes before the desired amount (1.2 to 1.4 times the number of mmoles of 90) of a 1.47 M n-butyllithium/hexane solution was syringed in down the side of the flask over a 1 minute period. The solution was then either a) stirred at -78° under argon for the desired length of time, or b) after having been stirred at -78° under argon for 5 minutes, warmed to -62° (chloroform slush bath), and stirred at that temperature for the desired length of time, or c) after having been stirred at -78° for 5 minutes, warmed to -43.5° (chlorobenzene slush bath) and stirred at that tempera-

ture for the desired length of time. Next, the solution was cooled back down to -78° and stirred for 10 minutes at that temperature. Then, it was quenched by syringing in 0.3 ml of methanol-O-d (99.5+ atom %D) over a 10 to 15 second period. After the solution had been stirred for an additional 10 minutes under argon at -78°, the cold bath was removed, and the stirring was continued for another 10 minutes. A few drops of water were added, and the solution was then carefully (avoiding volatilization of the products) concentrated on a rotary evaporator. The residue was partitioned between 35 ml of ether and 3 ml of water, plus 2 ml of saturated sodium chloride solution. The organic layer was washed with 3 ml of saturated sodium chloride solution, dried over anhydrous sodium sulfate, filtered, and carefully concentrated on a rotary evaporator. The resulting oil was analyzed by NMR and GC-MS. The product distribution is described after section e below.

b. Conditions E: n-butyllithium added at room temperature This procedure was the same as that for Conditions D above, except that no cooling bath was used. The n-butyllithium solution was syringed in down the side of the flask over a 1 minute period. After the solution had been stirred under argon at room temperature for the desired length of time, it was quenched with 10 drops of water, concentrated

carefully on a rotary evaporator, and worked up the same way as was described under Conditions D above.

c. Conditions F: n-butyllithium added at +53° A 25 ml 3-neck round-bottom flask, equipped with a magnetic stirring bar and an argon inlet, was argon-flushed and dried. It was then charged with a weighed amount (30 to 40 mg) of 7,7-dibromobicyclo [4.1.0] heptane (90), and the desired amount of triethylsilane, dissolved in enough dry (freshly distilled from LAH) THF to make up a total volume of 6 ml. The flask was next heated at +52° to +53° with an oil bath for 10 to 15 minutes. Then, the desired amount (1.4 times the number of mmoles of 90) of a 1.47 M n-butyllithium/hexane solution was syringed in through the center neck of the flask over a 1 to 1.5 minute period. After the solution had been stirred at +52° to +53° under argon for the desired length of time, it was quenched with 10 to 12 drops of water, either while the solution was maintained at +52° to +53°, or after it had been cooled to room temperature. The solution was then carefully concentrated on a rotary evaporator, and worked up the same way as was described under Conditions D above.

d. Experiments with 12-C-4 present (except for expt. IX-5) The desired amount (5 to 10 times the number of mmoles of 90) of 12-crown-4-ether (dried over 4A molecular sieves and stored in a desiccator) was either a) added to the

THF solution of 90 plus triethylsilane, before it was cooled or warmed to the reaction temperature, or b) added to the THF solution 5 minutes after the n-butyllithium was added, and at the same temperature at which the n-butyllithium was added.

e. Conditions G: n-butyllithium added at -100° (used only for expt. IX-5) A 25 ml 3-neck round-bottom flask, equipped with a magnetic stirring bar and an argon inlet, was argon-flushed and dried. It was then charged with 30.9 mg (0.122 mmol) of 7,7-dibromobicyclo[4.1.0]heptane (90) and 0.25 ml (1.57 mmol) of triethylsilane dissolved in 5.5 ml of dry (freshly distilled from LAH) THF. The flask was cooled to -100° to -105° ("Skelly B" hexane slush bath) for 15 minutes prior to the addition, via syringe, of 0.110 ml (0.162 mmol) of a 1.47 M n-butyllithium/hexane solution down the side of the flask over a 1 minute period. After the solution had been stirred under argon at -102° to -106° for 10 more minutes, a solution of 0.100 ml (0.618 mmol) of dry (stored over 4A molecular sieves) 12-crown-4-ether in 0.75 ml of hexane was syringed in through the center neck of the flask over a 15 second period. (The 12-crown-4-ether tended to freeze if it was added too slowly.) The resulting solution was stirred under argon at -102° to -105° for 5 more minutes, and then the "Skelly B" hexane slush bath was replaced with a -78° ("Skelly B" hexane-dry ice) bath. The solution was

stirred at -78° for 60 minutes, and then 0.3 ml of methanol-d was syringed in over a 10 to 15 second period. After 10 more minutes of stirring at -78° under argon, the cold bath was removed, and the solution was stirred under argon for another 10 minutes. A few drops of water were then added, and the solution was carefully concentrated on a rotary evaporator. The workup was then conducted in the same manner as was described under Conditions D above.

Examination of the product mixtures by GC, GC-MS, and NMR revealed the presence of the following compounds: anti-7-bromo-syn-7-deuterobicyclo[4.1.0]heptane (124-anti) and its C^7 epimer (124-syn), or their non-deuterated analogs 128-anti and 128-syn, respectively; dimers 95-syn and 95-anti; 7-n-butyl-7-deuterobicyclo[4.1.0]heptane (125), or its non-deuterated analog 102; 7-bromo-7-n-butyl-bicyclo[4.1.0]heptane (126); anti-7-triethylsilylbicyclo[4.1.0]heptane (127-anti), and its C^7-epimer (127-syn). Compounds 124-anti and 124-syn (and 128-anti and 128-syn) were identified by comparison of their GC retention times, GC-MS's, and crude NMR spectra with those of authentic samples. The position of deuteration was determined as H^7 by the weakness of that absorption in the NMR spectra of 124-anti (CCl_4, δ 2.50, t, J = 3.5 Hz) and 124-syn (CCl_4, δ 3.19, t, J = 8 Hz).

Compounds 127-anti and 127-syn were identified by comparison of their crude NMR spectra with their literature spectra. The observed NMR spectrum of 127-anti in carbon tetrachloride solution included a triplet at δ -0.76 (90 MHz ^{1}H NMR, Jeol FX-90Q), J = 6.7 Hz, and that of 127-syn included a triplet at δ -0.46. These compare well with the literature[65] data of δ -0.75, J = 7 Hz and δ -0.47, J = 10 Hz, respectively. For 127-syn, only the center peak of the triplet was visible, so its assignment is less certain. Compounds 127-anti and 127-syn were also observed by GC-MS (two GC peaks). The following mass spectrum is representative: 70 eV MS (Finnegan GC-MS), m/e (%RIC): 210 (P, 0.18), 181 (P-29, 7.59), 153 (5.05), 125 (2.24), 115 (P-95, 7.72), 109 (4.36), 95 (P-115, 5.44), 87 (P-95-28, 8.94), 67 (3.91), 59 (9.75), 55 (3.60).

Compound 126 was tentatively indentified by GC-MS. Two isomers were observed. The following mass spectrum is representative: 70 eV MS (Finnegan GC-MS, Column C), m/e (%RIC): 232 (P+2, 0.29), 230 (P, 0.24), 190 (0.17), 188 (0.20), 151 (P-79, 2.69), 109 (7.29), 95 (16.28), 81 (7.30), 79 (5.85), 68 (6.36), 67 (12.86), 55 (7.48), 53 (3.39).

Dimers 95-syn and 95-anti, and n-butylated compound 125 (or its non-deuterated analogue 102) have already been identified by Köbrich and Goyert[46a] as products from n-butyllithium

treatment of 7,7-dichlorobicyclo[4.1.0]heptane (100) in THF/ether solution. Their mass spectra are listed below.

For dimers 95-syn and 95-anti (two GC peaks), the following mass spectrum is representative: 70 eV MS (Finnegan GC-MS, Column C), m/e (%RIC): 188 (P, 0.11), 187 (P-1, 0.03), 173 (0.70), 159 (1.19), 145 (4.08), 131 (4.35), 117 (4.51), 109 (4.14), 105 (5.30), 95 (0.92), 94 (0.68), 93 (2.30), 92 (3.19), 91 (11.81), 79 (6.19), 77 (4.49), 67 (4.65), 65 (3.00), 55 (2.00), 53 (2.78), 51 (2.32).

For n-butylated compound 125 (two GC peaks), the following mass spectrum is representative: 70 eV MS (Finnegan GC-MS, Column C), m/e (%RIC): 153 (P, 1.72), 152 (P-1, 0.31), 110 (2.65), 97 (4.02), 96 (P-57, 6.78), 95 (P-1-57, 2.18), 82 (9.91), 81 (7.83), 68 (8.85), 67 (15.60), 56 (3.75), 55 (6.80), 54 (5.52).

In the THF experiments, THF insertion compound 103, already characterized by Köbrich and Goyert[46a] was also observed. Compound 103 (one GC peak), had the following 70 eV MS (Finnegan GC-MS, Column C), m/e (%RIC): 166 (P, 0.09), 165 (P-1, 0.12), 151 (0.07), 138 (0.48), 123 (2.97), 107 (0.62), 97 (3.83), 95 (P-71, 1.92), 91 (1.51), 85 (6.69), 84 (29.48), 79 (3.77), 71 (P-95, 5.64), 67 (4.14), 56 (4.84), 55 (7.09), 53 (2.81).

The order of elution of the compounds from Column C was: 128-anti, 128-syn, 125, 103, 126, (127-anti and 127-syn), (95-anti and 95-syn).

In the ether experiments, ether insertion compound 93 (only one GC peak) was eluted between the two 125 GC peaks. Compound 93 had the following 70 eV MS (Finnegan GC-MS, Column C), m/e (%RIC): 168 (P, 0.07), 153 (P-15, 3.79), 125 (1.11), 124 (1.79), 107 (1.63), 95 (P-73, 0.93), 93 (1.37), 86 (12.52), 81 (5.29), 79 (4.94), 67 (4.43), 58 (16.61), 57 (7.03), 55 (5.59).

No attempts were made to search for the intramolcular C-H insertion compounds 91 and 92.

5. Preparation of 7-bromobicylo 4.1.0 heptane (128-anti) and 128-syn)

A slight modification of the procedure of Seyferth et al.[26] was used, which involved a quench with methanol, instead of with concentrated hydrochloric acid.

A 50 ml 3-neck round-bottom flask, equipped with a magnetic stirring bar and a nitrogen inlet, was nitrogen-flushed and dried. The flask was then charged with a solution of 0.404 g (1.59 mmol) of 7,7-dibromobicyclo[4.1.0] heptane (90) in 25 ml of dry (freshly distilled from LAH) THF. The flask was cooled to -105° to -107° ("Skelly B" hexane slush bath) for 10 minutes prior to the addition,

down the side of the flask, over a 3.5 minute period, of 0.970 ml (1.68 mmol) of a 1.73 M n-butyllithium/hexane solution, via syringe. The resulting solution was stirred at -105° to -109° under nitrogen for 22 more minutes, and was then quenched by the addition of 0.4 ml of methanol, via syringe, over a 10 to 15 second period. After 5 more minutes of stirring at -106° to -108°, the solution was allowed to warm to $+15^{\circ}$, over a 2 hour period. Then, after 2 ml of saturated ammonium chloride solution had been added, the mixture was concentrated _in vacuo_, and extracted with 40 ml of ether. The organic layer was washed with 2 ml of saturated sodium chloride solution, dried (anhydrous magnesium sulfate), filtered, and concentrated on a rotary evaporator. Compounds _128-anti_ and _128-syn_ (ca. 1:1 ratio) were the only products detectable by GC. Their NMR spectra matched those reported in the literature[32b] for _128-anti_: δ 2.50 (t, 1H, J = 3.5 Hz), δ 0.9-2.2 (complex m, 10H); and for _128-syn_: δ 3.19 (t, 1H, J = 8.0 Hz), δ 0.9-2.4 (complex m, 10H).

The carbene/carbenoid chemistry of lithium and tin cyclopropylidenoids

by

Robert D. Herold

Volume 2 of 2

A Dissertation Submitted to the
Graduate Faculty in Partial Fulfillment of the
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DOCTOR OF PHILOSOPHY

Department: Chemistry
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Approved:
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Iowa State University
Ames, Iowa
1984

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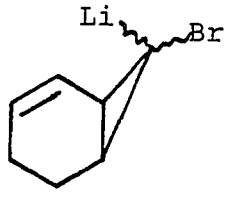
III. 7-BROMO-7-TRIMETHYLSTANNYL-BICYCLO[4.1.0]HEPT-2-ENE

A. Introduction

Chapter I of this dissertation, in conjunction with Chapter II, established that, in solution, the 1,3-rearrangements of 1-bromo-1-lithio-2-vinylcyclopropane derivatives such as 9 involve carbenoid intermediates, and not free carbenes. The mechanism for their rearrangements in the gas phase, studied by Brinker and Ritzer,[21] is still open to question.



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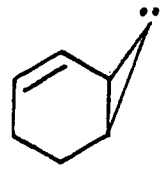

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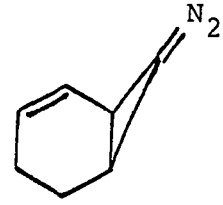
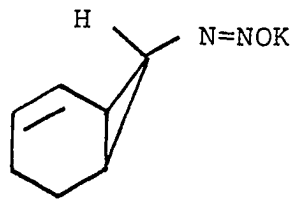


130

Another recently studied precursor of cyclopropylidene 10 is the diazo compound 130. It has reportedly been generated from the diazotate 131 (studied by Holm and Skattebol[66]) and from the nitrosourea 132 (studied by Kirmse and Jendralla[67] and by Kirmse et al.[68]). When 131 was treated with excess methanol, or when 132 was treated with lithium methoxide in methanol solution, products 133 and 134 were formed. They were rationalized[66-68] as being due to the methanol trapping of cation 135, which was itself a product



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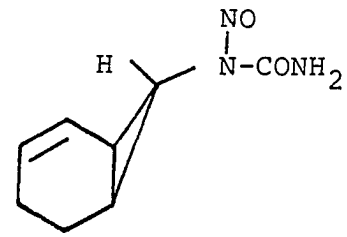

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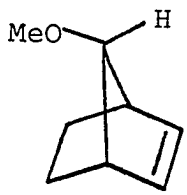

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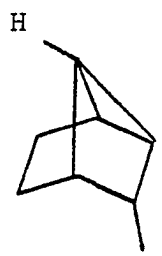
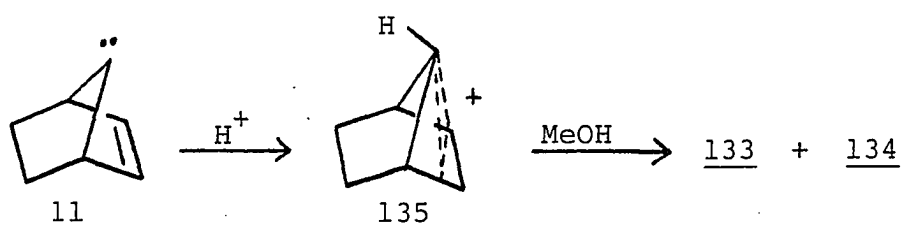


134 OMe

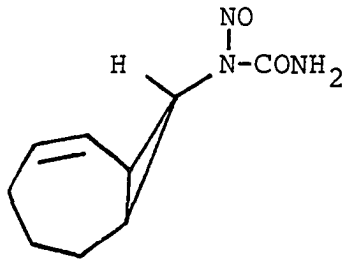
of the protonation by methanol of the rearranged carbene 11. These studies did not, however establish definitively that carbene 10 was actually rearranging to carbene 11. In fact, there was no proof that carbene 10 was necessarily involved in the reaction at all. (However, some results of Holm and Skattebol[66] did make it seem unlikely that a carbonium ion



11 135

rearrangement is involved, and some results of Kirmse and Jendralla[67] made it quite unlikely that a 1,3-rearrangement

of diazo compound 130 could explain the results.) Similar studies were conducted by Kirmse and Richarz of 136[69] and 137[70], and by Kirmse et al. of 138[71], all of which involved 1,3-rearrangements of the type discussed above.



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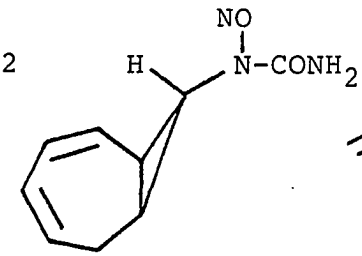
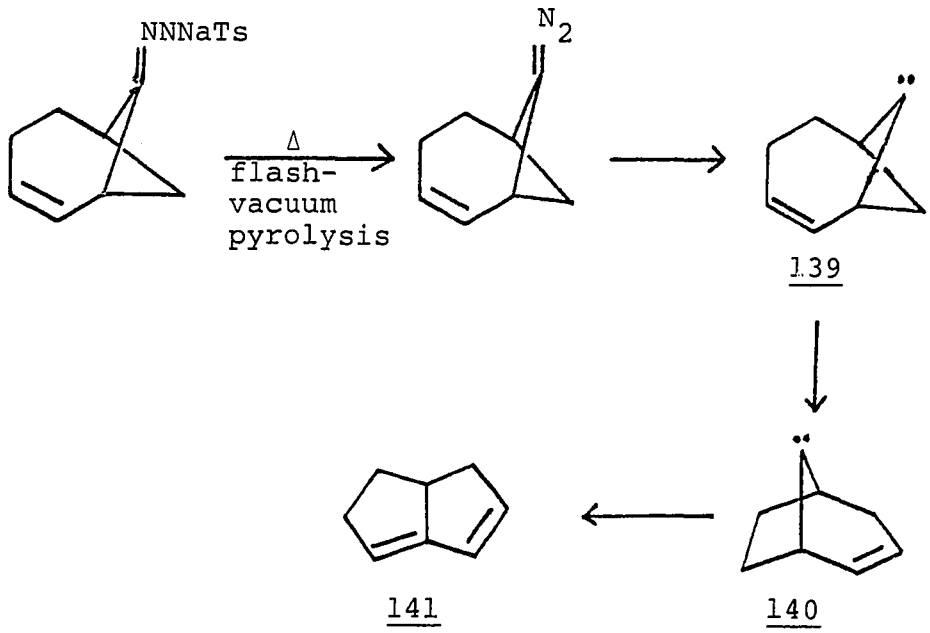


137

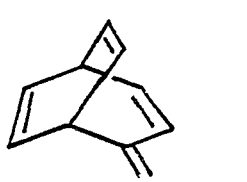
138

Chu[72] has recently obtained some kinetic evidence, through a study of the reaction of cyclopropylidene precursor 136 with methoxide ion, that the diazocyclopropanes just discussed do indeed produce the corresponding cyclopropylidenes, which then undergo the Skattebol 1,3-rearrangement.

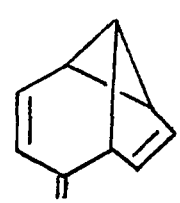
Other examples of type II carbene rearrangements (see the Introduction to Chapter I) can be found in the literature. An important example of a 1,3-rearrangement of a vinyl-substituted carbene is one provided by Brinker and König[73]. The generation of carbene 139 in the gas phase was apparently followed by a 1,3-rearrangement to carbene 140, which then generated diene 141. Since the reaction was



carried out in the gas phase, problems stemming from solvent interactions, such as reversible protonation of diazo compounds, were avoided. Nonetheless, the possibility remains that rearrangement of the diazo compound, or some other non-carbenic intermediate, could have been involved. Freeman and Swenson[74] reportedly generated the free carbenes from the tosylhydrazone salts 142 and 143 in aprotic solvent.



142

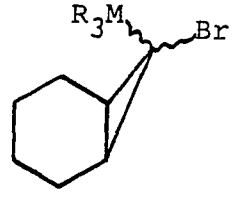


143

They rationalized their products by invoking type II carbene rearrangements which did not involve 1,3-rearrangements.

Returning now to the 1,3-rearrangements of 2-vinylcyclopropylidenes, it was felt that there was a need for a method of generating the required diazo compounds which is less ambiguous than those described above, i.e., the studies of 131, 132, 136, 137, and 138. (At the time the author of this dissertation began these studies, some ambiguities still existed in the diazocyclopropane studies.) However, because the need for an indirect means of diazocyclopropane generation (one not involving a ketone) is unavoidable, the search for such a method would in itself constitute a challenging research project. It was decided instead to take advantage of a different, seemingly more attractive, method of carbene generation, i.e., the pyrolysis of α-haloalkyltin compounds.

Seyferth and Lambert[65] pioneered the study of relatively stable α-haloalkyl derivatives of tin and lead, such as 144, as potential carbene sources. The advantages of these



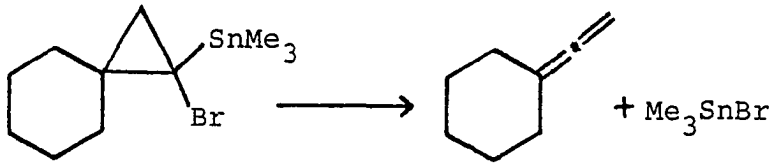
M = Sn, Pb
R = Me, Ph

144

cyclopropylidene precursors over the more well-known α-halocyclopropyllithium intermediates[75] include the facts that stereoisomers of the former can be isolated and studied

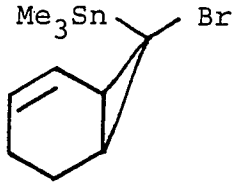
separately, and that they can be easily pyrolyzed in the gas phase, or in solution, under neutral, aprotic conditions.

Seyferth and Lambert[65] found that the tin derivatives of compounds such as 144 are much easier to prepare than the corresponding lead derivatives, and they therefore worked mainly with the former. They found that the pyrolysis of 144 (with M = Sn and R = Me) in an olefinic solvent such as cyclohexene, cyclooctene, or tetramethylethylene, gave, in high yield, a cyclopropanation product from the formal addition of bicyclo [4.1.0] heptan-7-ylidene (96) to the olefin. They also observed a Si-H carbene insertion product when the pyrolysis of 144 (with M = Sn and R = Me) was conducted in the presence of triethylsilane. Furthermore, allenes (generally thought of as typical cyclopropylidene products) were formed as major products in those cases in which they were not severely strained, e.g., compound 145.

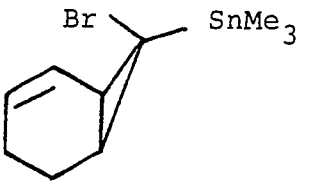


145

A pyrolytic study of 35-anti and 35-syn thus promised to provide a very appealing entry into the 10/11 carbene manifold.



35-anti



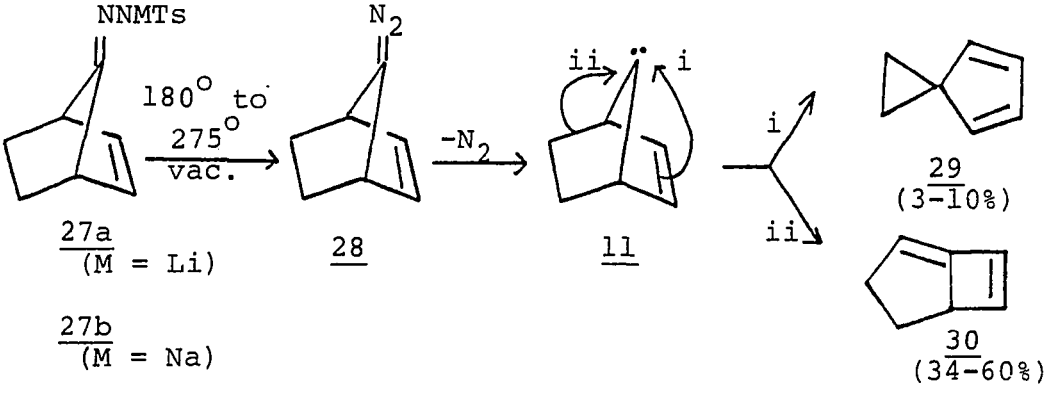
35-syn

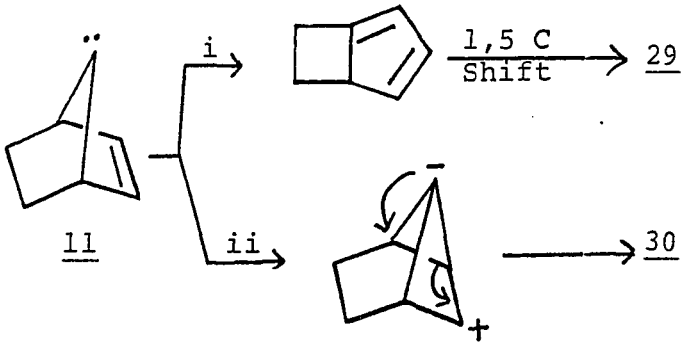
B. Results and Discussion

1. Gas-phase pyrolysis of anti-7-bromo-syn-7-trimethylstannylbicyclo [4.1.0]hept-2-ene (35-anti)

The gas-phase chemistry of carbene 11, already discussed briefly in the Introduction to Chapter I, is depicted in Scheme XXVI. Moss et al.[22,23] and Brinker and Ritzer[21] generated 11 via vacuum pyrolysis of the lithium tosylhydrazone salt 27a. The major products were the dienes 29 and 30. The suggested mechanisms are shown in Scheme XXVI. Product 29 was explained by pathway i, which is the migration of the ethano bridge, to give bicyclo [3.2.0] hepta-1,3-diene. The subsequent 1,5-alkyl shift of the intermediate, resulting in 29, is precedented.[76] Product 30 was rationalized by pathway ii, which results in the net migration of the etheno bridge. Moss et al.[22,23] obtained 30 and 29 in 34% and 3.5% yields, respectively, and Brinker and Ritzer[21] obtained them in 62% and 5% yields, respectively. Murahashi et al.[24] and Brinker and Ritzer[21] pyrolyzed the corresponding sodium tosylhydrazone salt 27b. Murahashi

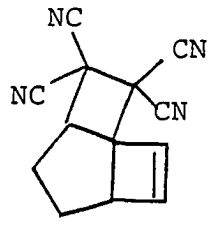
Scheme XXVI:





et al. obtained a 56% yield of 30 and a 9.6% yield of 29. Brinker and Ritzer similarly obtained a 51% yield of 30 and a 5% yield of 29. Treatment of 30 and 29 with tetracyanoethylene (TCNE) gave 146 and 147, respectively,[24] which aided in the structural identification of 30 and 29.

Since 35-anti is easier to obtain than 35-syn (see the Experimental of Chapter I), it was decided to study its gas-phase (vacuum) pyrolysis as a means of investigating the possibility of a 1,3-rearrangement of bicyclo[4.1.0]hept-



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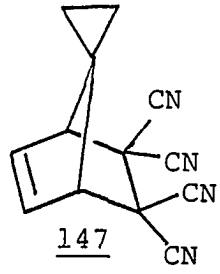
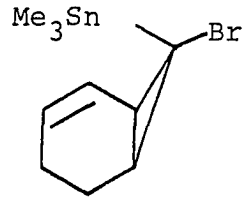


147



35-anti

2-en-7-ylidene (10) to bicyclo[2.2.1]hept-2-en-7-ylidene (11), i.e., the Skattebol rearrangement (see the Introduction to Chapter I). The observation of products 30 and 29, or trapping products from them such as 146 and 147, respectively, would constitute necessary, but not sufficient, evidence for such a carbene rearrangement.

In the first experiment, a solution of TCNE was placed in the cold trap during the vacuum pyrolysis of 35-anti at 205° to 280°, 0.016 Torr. No 146 could be detected, and only a trace amount (a ca. 1 to 3% yield) of 147 was formed, along with much larger amounts of other unidentified olefinic species.

Compound 35-anti was then pyrolyzed under various conditions (Table XXVIII, Experimental) and each crude pyrolysate was analyzed by low temperature (-78° to -50°) NMR, and by GC and/or GC-MS. Variable amounts of 29, toluene, cyclohepta-1,3,5-triene (148), benzene, a $C_{14}H_{16}$ species (149), and four other unidentified products (X_1 through X_4) were generated. NMR data for X_1 through X_4 are given in

the Experimental. Compound 30 could not be detected by NMR in any of the crude pyrolysates. (Note that the data in Table XXVIII are admittedly very unrefined. The reasons for not refining them any further will become apparent very shortly.)

When 29 and cyclohepta-1,3,5-triene (148) were subjected to vacuum pyrolysis at ca. 400° (through glass helices), they were recovered virtually unchanged. It is surprising that cyclohepta-1,3,5-triene was stable to the pyrolysis, since it has been reported[77] that flow pyrolysis of it at 475° results in its almost quantitative rearrangement to toluene. Evidently, the vacuum pyrolysis conditions used here did not cause the direct rearrangement of ground-state (non-vibrationally excited) cyclohepta-1,3,5-triene.

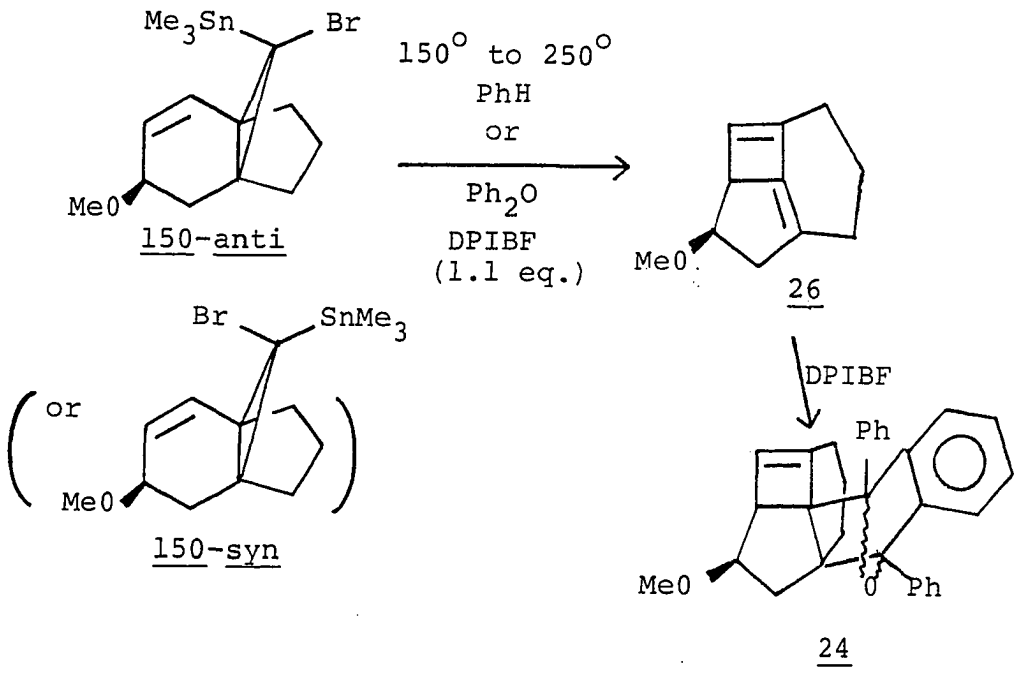
The very sketchy results presented in Table XXVIII were not refined because, during the course of this investigation, Brinker and Ritzer[21] reported some similar vacuum pyrolysis results. They studied 7-bromo-7-trimethylstannylbicyclo-[4.1.0] hept-2-ene of unspecified stereochemistry. Careful comparison of their product data with those for 35-anti and 35-syn (see the Experimental) reveals that their compound was actually 35-anti. By pyrolyzing 35-anti at 265° to 275°, at 5 x 10^{-3} mm, they obtained 30, 29, toluene,

and cyclohepta-1,3,5-triene (148) in 1%, 0.1%, 2.7%, and 3.8% yields, respectively. Using higher pressures during the pyrolysis resulted in smaller yields of toluene.[78a] Brinker and Ritzer[21] made note of the fact that the high temperature required for the decomposition of 35-anti was a major drawback for a study of this type because, when diene 30 (the product of major interest) was subjected to the same pyrolysis conditions, only a trace of it survived.

Because the gas-phase pyrolysis of 35-anti gave such extremely low yields of 29 and 30, attention was next directed toward the solution-phase pyrolyses of 35-anti and 35-syn.

2. Solution-phase pyrolyses of anti-7-bromo-syn-7-trimethylstannylbicyclo [4.1.0] hept-2-ene (35-anti) and syn 7-bromo-anti-7-trimethylstannylbicyclo [4.1.0] hept 2-ene (35-syn)

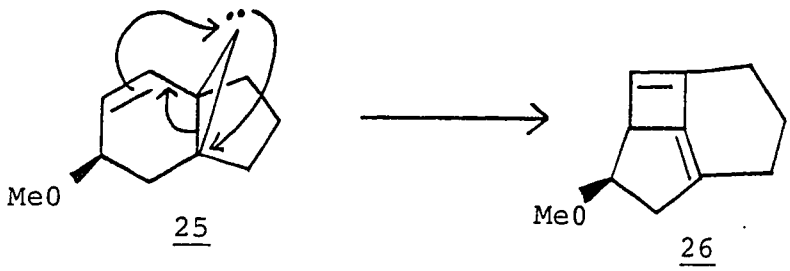
Diene 30 was expected to be the major product of the solution-phase pyrolysis of 35-anti or 35-syn because of the results obtained by Chang[20] with tricyclic derivatives, 150-anti and 150-syn, respectively. The pyrolysis of either 150-anti or 150-syn in a solution containing 1.1 equivalents of DPIBF led to a high yield of product 24, which obviously arose from the Diels-Alder trapping of diene 26 by DPIBF. The formation of diene 26, which is analogous to diene 30



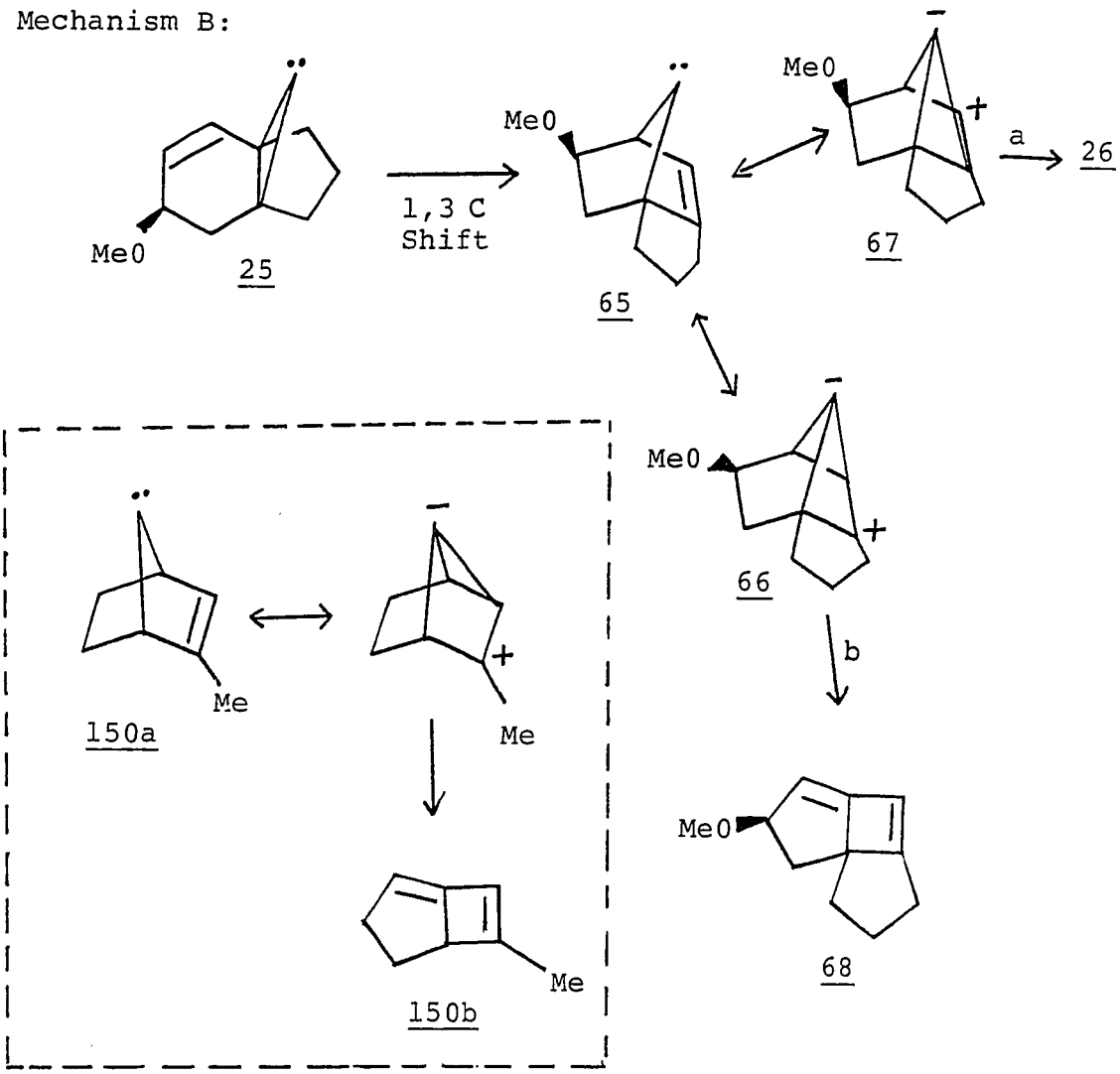
(the major product from bicyclo [4.1.0] hept-2-en-7-ylidene, 11), appears, on the surface, to indicate that the Skattebol rearrangement of carbene 25 to 65 (Mechanism B of Scheme XXVII) has occurred. However, as was already discussed in section 4 of Chapter I (Scheme XV), one is forced to favor Mechanism A, the direct rearrangement of carbene 25 to diene 26, over Mechanism B for the following reasons. Since only diene 26 was formed, and not diene 68, Mechanism B would require that carbene 65 react via pathway a, but not by pathway b. If anything, one would expect resonance form 66 to be more stable than 67. (This expectation is born out by some results[78b] obtained with 2-methylbicyclo[2.2.1] hept-

Scheme XXVII:

Mechanism A:



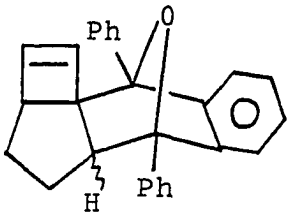
Mechanism B:



2-en-7-ylidene (150a), generated from its diazo precursor. It rearranged preferentially to 6-methylbicyclo [3.2.0] hepta-1,6-diene (150b), as shown in Scheme XXVII.) Furthermore, diene 68 should be less strained than diene 26. It was anticipated that a deuterium labelling study of the pyrolysis reaction of the parent system (35-anti and 35-syn) might provide for a conclusive way of deciding upon Mechanism A or B of Scheme XXVII.

Unfortunately, in practice, neither the solution-phase pyrolysis of 35-anti nor of 35-syn (in the presence of 1.1 equivalents of DPIBF) produced 31 (the trapping adduct from the desired diene 30). To make matters worse, the two epimers of the starting material displayed totally different

30

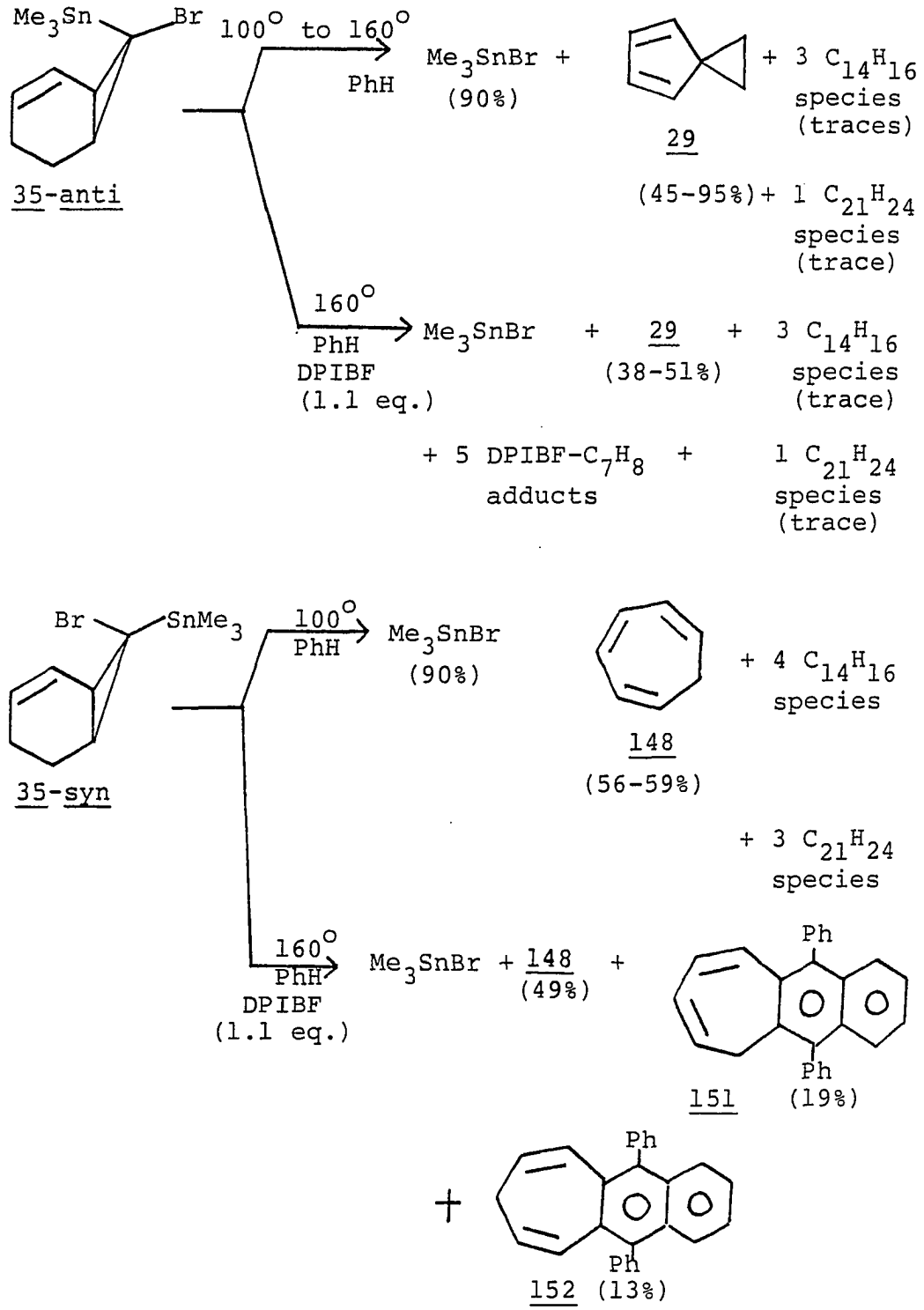


31

chemistry upon solution-phase pyrolysis. As shown in Scheme XXVIII, 35-syn produced mainly cyclohepta-1,3,5-triene (148), plus either DPIBF products 151 and 152 or C_7H_8 oligomers ($C_{14}H_{16}$ and $C_{21}H_{24}$ species) if DPIBF was absent.

The yield of 29 obtained from 35-anti varied greatly (45 to 95%) from one batch of solvent to another, as well

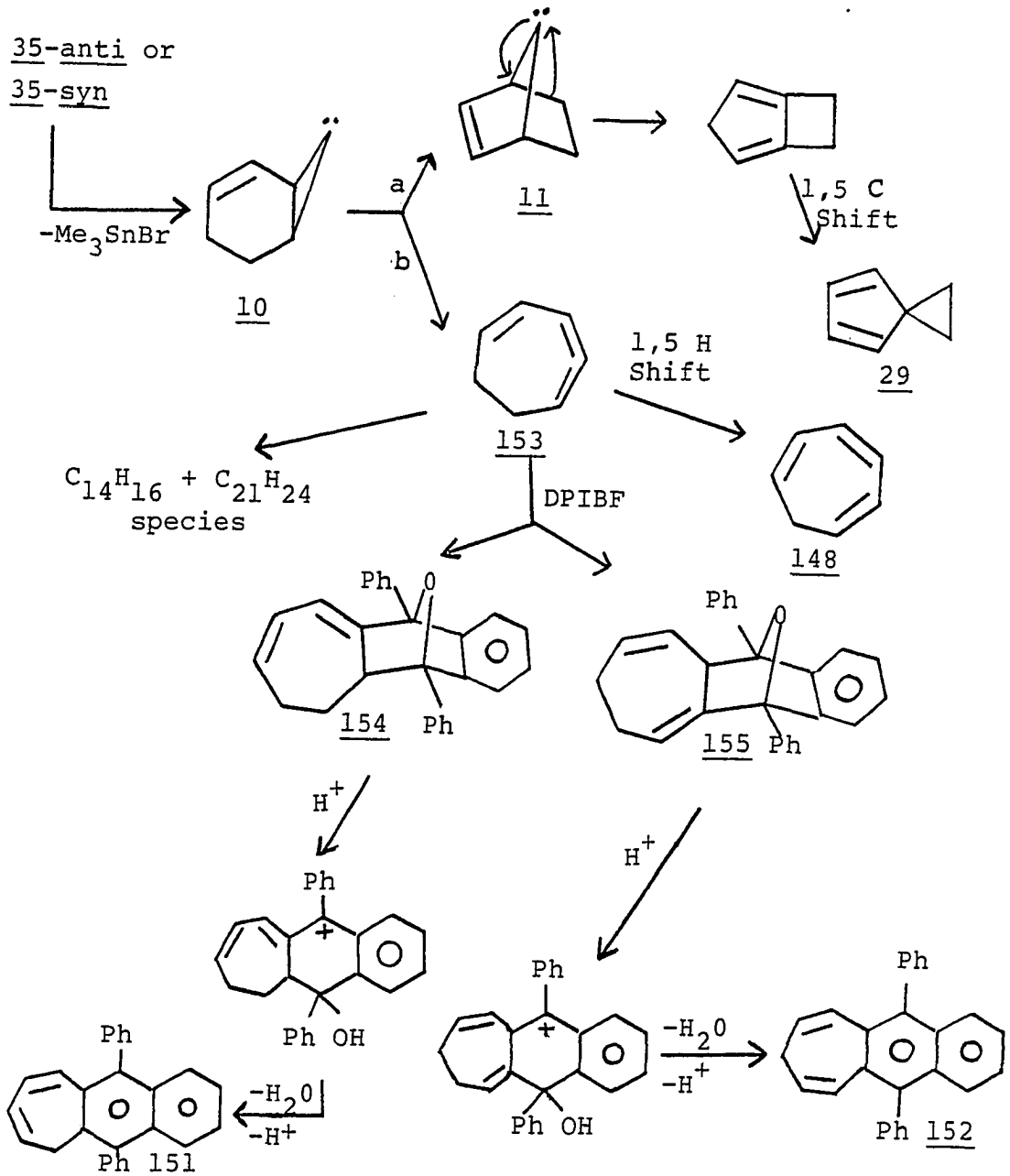
Scheme XXVIII:



as from one batch of 35-anti to another. As will be discussed in more detail later, the reaction rate of 35-anti was also strongly dependent upon these two variables. Since product 29 slowly polymerized during prolonged heating periods, it is easy to understand why the "slower" samples of 35-anti gave lower yields of 29.

Mechanisms which invoke carbene 10 as the key intermediate can in principle explain either diene 29 (from 35-anti) or cyclohepta-1,3,5-triene (148), and DPIBF trapping compounds 151, and 152 (from 35-syn). They are outlined in Scheme XXIX. (Obviously, the same carbene intermediate cannot be responsible for both reaction pathways a and b.) In pathway b, carbene 10 ring-opens to form allene intermediate 153, which can then go on to generate all of the products observed in the pyrolysis of 35-syn. (Note that the absence of the $C_{14}H_{16}$ and $C_{21}H_{24}$ species in the pyrolyses with DPIBF supports the contention that 151, 152, and the $C_{14}H_{16}$ and $C_{21}H_{24}$ species all originate from the same intermediate, i.e., allene 153.) The proposed dehydration of intermediates 154 and 155 is well precedented.[79-83] In this particular reaction, it could be catalyzed either by traces of protonic acid, as shown in Scheme XXIX, or by traces of Lewis acids[79], present as impurities either in the starting material, or in the solvent.

Scheme XXIX:

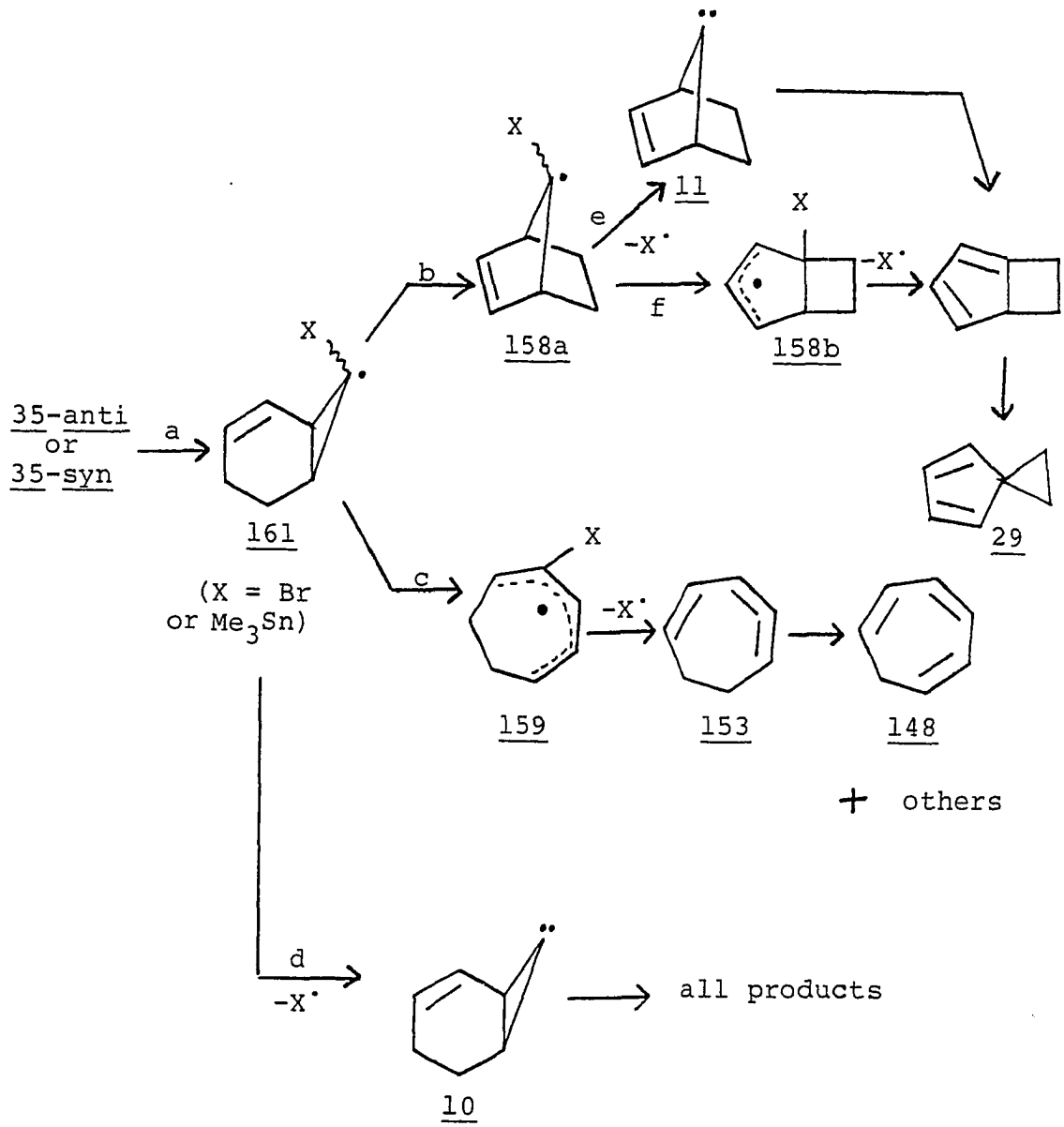


In pathway a of Scheme XXIX, carbene 10 undergoes the Skattebol rearrangement to carbene 11, which could then give rise to diene 29 through migration of its ethano bridge, followed by the precedented[22-24,76] 1,5-sigmatropic rear-

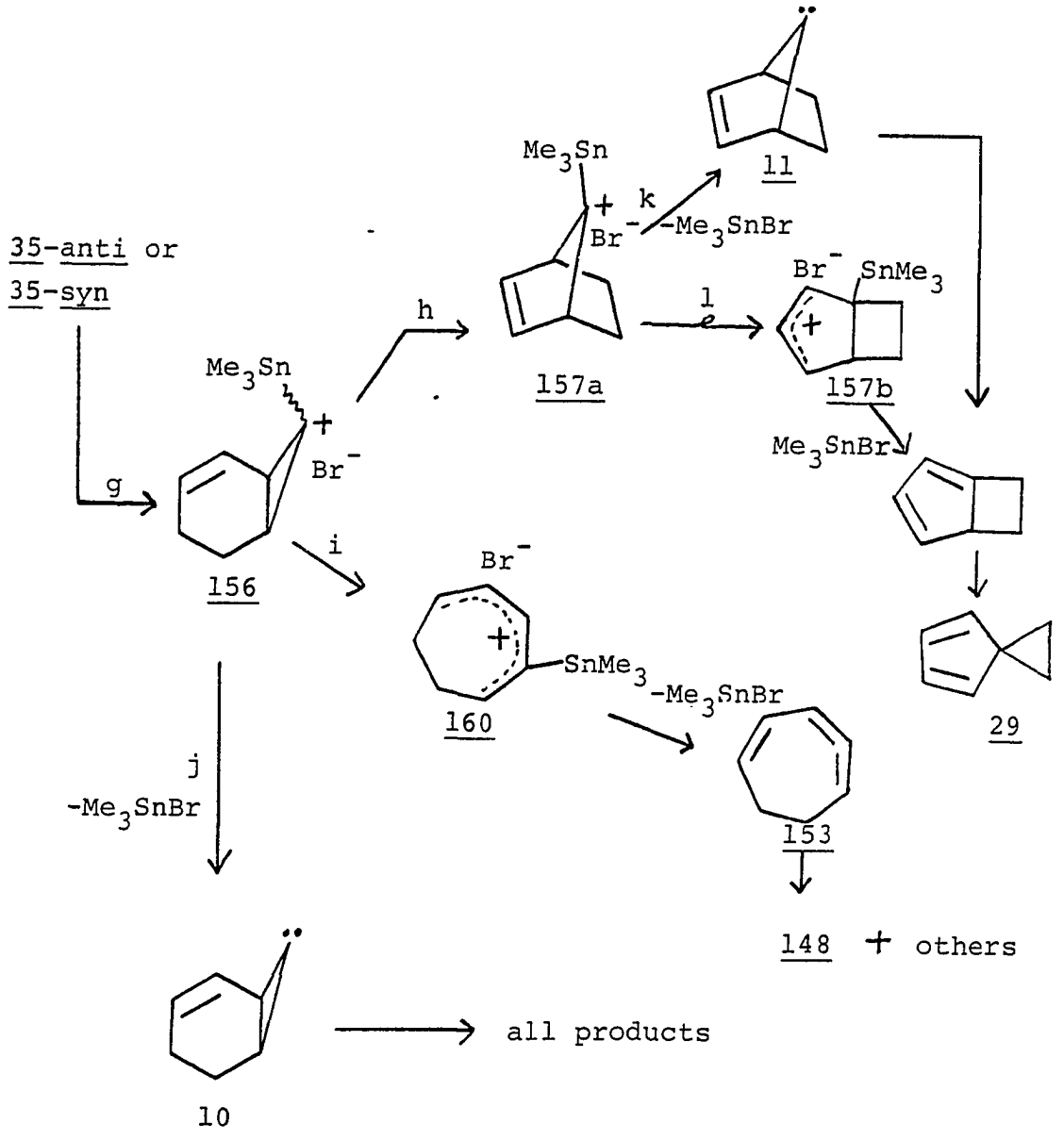
rangement of bicyclo[3.2.0]hepta-1,3-diene to 29, as has already been discussed. However, such a preferred migration of the ethano bridge would be very perplexing because, in the gas phase, migration of the etheno bridge of 11 is preferred.[21-24] Could the benzene solvent, because of its highly polarizable π-cloud, be producing some special solvent effect which causes the ethano bridge migration to be preferred? The answer is no! When 35-anti was pyrolyzed in cyclohexane solution, 29 was still the major product. In order to explain the apparent reversal of product preference upon changing from the gas-phase to solution, one either has to invoke a) a general profound solvent effect on the rearrangement of the carbene (for instance, the gas phase rearrangement of 11 to 30 might involve a vibrationally or electronically excited state of 11), or b) rearrangement of 30 to 29 in solution.

Alternatively, as shown in Scheme XXX, the products could be explained by either radical (path a) or ionic (path g) processes. For simplicity, the stereochemistry of the bromide in ionic intermediates 156 and 157a has been ignored in Scheme XXX. Product 29 (from 35-anti) could be explained in terms of either the rearranged radical intermediates 158a and 158b, or the rearranged ionic intermediates 157a and 157b. The products from 35-syn could be explained in terms of the ring-opened radical intermediate 159, or the ring-opened

Scheme XXX:

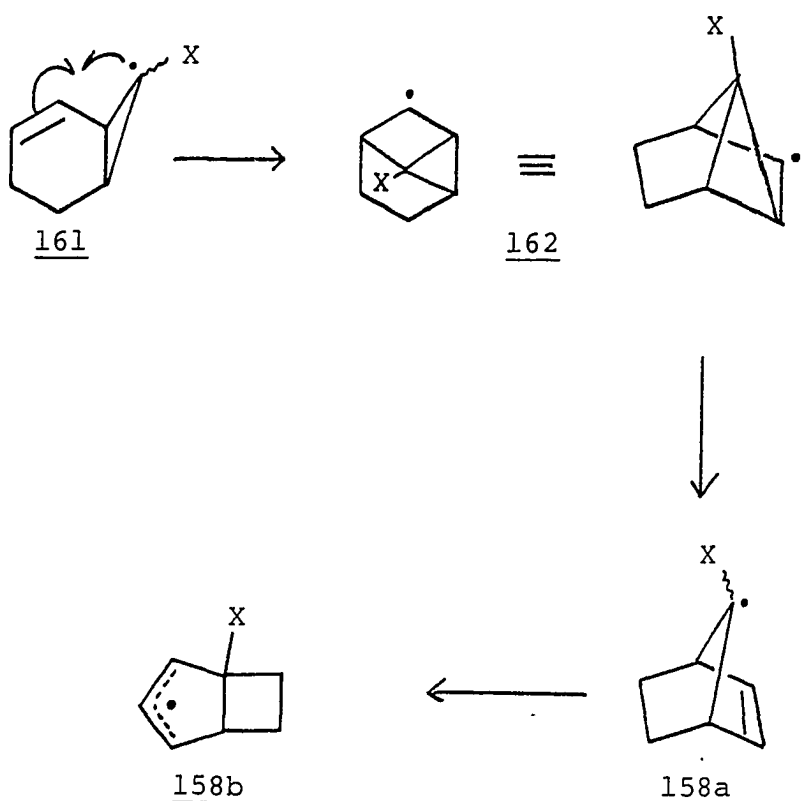

35-anti
or
35-syn
a
X
161
(X = Br
or Me3Sn)
b
158a
e
11
-X·
f
158b
X
-X·
29
c
159
-X·
153
148
+ others
d
-X·
10
all products

Scheme XXX (Continued):



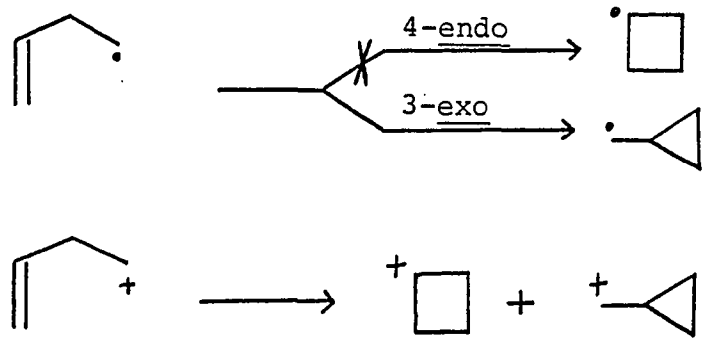
ionic intermediate 160. In principle, radical intermediate 161 and ionic intermediate 156 could generate the carbene 10 (pathways d and j, respectively), or the radical intermediate 158a and the ionic intermediate 157a could generate carbene 11 (pathways e and k, respectively).

The most reasonable way to visualize the rearrangement of radical 161 to 158a is that pictured below, with double bond participation resulting in the generation of cyclobutyl radical 162. Radical 161 can be thought of as a homoallyl radical, and the rearrangement of 161 to 162



161 162 158a 158b

as constituting a 4-endo radical ring-closure reaction. In simpler systems, a 4-endo radical ring closure is disfavored relative to a 3-exo closure,[84] as is illustrated below.



Homoally cations, on the other hand, can undergo ring closure in either sense. Furthermore, it has been found[85] that, in solution, bicyclo[2.2.1]hept-2-en-7-yl apparently does not rearrange to bicyclo[3.2.0]hept-2-en-3-yl (making the rearrangement of 158a to 158b seem unlikely). Thus, on the basis of these very simple considerations, the rearrangements of radical 161 to 158a and 158a to 158b seem unlikely, but the rearrangements of ion pair 156 to 157a and 157a to 157b seem plausible.

The transformation of radical 161 to 159 constitutes the ring opening of a cyclopropyl radical, a process which does not occur readily.[84] The ring opening of cyclopropyl cations, on the other hand, is a well-precedented, disrotatory process.

Thus, if radical reactions are involved, one would expect them to be only in the form of pathway a/d of Scheme XXX. More detailed analyses of the various cation rearrangements and of the cation ring-opening reaction (Scheme XXX) are necessarily more complex than the corresponding radical reactions, because of the greater importance of the stereochemistry of the bromide in the former. Such analyses will be discussed as they apply to the specific results presented later in this chapter.

In order to test for ionic processes, pyrolyses of 35-anti and 35-syn were conducted in solvents of various polarities. The results are summarized in Table XV. The fact that the pyrolysis reactions are first order in starting material will be discussed in more detail later. For 35-syn, there was a definite rate increase with increasing solvent polarity (going from triethylsilane to acetonitrile), which is suggestive of an ionic mechanism (path g/i of Scheme XXX). For 35-anti, however, there was no clear trend. Furthermore, the complex product mixture obtained from 35-anti in acetonitrile solvent (probably resulting from reactions between

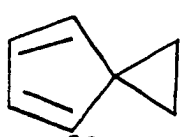


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Table XV. Pyrolyses of 35-anti and 35-syn in solvents of varying polarity

Expt.	SM	Amt. of SM (mg)	Solv.	Temp.
1[c]	35-syn	19.7	Et_3SiH	100°
2[e,f]	35-syn	33.8	C_6D_6	100°
3[e,f]	35-syn	27.7	Ph_2O	100°
4[e,f]	35-syn	20.4	CD_3CN	100°
5[c]	35-anti	25.2	Et_3SiH	160°
6[e,h]	35-anti	21.3	C_6D_6	160°
7[e,h]	35-anti	17.4	Ph_2O	160°
8[e,h]	35-anti	26.8	CD_3CN	160°

[a]Least squares anal. of a plot of ln [SM] (monitored by NMR meas. of Me_3SnBr and starting material) vs. time.

[b]Yield measured by NMR integration vs. an internal std. (For structures, see previous page.)

[c]Sample dissolved in 0.3 ml of solvent, flushed with N_2, and sealed under N_2 in an NMR tube.

[d]This reaction was finished by heating at 130°.

[e]Sample dissolved in 0.3 ml of solv.; degassed by 3 freeze-high vac.-thaw cycles; sealed under N_2 (NMR tube).

[f]These experiments used the same batch of 35-syn.

[g]The product obtained in Et_3SiH is discussed later.

[h]These experiments used the same batch of 35-anti.

[i]Cyclohexa-1,3-diene, plus 6 unidentified products were observed by GC and GC-MS analysis.

k^{a} (sec_5^{-1}) x10^5	No. of data points	Uncer-tainty[a] X10^5	r^{a} (Correl. factor)	%Yield[b] 148	%Yield[b] 29
<1.1	2	--	--	40[d]	0
11.3	3	±0.2	0.9998	56	0
24	4	±2	0.9759	58	0
190	2	--	--	84	0
>20	2	--	--	0	0[g]
62.9	3	±0.2	0.9999	0	69
28	4	±3	0.9919	0	28
61	3	±5	0.9907	0	0[i]

acetonitrile and reactive intermediates from 35-anti) points toward a more complex mechanism for 35-anti than for 35-syn.

Because of an observation that the reaction rate of 35-anti was strongly dependent upon the particular batch of benzene solvent used, there was some reason to suspect a radical chain mechanism. (Different batches of solvent could contain variable amounts of radical chain inhibitors.) The results obtained with 35-anti and 35-syn in different batches of benzene with and without benzoyl peroxide initiator are presented in Table XVI.

The thermal decomposition of 35-anti was strongly accelerated by the presence of 0.1 equivalent of benzoyl peroxide, while the decomposition rate of 35-syn was virtually unaffected. Also, the reaction rate of 35-anti was strongly dependent upon the particular batch of benzene solvent employed, which might suggest a sensitivity to trace amounts of radical chain inhibiting impurities.

To further test for the possibility of a radical chain mechanism in the reaction of 35-anti, attempts were next made to independently generate radical 161 (Scheme XXX), with X = bromine and with X = trimethyltin. The pyrolysis of 7 (Scheme XXXI) in the presence of tri-n-butyltin hydride should generate radical 161 (with X = bromine). Scheme XXXI

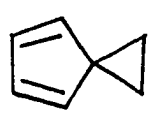
Table XVI. Pyrolyses of 35-anti and 35-syn in benzene solution with and without benzoyl peroxide

Expt.	SM	Amt. of SM (mg)	Solv.	Additive	Temp.
1[c]	35-syn	33.8	C_6D_6[d]	None	100°
2[c,e]	35-syn	16.0	C_6H_6[f]	None	100°
3[c,e]	35-syn	19.4	C_6H_6[f]	$(PhCO)_2O$, 0.1 eq.	100°
4[c,g]	35-anti	21.3	C_6D_6[d]	None	160°
5[c,g]	35-anti	21.6	C_6H_6[f]	None	160°
6[c,g]	35-anti	14.3	C_6H_6[f]	$(PhCO)_2O$, 0.1 eq.	160°

[a]Least squares anal. of a plot of ln [SM] (monitored by NMR meas. of Me_3SnBr and starting material) vs. time.

[b]Yield measured by NMR integration vs. an internal std.

Structures:



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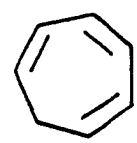

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[c]Sample dissolved in 0.3 ml of solv.; degassed by 3 freeze-high vac.-thaw cycles; sealed under N_2 (NMR tube).

[d]Same batch of benzene-d_6 for these expts.

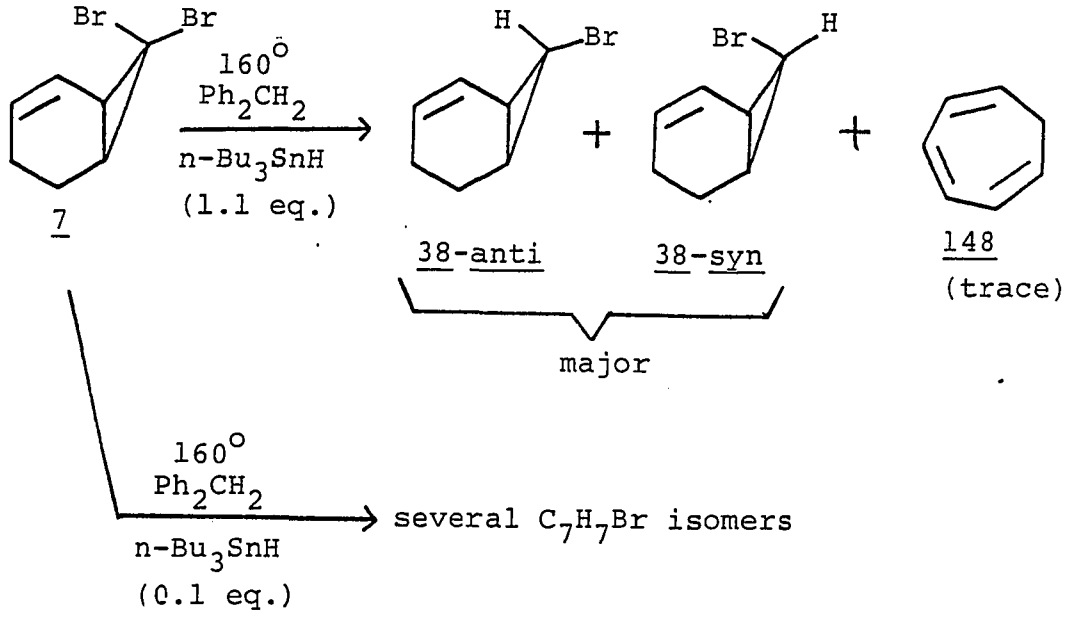
[e]Same batch of 35-syn for these expts.

[f]Same batch of benzene for these expts.

[g]Same batch of 35-anti for these expts.

k^a (sec_5^{-1}) x10^5	No. of data points	Uncer-tainty[a] x10^5	r^a (Correl. factor)	%Yield[b] 148	%Yield[b] 29
11.3	3	±0.2	0.9998	56	0
8.9	5	±0.6	0.9852	50	0
9.4	5	±0.3	0.9954	43	0
62.9	3	±0.2	0.9999	0	69
8.0	6	±0.2	0.9989	0	45
143	3	±6	0.9979	0	74

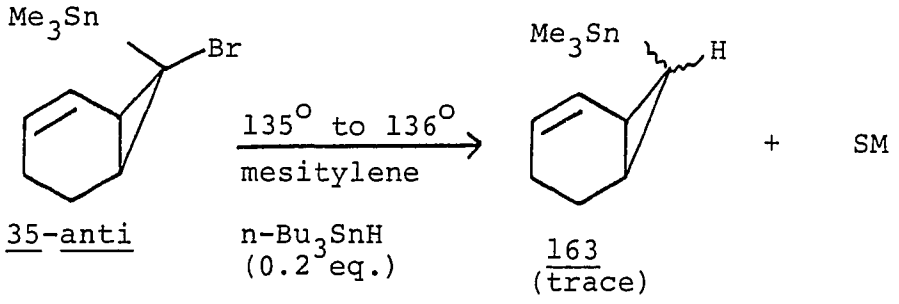
Scheme XXXI:



shows the results of pyrolyses conducted in the presence of 1.1 and 0.1 equivalents of tri-n-butyltin hydride. None of the spirodiene 29 was obtained in either case, and the experiment with 0.1 equivalent gave a product mixture virtually identical to one run with no tri-n-butyltin hydride.

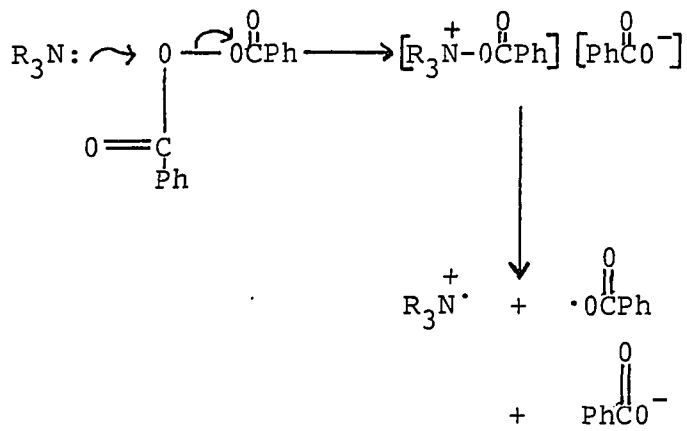
The pyrolysis of 35-anti in the presence of 0.2 equivalent of tri-n-butyltin hydride, which would be expected to generate radical 161 (with X = trimethyltin), at 135° (a temperature which is lower than that normally used for the pyrolysis of 35-anti alone) resulted in virtually no reaction. Mostly starting material, plus a trace of re-

duction product 163 were recovered. Thus, tri-n-butyltin hydride was ineffective as a radical chain initiator.



Furthermore, heating 35-anti in benzene solution containing 0.2 to 0.7 equivalent of azo-bis-isobutyronitrile (AIBN) also resulted in no rate enhancement.

Because only benzoyl peroxide had been an effective accelerator for 35-anti, it was suspected that a radical chain mechanism might not really be involved at all. In fact, in some later experiments (Table XVII), benzoyl peroxide caused no acceleration. The earlier observed rate enhancement by benzoyl peroxide had involved "slower" samples of 35-anti, and was probably due to the destruction of traces of Lewis base inhibitors by benzoyl peroxide. (As will be seen later, the decomposition of 35-anti was strongly inhibited by amines, and presumably by other Lewis bases as well.) Trialkylamines are well known to react with benzoyl peroxide in the manner shown below.[86,87] Trimethylamine undergoes the reaction at temperatures as low as -5°![87]



Furthermore, the presence of radical chain inhibitors (4-methyl-2,6-di-tert-butylphenol and 2,6-di-tert-butylbenzoquinone) in the pyrolysis of 35-anti caused no rate reduction (Table XVII). One can therefore confidently rule out a radical chain mechanism for 35-anti.

Next, 35-anti was pyrolyzed in the presence of methanol in order to see whether any of the ionic intermediates of pathway g/h/k or g/h/l of Scheme XXX could be trapped. (There was the further possibility that carbene intermediates, particularly singlet carbenes, would insert into the O-H bond of methanol.[88]) Three products (38-anti, 164, and 165) other than 29 were obtained (Scheme XXXII). As is shown in Scheme XXXII, product 38-anti most likely arose from cleavage of the trimethyltin group of 35-anti by hydrogen bromide, and 165 could result from a similar acid cleavage reaction of 164.[89] Results obtained with different concentrations of methanol are presented in Table XVIII.

Table XVII. Pyrolysis of 35-anti in benzene solution[a] with and without benzoyl peroxide and radical chain inhibitors

Expt.	Amt. of SM (mg)	Temp.	Total time heated (min).
1[c](X-40)[d]	5.0	100.5-101.5°	30
2[c](X-42)[d]	3.4	100.5-101.5°	30
3[c](X-43)[d]	4.2	100.5-101.5°	30
4[c](X-46)[d]	4.2	100.5-101.5°	30
5[c](X-47)[d]	3.8	100.5-101.5°	30
6[c](X-48)[d]	4.7	100.5-101.5°	30
7[c](X-51)[d]	3.2	100.5-101.5°	30
8[g](X-26-1)[d]	6.9	160-164°	30
9[g](X-23-1)[d]	6.2	160-164°	30
10[g](X-23-2)[d]	6.4	160-164°	30
11[c](X-34)[d]	7.2	160-164°	30
12[c](X-35)[d]	7.3	160-164°	30
13[c](X-38)[d]	4.5	160-164°	30

[a]Base-washed glassware. Benzene dist. from sodium benzophenone ketyl; stored over sodium. Each sample dissolved in 0.3 ml solvent, sealed under N_2. One batch SM.

[b]Yield measured by NMR integration vs. internal std.

[c]Same purified batch of benzene for these expts.

[d]Notebook number, followed by page number.

[e]Small amts. of 2 unident. trimethyltin compds (NMR).

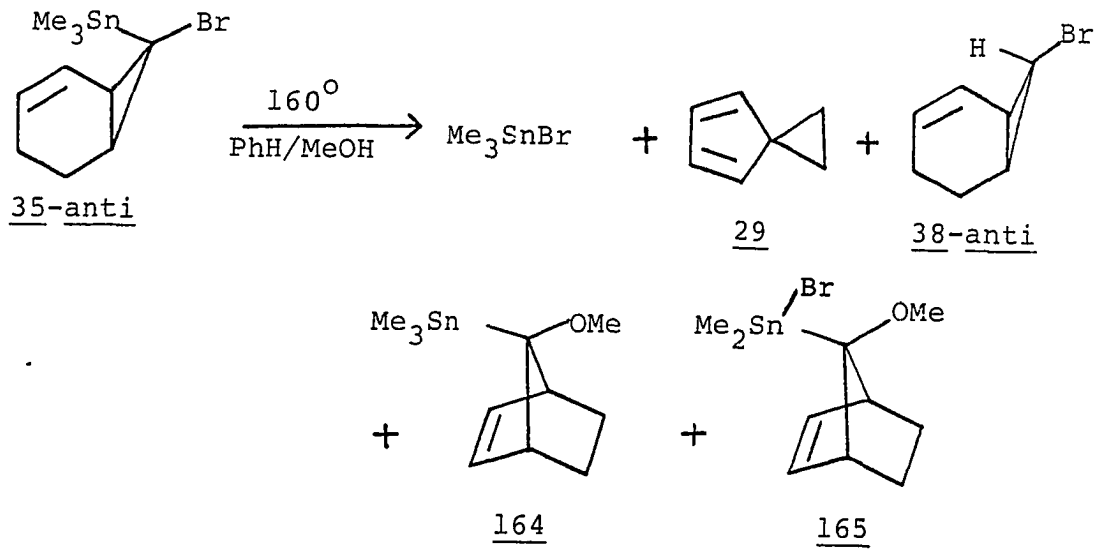
[f]2,6-di-tert-butylbenzoquinone.

[g]Same purified batch of benzene for these expts.

[h]4-Methyl-2,6-di-tert-butylphenol.

Additive	%Recov.[b] SM	%Yield[b] Me_3SnBr	%Yield[b] 29
None	70	17	15
None	63	19	17
$(PhCO)_2O$; 1.2 eq.	53	10	6[e]
$(PhCO)_2O$; 0.2 eq.	65	6	4[e]
None	61	21	18
Inhibitor[f]; 0.2 eq.	61	19	19
None	69	16	14
None	31	64	57
None	28	66	62
$(PhCO)_2O$; 1.0 eq.	31	51	39
None	23	73	67
None	16	79	73
Inhibitor[h]; 1.6 eq.	8.6	69	65

Scheme XXXII:



35-anti 29 38-anti 164 165

35-anti $\xrightarrow{MeOH}$ 164 + HBr

35-anti $\xrightarrow{HBr}$ 38-anti + Me_3SnBr

164 $\xrightarrow{HBr}$ 165 + CH_4

One might be tempted to argue that product 164 resulted from insertion of bicyclo[2.2.1]hept-2-en-7-ylidene (11) into the Sn-O bond of trimethyltin methoxide (generated from a reaction between methanol and trimethyltin bromide). Such an argument is untenable, however, because trimethyltin methoxide is known[90] to be thermally unstable. A reasonable explanation for the formation of product 164,

Table XVIII. Pyrolysis of 35-anti at 160° in the presence of methanol (run to completion)

Expt.	No. mg SM	Vol. ratio MeOH: C_6H_6	%Yield[a] Me_3SnBr	%Yield[a] 29	%Yield[a] 164	%Yield 165	%Yield[b] 38-anti
1	30	4:96[c]	86	61	9	0[a]	?
2	29	29:71[c]	73	41	23	0[a,b]	0
3	31	100:0[d]	24	0	28	44[a]	20

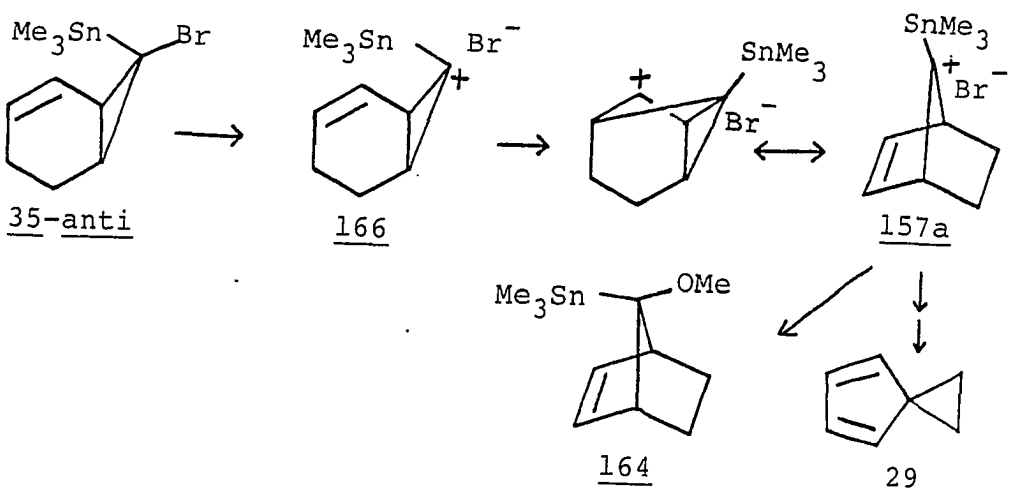
[a]Yield measured by NMR integration vs. internal std. (For structures, see Scheme XXXII.)

[b]Yield measured by GC integration vs. internal std., with correction factors. (For structures, see Scheme XXXII.)

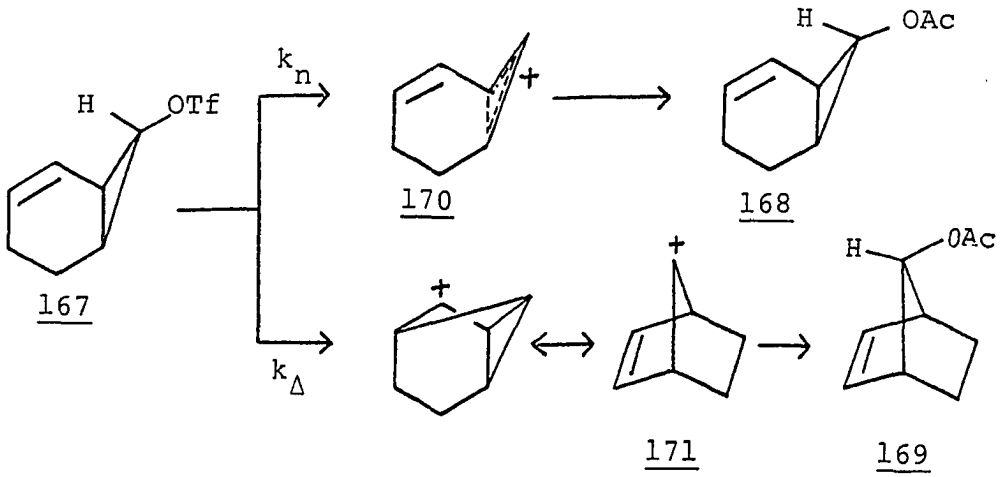
[c]Sample dissolved in 0.3 ml of the solv.; degassed (3 freeze-high vac.-thaw cycles); sealed under N_2 (NMR tubes).

[d]Sample dissolved in 0.3 ml of the solvent; flushed with N_2; sealed under N_2 (NMR tube).

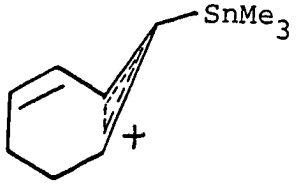
as shown below, is a rearrangement of an initially formed ion pair (166)[91] to 157a, followed by trapping of 157a by methanol.



(Carbene 10, bicyclo [4.1.0] hept-2-en-7-ylidene, is thus by-passed in this reaction.) The exclusive formation of a bicyclo [2.2.1] hept-2-en-7-ylium cationic intermediate (157a) is somewhat surprising when one considers the acetic acid solvolysis of triflate 167, shown below, in which



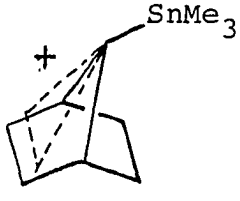
acetates 168 and 169 were obtained in a 2.3 to 1 ratio (90% combined yield).[92] Product 168 was proposed to arise from the k_n process, a σ-assisted ionization (involving partially ring-opened ion 170), while product 169 was rationalized by the k_Δ process, in which anchimeric assistance by the double bond produces ion 171. Why does 35-anti produce exclusively the norbornenyl-type cation 157a? One explanation is that, for the ionization of 35-anti to cyclopropyl cation 166, the incipient cationic center is sufficiently stabilized by the tin group (perhaps via hyperconjugation), that participation by the cyclopropyl ring (as in partially ring-opened



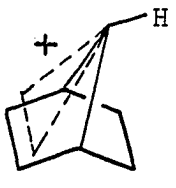
172

cation 172) is not required. Because the partially ring-opened cation is not involved, the double bond is able to participate more readily, resulting in rearrangement to the norbornenyl cation 157a. An alternative explanation is that the steric relief attained because of the decreasing steric interaction between the trimethyltin group and the cyclohexyl ring during the ionization of 35-anti negates the need for participation by the cyclopropyl ring, also allowing the double bond to participate more readily.

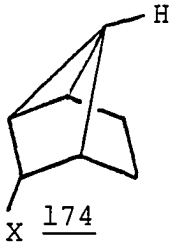
The stereoselective formation of the cation trapping products 164 and 169 is a result of the resonance hybrids 173 and 135, respectively.[93] In each case, the approach of



173



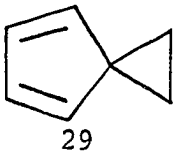
135



174

a nucleophile anti to the double bond is strongly favored. Since products such as 174 are sometimes observed in solvolysis reactions involving bicyclo [2.2.1] hept-2-en-7-ylium ions (such as 171), one might wonder why the reaction of 157 with methanol, and of 171 with acetic acid, did not result in any products of the 174-type. The answer is that a strong necleophile (such as methoxide or hydride ion) can cause product 174 to form, but a weak nucleophile cannot.[66,67,93-95]

If the rate determining step in the reaction of 35-anti is its ionization, then Lewis acid catalysts which are capable of coordinating with the bromine should cause accelerations. This was indeed found to be true. As is shown in Table XIX, tin tetrachloride and aluminum trichloride are both effective catalysts. Their presence resulted in increases both in the rate of disappearance of 35-anti, and in the yield of spirodiene 29. It was observed that, during the overnight freezer storage of a crude solution of 29 plus tin tetrachloride, the 29 disappeared, presumably via polymerization. Tin tetrachloride and alumi-



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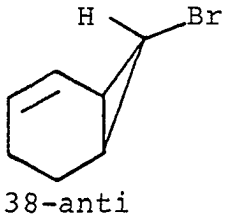


38-anti

Table XIX. Effect of Lewis acids on the pyrolysis of 35-anti in benzene solution[a] at 100.5° to 101.5°

Expt.	Amt. of SM (mg)	Soln. vol. (ml)	Additive	Total time heated (min.)
1(X-40)[c]	5.0	0.3	None	30
1(X-40)[c]	5.0	0.3	None	385
2(X-42)[c]	3.4	0.3	None	30
3(X-47)[c]	3.8	0.3	None	30
4(X-49)[c]	4.2	0.3	$SnCl_4$[d], 0.27 eq.	30
5(X-51)[c]	3.2	0.3	None	30
6(X-52)[c]	4.8	0.3	$SnCl_4$[d], 0.12 eq.	10
7(X-51)[c]	3.2	0.3	None	10
8(X-53)[c]	3.4	0.3	$AlCl_3$[d], trace	10

[a,b]See footnotes a and b, respectively, under Table XVII. (For structures of 29 and 38-anti, see previous pg.)

[c]Notebook number, followed by page number.

[d]Anhydrous.

[e]Yield measured by GC integration vs. an internal std., with correction factors.

[f]Many tetrahalo-/tetraalkyltin disproportionation products[96] were observed by NMR.

[g]Trimethyltin bromide appeared to be initially formed cleanly in 60% yield, according to NMR anal. within the sealed tube. After the tube was opened to air, the "trimethyltin bromide" NMR peak became very broad. GC-MS analysis showed the presence of trimethyltin bromide and chloride in a 1:2 ratio, respectively.

%Recov. SM	%Yield[b] Me_3SnBr	%Yield[b] 29	%Yield 38-anti
70[b]	17	15	0[b]
12[b]	75	67	0[b]
63[b]	19	17	0[b]
61[b]	21	18	0[b]
1[e]	?[f]	43	0[e]
69[b]	16	14	0[b]
20[e]	?[f]	20	0[e]
81[b]	4.3	3.9	0[b]
3[e]	60[g]	10	9[e]

num trichloride probably caused polymerization of spirodiene 29 during the pyrolysis as well. (The polymerization of dienes by Lewis acid catalysts is known to occur.[97]) Had this polymerization not occurred, the yield of 29 in the presence of Lewis acids would undoubtedly have been even higher, and the accelerating effect of the Lewis acids would have been even more dramatically demonstrated. The 38-anti observed in experiment 8 must have been the result of cleavage of the Sn-C bond of 35-anti by hydrogen chloride (generated by hydroysis of some of the aluminum trichloride by adventitous moisture).[89]

Note that the average total trimethyltin group recovery in Table XIX was only 84% for those experiments which involved no additives (experiments 1 through 3, 5, and 7); but, the fact that this recovery was usually the same, regardless of at which point of the reaction the measurements were made (20% or 85% completion) suggests a systematic error. (For most of the larger scale experiments in Table XVII, i.e., experiments 8, 9, 11, and 12, the average total trimethyltin group recovery was ca. 95%.)

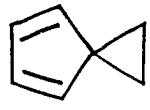
Since Lewis acids accelerated the decomposition of 35-anti, it was wondered whether protonic acids could do the same. As can be seen from the data in Table XX, protonic acids merely cleaved off the trimethyltin group, re-

Table XX. Effect of protonic acids on[a] the pyrolysis of 35-anti in benzene solution[a] at 100.5° to 101.5°

Expt.	Amt. of SM (mg)	Additive	Total time heated (min.)
1(X-42)[d]	3.4	None	30
2(X-44)[d]	3.7	TsOH[e]; 1.1 eq.	30
3(X-45)[d]	4.5	$PhCO_2H$; 1.0 eq.	30

[a,b]See footnotes a and b, respectively, under Table XVII.

Structures:



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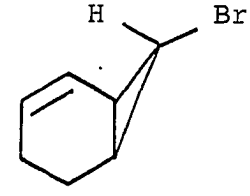


38-anti

[c]Yield measured by GC integration vs. an internal standard, with correction factors.

[d]Notebook number, followed by page number.

[e]p-Toluenesulfonic acid.

[f]Broad peaks were in this region of the NMR spectrum, probably due to several different trimethyltin compounds.

%Recov.[b] SM	%Yield[b] Me_3SnBr	%Yield[b] 29	%Yield[c] 38-anti
63	19	17	0
9.5	?[f]	9.0	44
29	?[f]	17	20

sulting in anti-7-bromobicyclo[4.1.0]hept-2-ene (38-anti). Such stereospecific acid cleavage of trialkyltin groups is well precedented.[89]

Since Lewis acids were observed to accelerate the reaction of 35-anti, it was of concern that the reaction might be autocatalytic, due to the formation of one equivalent of trimethyltin bromide, a potential Lewis acid. For this reason, the kinetics of the reaction were investigated. The rate plot shown in Figure 19 illustrates

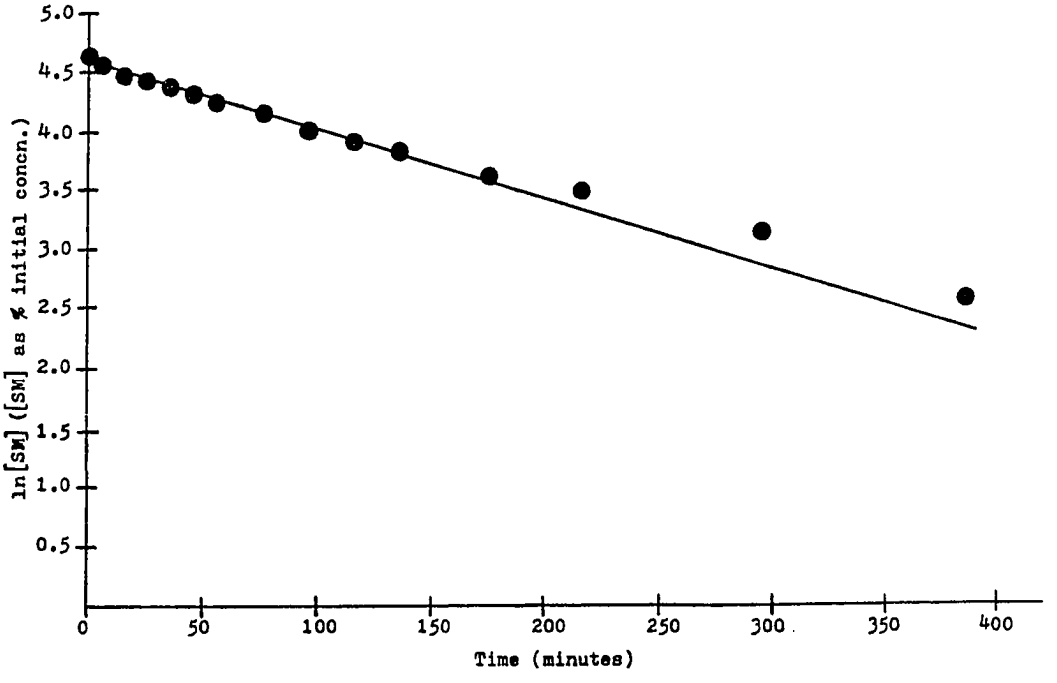


Figure 19. First order rate plot of the thermal decomposition of 35-anti in benzene solution at 100.5° to 101.5°

the clean first order nature of the thermal decomposition of 35-anti. Least squares analysis (See the Experimental, entry 1) showed the rate constant to be $k = 9.0 \pm 0.2 \times 10^{-5}$ sec^{-1}. Autocatalysis can thus be ruled out.

Since rate measurements at two different temperatures (100° and 160°) were available, it was possible to estimate the activation parameters. Values of k obtained at the two different temperatures are listed in Table XXI. (In spite of

Table XXI. Values of k for the thermal decomposition of 35-anti in benzene solution at two temperatures (using the same batch of 35-anti)

Temp.[a]	Av. k (sec^{-1}) x 10^5
$100.2\text{-}101.8^{\circ}$	$12 \pm 25\%$[b]
$160\text{-}164^{\circ}$	$260 \pm 12\%$[c]

[a]Thermometers were calibrated with ice water and boiling water, and found to be correct at both temperatures to within 0.2° to 0.3°. They were then assumed to be linear throughout the 0° to 164° range.

[b]Based on four rate measurements (least squares analyses of ln[SM] vs. time).

[c]Based on two rate measurements.

the fact that the total trimethyltin group recovery measured in the 100° reactions averaged only ca. 84%, because of an apparent systematic error, as discussed earlier, the assumption of a 100% yield of trimethyltin bromide seemed the most

reasonable to use for the rate constant calculations. Changing from an assumption of a 100% yield to an 84% yield was found to cause a negligible difference in the calculate rate constant.) From the values in Table XXI, $\Delta G^{\ddagger}$ was estimated as 31.0 $\pm$ 0.2 kcal-mol^{-1}, $\Delta H^{\ddagger}$ as 16 $\pm$ 3 kcal-mol^{-1}, and $\Delta S^{\ddagger}$ as -35 $\pm$ 6 eu. This large negative entropy of activation could be explained by a reorganization of the solvent surrounding the polar transition state leading to the ion pair. However, there is also a second equally viable explanation, which involves the proposal that, since the reaction of 35-anti can be accelerated by Lewis acid impurities, the observed rate constant (k_{obs}) might actually be the sum of two terms, i.e., k_i (ionization) and $k_{cat.}$ (catalysis). (Some data will be presented shortly that supports this proposal.) The two rate constants k_i and $k_{cat.}$ could very well have different temperature dependencies. If this were the case, then the above calculation of $\Delta S^{\ddagger}$, which assumed a linear relationship between $\ln(k_{obs})$ and $1/T$, would not be valid. Thus, the calculated negative entropy of activation might simply have resulted from such a non-linear relationship. Obviously, much more extensive data, taken over at least four different temperatures, would be required in order to resolve this question.

At this point, it was hypothesized that Lewis bases, such as amines, might inhibit the reaction by deactivating

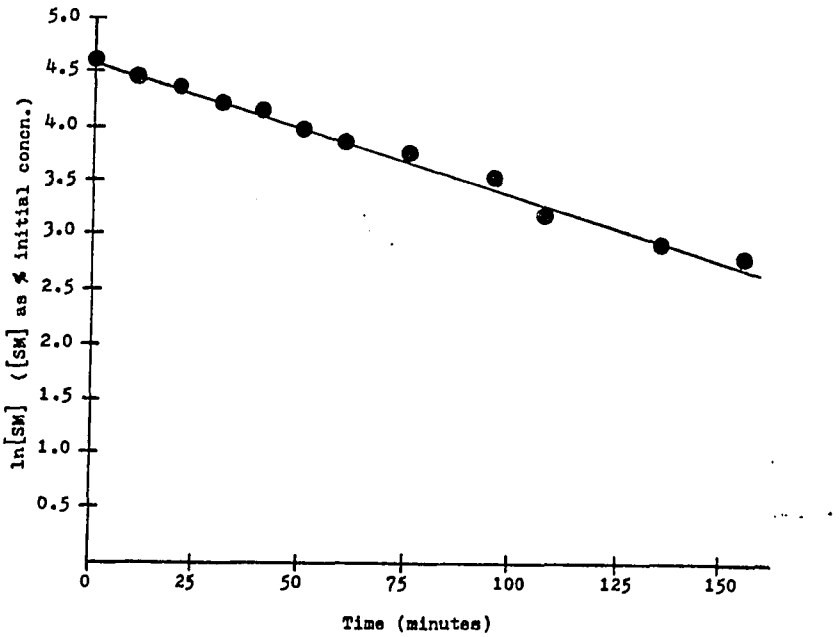


Figure 20. First order rate plot of the thermolysis of 35-anti in benzene containing 0.09 equivalent of Et_3N (160°-164°)

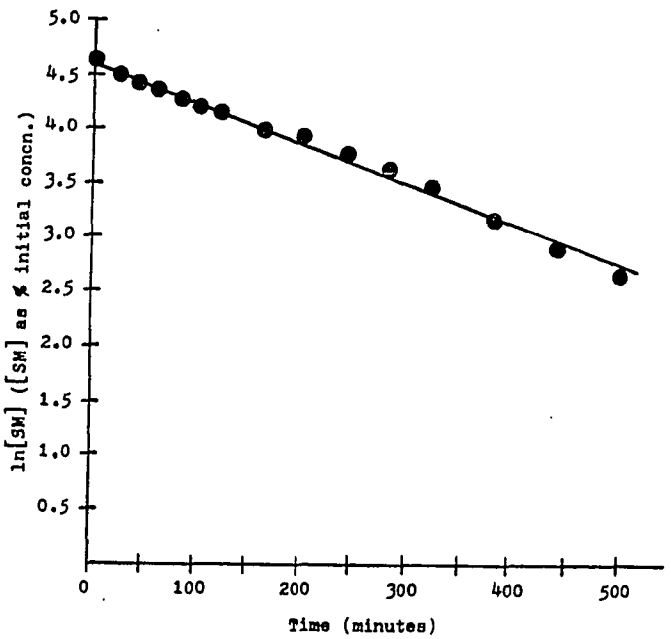


Figure 21. First order rate plot of the thermolysis of 35-anti in benzene containing 0.52 equivalent of Et_3N (160°-164°)

any Lewis acid impurities. In practice, triethylamine did indeed give very strong inhibition, as can be seen in Table XXII.

The first order rate plots of experiments 7 and 5 of Table XXII are given in Figures 20 and 21, respectively, and show that the thermolysis reaction of 35-anti is cleanly first order even if it is run in the presence of triethylamine. For the purpose of calculating rate constants, the assumption of a 100% yield of trimethyltin bromide (rather than the measured average value of 82%) seemed the most reasonable to use, for reasons which have already been discussed in connection with Table XXI. Least squares analysis (see the Experimental, entry 1) showed the rate constants for Figures 20 and 21 to be $20.2 \pm 2 \times 10^{-5}$ sec^{-1} and $6.33 \pm 0.08 \times 10^{-5}$ sec^{-1}, respectively.

There appear to be three reasonable explanations for the observed triethylamine inhibition of the reaction of 35-anti (Table XXII): a) deactivation of a Lewis acid catalyst by triethylamine, b) coordination of triethylamine with the tin group of 35-anti (resulting in structure 175, shown below, which would prevent facilitation of the C-Br heterolysis by interaction between the bromine and the tin group, and c) coordination of triethylamine with the tin group during the ionziation of 35-anti, (which results in complex

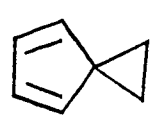
Table XXII. Effect of triethylamine concentration on the reaction rate of 35-anti in benzene solution[a] at 160° to 164°

Expt.	mmol of SM	mmol of Et_3N	Soln. vol. (ml)
1(X-23-1)[c]	0.0185	0	0.30
2(X-26-1)[c]	0.0206	0	0.30
3(X-26-2)[c]	0.0209	0.0215	0.30
3(X-26-2)[c]	0.0209	0.0215	0.30
4(X-62)[c]	0.0170	0.0140	0.27
5(X-60)[c]	0.0179	0.0093	0.32
5(X-60)[c]	0.0179	0.0093	0.32
6(X-57)[c]	0.0122	0.0029	0.29
7(X-59)[c]	0.0176	0.0016	0.27
7(X-59)[c]	0.0176	0.0016	0.27

[a]Base-washed glassware. Benzene distilled from sodium benzophenone ketyl, stored over sodium. Each sample flushed with N_2; and sealed under N_2 (NMR tube). Same SM batch, and same batch of benzene for all experiments.

[b]Yield measured by NMR integration vs. internal std.

Structure of 29:

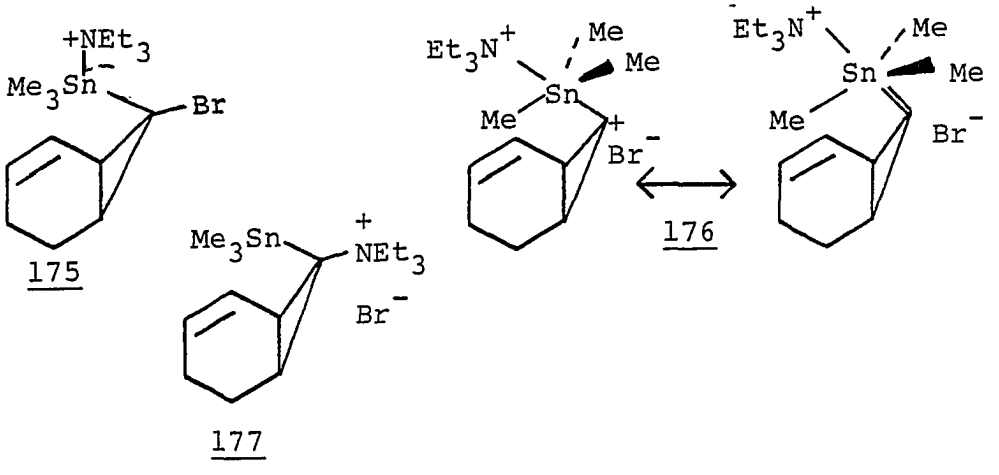


29

[c]Notebook number, followed by page number.

Total time heated (min.)	%Recov.[b] SM	%Yield[b] Me_3SnBr	%Yield[b] 29
10	28	66	62
10	31	64	57
10	79.4	0.6	ca. 0
150	74	5.9	trace
10	77	7.1	6.2
10	75	4.7	4.0
500	11	69	57
10	66	16	15
10	70	11	10
155	13	68	61

176), before rearrangement. The resulting stabilization of the cationic center by a combination of inductive, resonance, and hyperconjugative effects might preclude interaction with the double bond, so that the rearrangement no longer occurs readily. Re-attack of the bromide ion on the positively charged carbon might then result in a return of intermediate 176 to starting material. (Structure 177 is a very unlikely explanation for the inhibition because there was no detectable isomerization of 35-anti to 35-syn in the presence of triethylamine, and the stereospecific return of 177 to starting material would be difficult to explain. Furthermore, as will be seen in Chapter IV, the saturated analog of 35-anti, which also displays inhibition by triethylamine, gave no isolable product with diethylamine, despite strong inhibition by diethylamine. A mechanism involving an intermediate analogous to 177 would predict an isolable product from diethylamine.) The proposed formation of complexes between

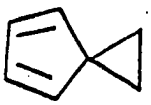


triethylamine and a tin group is precedented.[98] In addition, the formulation of complex 176 is reasonable, since trigonal bipyramidal tin intermediates (with an electronegative group and an electron-donating group in the apical positions) are known.[99] Because the incipient cationic center which evolves during the ionization of 35-anti is very electronegative, it is reasonable to propose that the tin atom of an ionized form of 35-anti (166) would have an open coordination site (probably filled initially by benzene) for a good nucleophile like an amine molecule. Furthermore, since tin possesses filled low-lying d-orbitals, it is not inconceivable that there is some stabilization via a resonance interaction between tin and the cationic center, as shown in structure 176; also, hyperconjugative stabilization of the positive charge may occur. The kinetic analyses in Scheme XXXIII show that the inhibition mechanisms involving complexes 175 (Model A) and 176 (Model B) are kinetically indistinguishable.

However, intermediate 175 should be spectroscopically differentiable from 35-anti. Since one equivalent of triethylamine (experiment 3, Table XXII) virtually shut off the reaction, if the true inhibition mechanism really involves 175, then mixing 35-anti with at least one equivalent of triethylamine should result in a quantitative yield of

Scheme XXXIII:

Model A:



$$SM\cdot Et_3N \;(\underline{175}) \underset{}{\overset{K_t^{*}}{\rightleftharpoons}} SM\ (\underline{35}\text{-}\underline{anti}) \xrightarrow{k_1} Me_3SnBr + \underline{29}$$

$$[SM]_{total} = [SM] + [SM\cdot Et_3N]$$

$$K_t = \frac{[SM\cdot Et_3N]}{[SM]\cdot[Et_3N]}^{**}$$

$$[SM] = \left(\frac{1}{1 + K_t[Et_3N]}\right)[SM]_{total}$$

$$-\frac{d[SM]}{dt} = k_i[SM] = \left(\frac{k_i}{1 + K_t[Et_3N]}\right)[SM]_{total}$$

$$= k_{obs}[SM]_{total}$$

$$\therefore k_{obs} = \frac{k_i}{1 + K_t[Et_3N]}$$

---

*Acid-base equilibria of this type are established rapidly.[100]

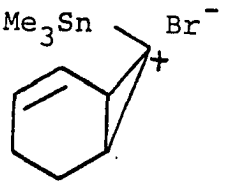
** $[Et_3N]$ is assumed to be constant throughout the reaction.

Scheme XXXIII (Continued):

Model B:

$$\underset{(\underline{35}\text{-anti})}{SM} \xrightarrow{k_i} I \longrightarrow Me_3SnBr + \underline{29}$$

$$I \xrightarrow{k_t[Et_3N]} I\cdot Et_3N \quad (\underline{176})$$

I = 

$\underline{166}$

assume $\frac{d[I]}{dt} = 0$ (steady state approx.)

$$\frac{d[I]}{dt} = k_i[SM] - (k_2 + k_t[Et_3N])[I] = 0$$

$$I = \frac{k_i[SM]}{k_2 + k_t[Et_3N]}$$

$$\frac{-d[SM]}{dt} = \frac{k_i k_2}{k_2 + k_t[Et_3N]}[SM] = k_{obs}[SM]$$

$$\therefore k_{obs} = \frac{k_i k_2}{k_2 + k_t[Et_3N]} = \frac{k_i}{1 + (k_t/k_2)[Et_3N]}$$

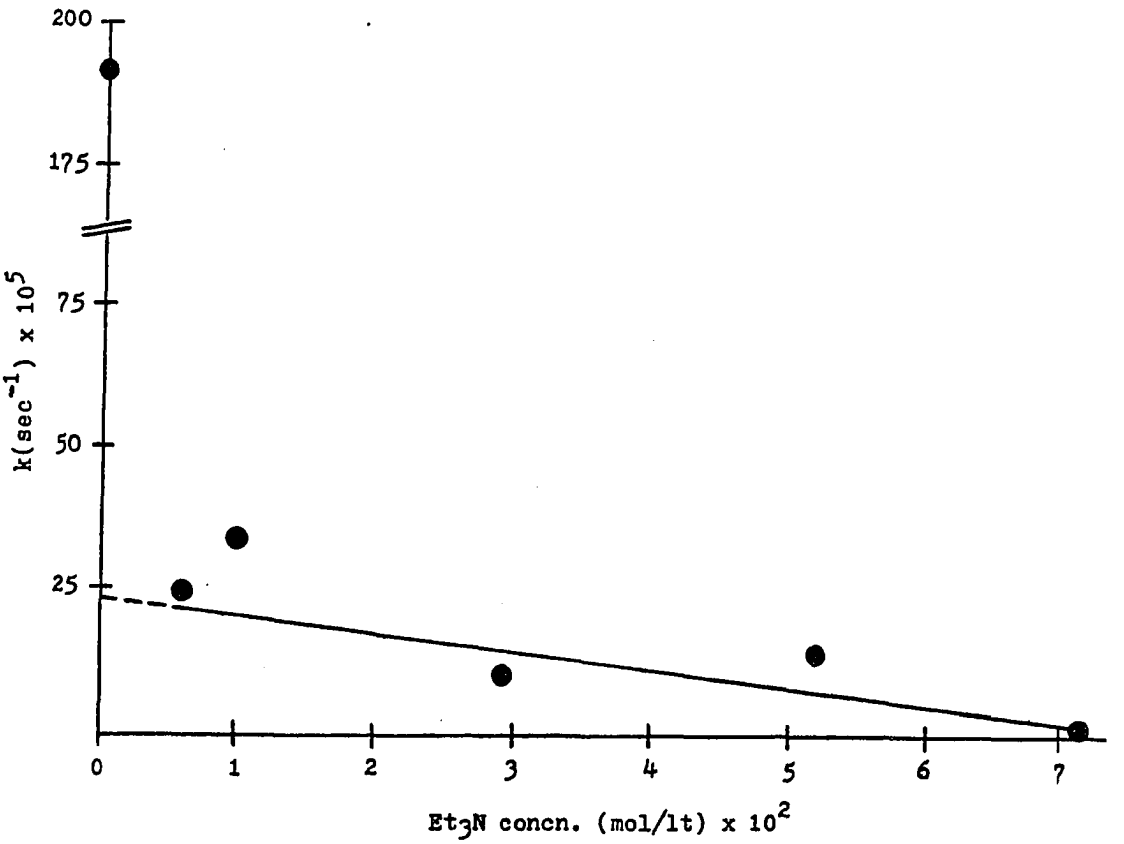


Figure 22. Plot of the rate constants of the thermal decomposition of 35-anti in benzene solutions containing variable concentrations of triethylamine, at 160° to 164° (All experiments used the same batch of 35-anti and of solvent.)

complex 175. There was, however, no detectable change in the NMR spectrum of 35-anti or of triethylamine either when 2 equivalents of triethylamine were added to a benzene solution of 35-anti at room temperature, or when the NMR spectrum of the resulting mixture was monitored between room temperature and 120°. (The variable temperature ^{1}H NMR spectrum was studied by placing a sealed NMR tube of the benzene solution of 35-anti plus 2 equivalents of triethylamine in the probe of a Varian EM-360L 60 MHz NMR spectrometer. The benzene solvent peak was used for the lock signal. Pyrolysis of this same 35-anti/triethylamine sample at either 100.5° to 101.5° for 30 minutes, or at 160° to 164° for 10 minutes, resulted in no reaction, whereas a similar pyrolysis of 35-anti in the absence of triethylamine for 10 minutes at 160° to 164° gave a 67% conversion of 35-anti to trimethyltin bromide plus spirodiene 29, and a pyrolysis for 30 minutes at 100.5° to 101.5° gave a 20% conversion.)

One can ascertain whether a portion of the inhibition is due to deactivation of a Lewis acid catalyst impurity by plotting the rates of the reactions shown in Table XXII vs. triethylamine concentration. Such a plot is presented in Figure 22. Since the intercept of the plot at zero triethylamine ($k_i = 24 \pm 6 \times 10^{-5}$ sec^{-1}, from a least squares analysis, as described in the Experimental, entry 1), is much

lower than the actual observed rate in the absence of triethylamine (k_{obs} = 190 ± 15 x 10^{-5} sec^{-1}, calculated from experiments 1 and 2 of Table XXII, one must conclude that the initial rapid decrease in rate at very low triethylamine concentration is due to the deactivation of a Lewis acid catalyst impurity. The later, much more gradual decrease in rate with increasing triethylamine concentration is likely due to the generation of triethylamine complex 176, followed by its return to starting material.

In order to obtain an estimate of the activation parameters, the pyrolysis of 35-anti in the presence of triethylamine was also conducted at 130°. The rate data at 130° and 160° are listed in Table XXIII.

The value of $\Delta G^{\ddagger}$ was estimated as 33.7 ± 0.6 kcal-mol^{-1}, that of $\Delta H^{\ddagger}$ as 42 ± 10 kcal mol^{-1}, and that of $\Delta S^{\ddagger}$ as 19 ± 23 eu. The non-zero entropy of activation could simply be the result of a non-linear relationship between $\ln(k_{obs})$ and 1/T, as was discussed earlier for the $\Delta S^{\ddagger}$ calculation in the absence of triethylamine. (In the present case, the expression for k_{obs} is of the form $k_i/(1 + K_t[Et_3N])$. Since k_i and K_t could easily display different temperature dependencies, the relationship between $\ln(k_{obs})$ and 1/T might not be linear.) Again, much more extensive data would be required to obtain understandable results.

Table XXIII. Values of k for the thermal decomposition of 35-anti in benzene solution containing 0.6 equivalent of triethylamine, at two temperatures (using the same batch of 35-anti, and of solvent)

Temp.[a]	Av. $k(sec^{-1}) \times 10^5$
130-132°	0.36 ± 25%[b]
160-164°	14 ± 25%[c]

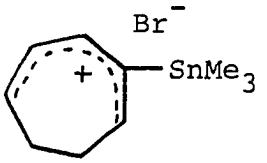
[a]Thermometer was calibrated as described in footnote a, under Table XXI.

[b]Based on one rate measurement. The 25% error limit was assumed from the error limit of the 160° reactions. Et_3N concn. = 0.031 M; 35-anti concn. = 0.051 M.

[c]Based on the plot in Figure 22 (least squares anal.) Et_3N concn. = 0.031 M; 35-anti concn. = ca. 0.05 M (see Table XXII).

Good evidence has been obtained for an ionic mechanism for the pyrolysis of 35-anti, but what about 35-syn? The solvent polarity study of 35-syn, vide supra, had strongly suggested an ionic mechanism (pathway g/i of Scheme XXX). Woodward-Hoffman rules predict that, for 35-syn, a concerted ionic ring opening is favored, because a cis-double bond is formed. (For 35-anti, such a concerted ionic ring opening would form a strained trans double bond.) In order to further verify that the ionic mechanism was really operative,

35-syn was next pyrolyzed in the presence of methanol, in an attempt to trap the ionic intermediate 160.

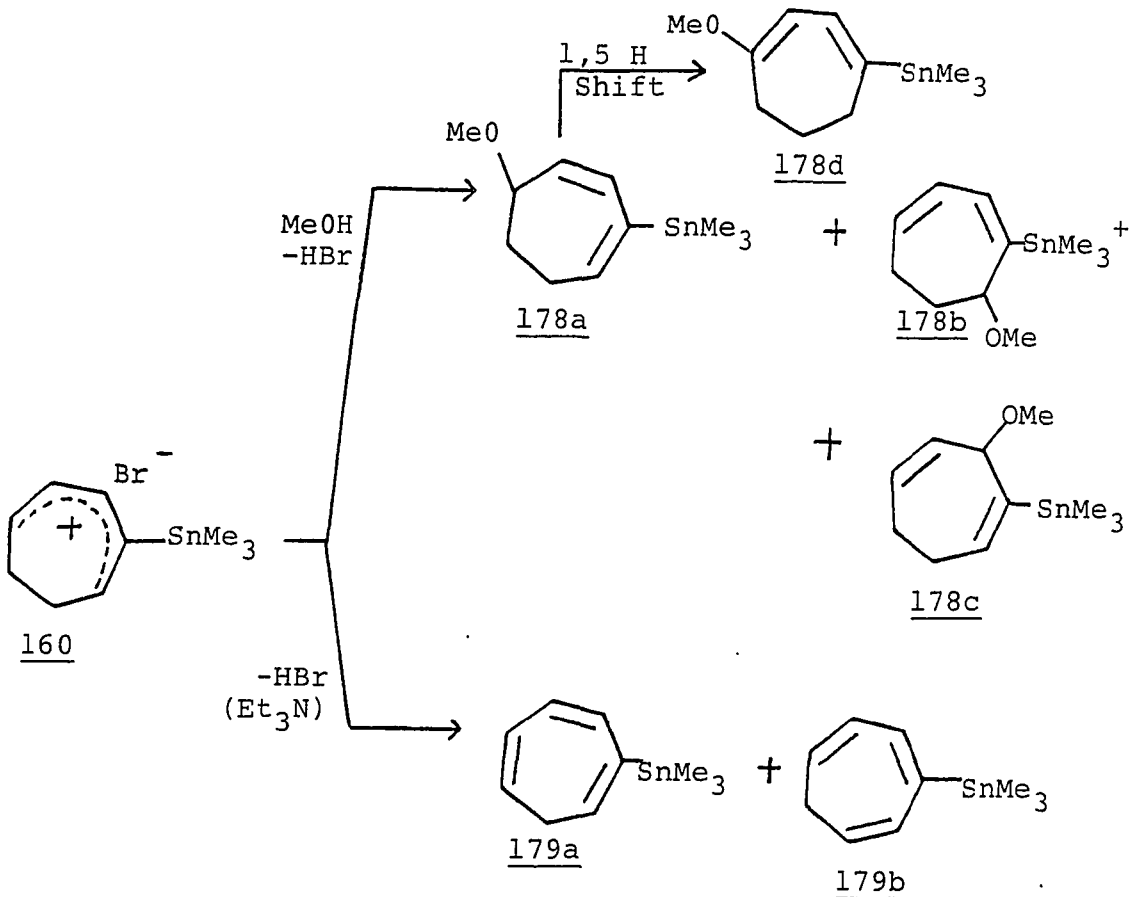


160

When 35-syn was pyrolyzed at 100° to 102° in 71% methanol/29% benzene-d_6 (measured by volume), containing 1.0 equivalent of triethylamine as a buffer (see the Experimental), 6 tin-containing products were obtained (in ca. 3% yield each) and were tentatively identified (by GC-MS and by mechanistic considerations) as the cation trapping products 178a through 178d, 179a, and 179b (Scheme XXXIV). Possible mechanisms for their formation are offered in Scheme XXXIV. There was no evidence for products from insertion of bicyclo[4.1.0]-hept-2-en-7-ylidene (10) into methanol. Importantly, there was a substantially larger rate constant for this 71% methanol/29% benzene-d_6 reaction ($k = 117 \pm 2 \times 10^{-5}$ sec^{-1}, according to a least squares analysis, as described in the Experimental, entry 1) than for a benzene-d_6 reaction ($k = 9.33 \pm 0.08 \times 10^{-5}$ sec^{-1}) run at the same temperature with the same batch of 35-syn, and of benzene-d_6. This rate increase is expected for the increased solvent polarity.

It is interesting to note that only a trace of cyclohepta-1,3,5-triene was obtained in the above methanolic ben-

Scheme XXXIV:



zene reaction, whereas cyclohepta-1,3,5-triene is the major product (in ca. 57% yield, as shown in Scheme XXVIII) in the benzene reaction. When a sample of cyclohepta-1,3,5-triene was heated under the same reaction conditions (100° to 102°, in 65% methanol/35% benzene-d_6), it was found to be stable. The difference between the normal yield of cycloheptatriene (57%), and the combined yield of cation trapping products 178a through 178d, and deprotonation products 179a and 179b

(ca. 18%), is apparently made up by an increased amount of oligomerization of allene 153. (GC analysis revealed that the yield of one of the dimers was ca. 4 times larger in the methanolic benzene reaction than in a benzene reaction, run at the same temperature and with the same concentration of 35-syn.)

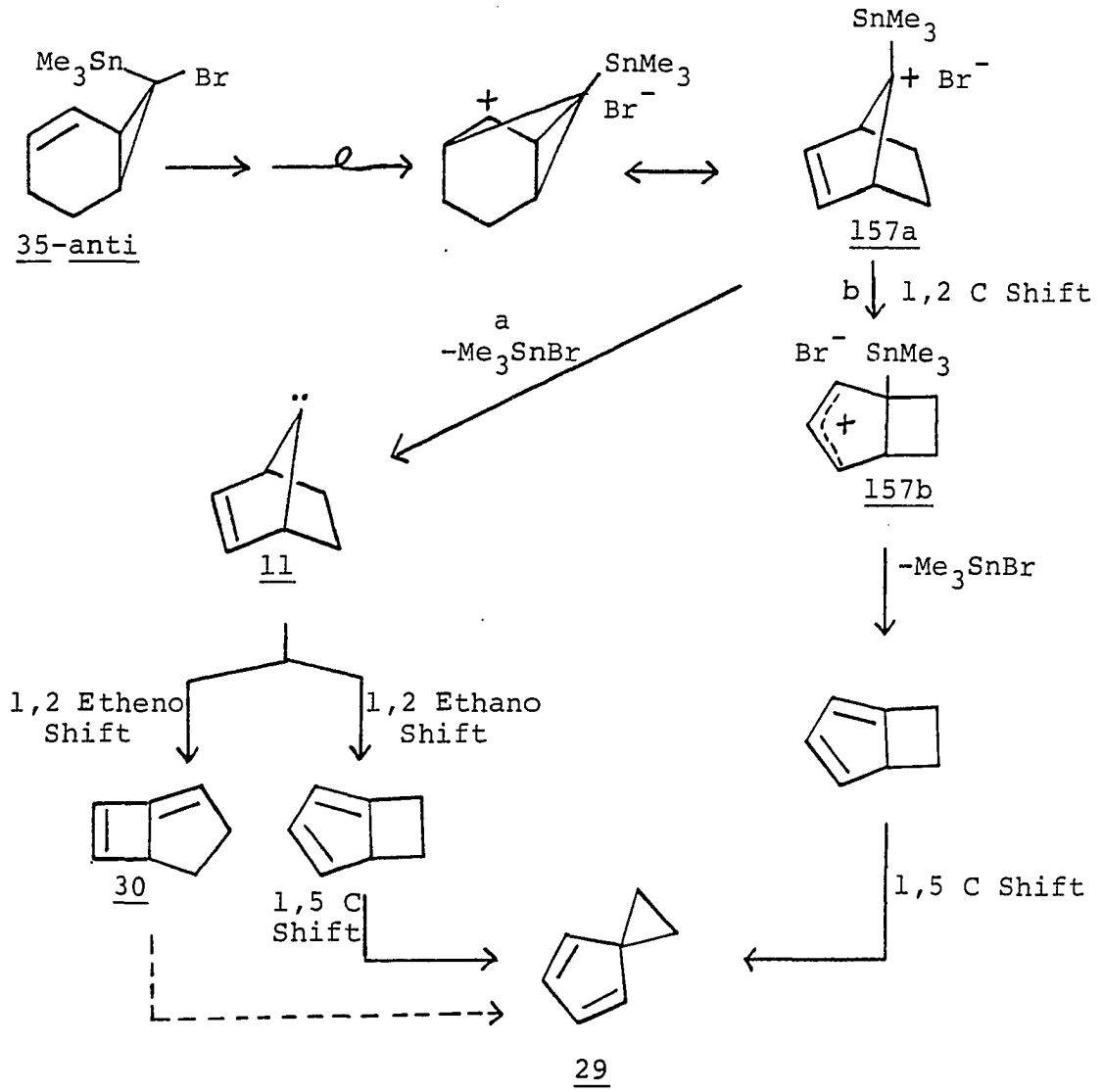
Because the reaction rate of 35-syn was much less sensitive than that of 35-anti to changes from one batch of a solvent to another (see Table XVI), it was hypothesized that triethylamine should probably have very little effect upon the pyrolysis rate of 35-syn (presumably because of the fundamentally different nature of the ionic intermediates formed from the two starting materials). The pyrolysis of 35-syn was next conducted with and without triethylamine, in order to test this hypothesis. The rate constant measured for the pyrolysis of 4.5 mg of 35-syn at 100° to 102° in 0.34 ml of benzene-d_6 was $9.33 \pm 0.08 \times 10^{-5}$ sec^{-1} (according to a least squares analysis, as described in the Experimental, entry 1), while that for the pyrolysis of a sample of 4.5 mg of 35-syn in 0.36 ml of benzene-d_6 containing 1.0 equivalent of triethylamine at the same temperature was $7.6 \pm 0.2 \times 10^{-5}$ sec^{-1}. The ratio of $k_{triethylamine)}/: k_{(no\ additive)}$ for 35-syn in benzene solution, 0.82, was thus much closer to 1 than that for

35-anti, 0.004 (calculated from experiments 1 through 3 of Table XXII). The hypothesis that the reaction rate of 35-syn should be much less sensitive to triethylamine than that of 35-anti has been proven to be true.

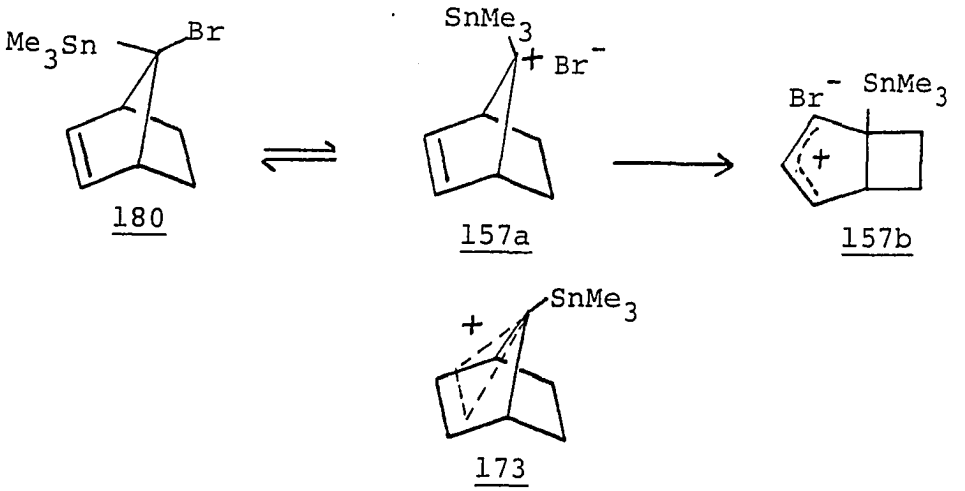
Returning now to the pyrolysis of 35-anti, it was concluded earlier in this section that the reaction mechanism begins with C-Br bond heterolysis, accompanied by rearrangement of 35-anti to ion pair 157a, as is shown in Scheme XXXV.

But how is spirodiene 29 formed? It could arise either from path a, i.e., formation of free carbene 11 (which can then go on to form 29 by a series of rearrangements), or from path b, i.e., Wagner-Meerwein rearrangement of 157a to 157b, followed by loss of trimethyltin bromide, and rearrangement to form 29. Regarding pathway a, it has already been discussed that, in order to explain why carbene 11 apparently switches from preferring 1,2-etheno bridge migration in the gas phase to preferring 1,2-ethano bridge migration in solution, one must invoke either a profound solvent effect upon the rearrangement of 11, or a rearrangement of diene 30 to 29 in solution. Regarding pathway b, one could write ion pair 157a as being in equilibrium with the covalent form 180, shown below, with the specific stereochemistry drawn, because, as was already discussed, resonance hybrid 173 is expected to dominate the characteristics of 157a. But

Scheme XXXV:

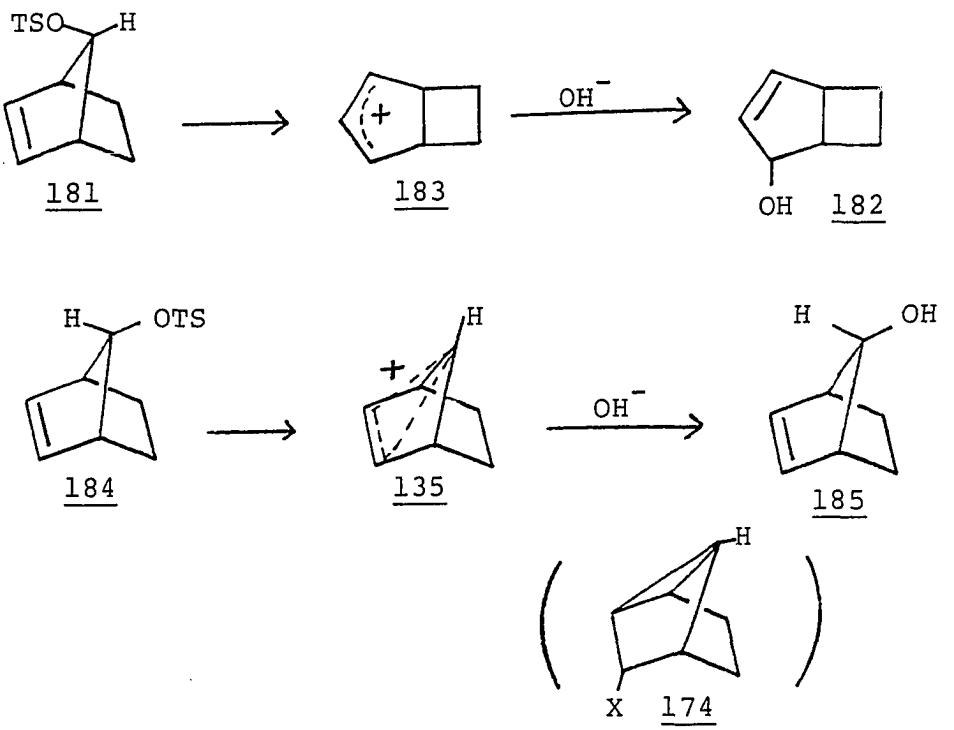


if such is the case, then the proposed rearrangement of 157a to 157b is perplexing because of the results shown in Scheme XXXVI. It is known that the solvolysis of syn-tosylate 181 in the presence of aqueous sodium bicarbonate results in a 90% yield of alcohol 182, which is obtained through trapping of



180 157a 157b 173

allylic cation 183.[101] The solvolysis of 181 was 10^4 times faster than that of its saturated analog, evidently because of anchimeric assistance by the ethano bridge of 181, with concomitant formation of an allylic cation. The solvolysis Scheme XXXVI:

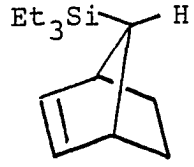


181 183 182 184 135 185 174

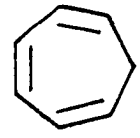
of the anti-tosylate 184 in the presence of aqueous sodium bicarbonate, on the other hand, gave only alcohol 185, as a result of the trapping of cation 135.[93] The presence of methoxide ion[94] or hydride ion [93] as the nucleophile, instead of hydroxide, resulted in the additional formation of a tricyclic trapping product, 174 (with X = MeO or H, respectively). In short, a trapping product from allylic cation 183 has apparently never been observed before in the solvolysis reaction of an anti-7-substituted bicyclo[2.2.1]hept-2-ene such as 184, from which the formation of resonance hybrid 135 determines the predominant mode of reaction. However, the formation of an allylic cation from an anti-7-substituted bicyclo[2.2.1]hept-2-ene is precisely what is postulated in pathway b of Scheme XXXV. There are three plausible explanations for why pathway b might occur: a) one cannot be sure what cation 173 (or 135, for that matter) would do in the absence of a strong nucleophile. Perhaps, given enough time, 157a could rearrange to allylic ion pair 157b. b) The presence of the tin group in ion pair 157a could profoundly affect its chemistry. Specifically, one could speculate that perhaps the formation of the allylic cation is more favorable for 157 than for the unsubstituted case, 135, because in the rearrangement of 157a, the tin group helps to stabilize the incipient allylic cationic center via a β-effect. c) Per-

haps cation 157a is long-lived enough to allow for leakage into the epimeric syn-7-bromo system.

Since no cationic intermediates other than 157a were trapped by methanol during the pyrolysis of 35-anti, the most likely way of distinguishing pathways a and b of Scheme XXXV was to attempt to trap free carbene 11 (pathway a). For comparison purposes, both 35-anti and 35-syn were pyrolyzed in the presence of triethylsilane, which can trap carbenes via Si-H insertion.[54] As shown in Table XXIV, only 35-anti gave an appreciable amount of the apparent Si-H insertion product 186. (The stereoselectivity will be discussed later.) Compound 35-syn gave mainly the usual



186



148

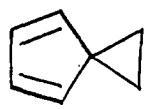
products, i.e., cyclohepta-1,3,5-triene (148) and C_7H_8 oligomers.

The small amount of 186 obtained from 35-syn must have been due to the traces of 35-anti which contaminated the 35-syn samples. (See footnotes e and h under Table XXIV.) It was concluded that bicyclo[4.1.0]hept-2-en-7-ylidene (10) is not involved in the pyrolysis of either 35-syn or 35-anti. (It was not trapped by either triethylsilane or metha-

Table XXIV. Pyrolyses of 35-anti and 35-syn in the presence of triethylsilane

SM	Temp.	Conditions	%Yield 29[a]	%Yield 148[a]	%Yield 186[a]
35-anti	160°	H[b]	25[c]	0[c]	49[c]
35-anti	160°	I[d]	0[c]	0[c]	74[c]
35-syn[e]	100°	H[b]	0[c]	?[f]	4.8[g]
35-syn[h]	100°	I[d]	0[c]	40[c]	0.9[g]

[a]



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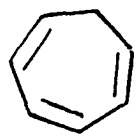

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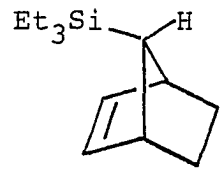


186

[b]Conditions H: The starting material (ca. 0.08 mmol) and 3.5 equiv. of triethylsilane were dissolved in 0.3 ml of benzene-d_6, placed in an NMR tube, and degassed with 3 freeze-high vac.-thaw cycles, and sealed under nitrogen. The reaction was carried out to ca. 100% completion.

[c]Yield measured by NMR integration vs. an internal std.

[d]Conditions I: The starting material (ca. 0.08 mmol) was dissolved in 0.3 ml of triethylsilane, in an NMR tube, flushed briefly with nitrogen, and sealed under nitrogen. The reaction was carried out to ca. 100% completion.

[e]Contaminated with a trace (ca. 4%) of 35-anti.

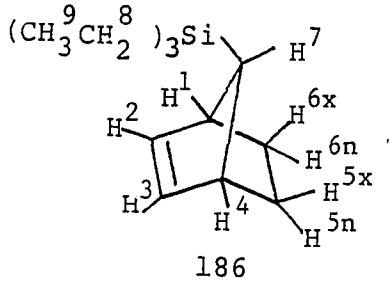
[f]Not measured.

[g]Yield measured by GC integration vs. an internal standard, with correction factors.

[h]Contaminated with a trace (ca. 1%) of 35-anti.

nol.) While on the surface the formation of product 186 implicates the intermediacy of bicyclo[2.2.1]hept-2-en-7-ylidene in the pyrolysis of 35-anti, it is disturbing that it was formed in such high stereoselectivity, a point which will be discussed in more detail shortly. In a control experiment, spirodiene 29 was pyrolyzed in triethylsilane solvent at 160°, and found to give no reaction.

The stereochemistry of 186 was verified by a combination of NMR and mass spectral analysis. Firstly, the ^{13}C NMR spectrum showed the expected 6 lines (see the Experimental), which verified the presence of only one epimer (to within the detection limits of NMR spectroscopy). Secondly, the 300 MHz ^{1}H NMR spectrum strongly suggested that the triethylsilyl group is syn to the double bond. The H^7 of 186 appeared as a slightly broadened singlet ($w_{1/2}$ = 2.7 Hz), while for the other epimer, 187, there should be a long-range coupling interaction (2 to 3 Hz[28]) between the H^7 and the



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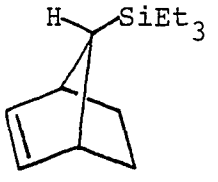

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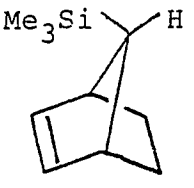
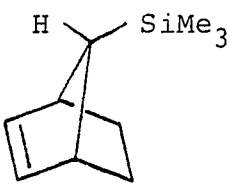


188-syn



188-anti

endo-$H^{5,6}$. Comparison of the chemical shift data of 186 with those of 188-syn and 188-anti (see Table XXV) also supports the stereochemistry of 186 as drawn. Additionally, a 2D-NOE ^1H NMR study (Nicolet NT-300 NMR spectrometer) of 186 supported the stereochemistry as drawn. There was no NOE between $H^{5x,6x}$ and H^8, or between $H^{5x,6x}$ and H^9. There

Table XXV. Comparison of NMR data for 186[a], 188-syn[b], and 188-anti[b]

Proton(s)	Chemical shift(δ) 186	188-syn	188-anti	Description (spacing, Hz) 186	188-syn	188-anti
1,4	2.865	2.90	2.89	m	m	m
2,3	5.782	5.85	6.10	t (1.95)	t (1.9)	t (1.7)
7	0.724	0.71	0.86	sl.br.[c] s ($w_{1/2}$ = 2.7)	t (1.4)	m[d]

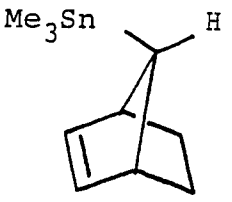
[a]Run on the Nicolet NT-300 (300 MHz) NMR spectrometer.

[b]NMR data taken from the literature.[102]

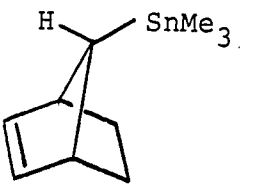
[c]The usual anti-H^7-$H^{1,4}$ coupling constant is 1.2 to 1.5 Hz. The unusually small anti-H^7-$H^{1,4}$ coupling constant for 186 (apparently less than ca. 1 Hz, based on the $w_{1/2}$ of 2.7 Hz) must be due to some bending of the C^7 bridge because of the bulky triethylsilyl group.

[d]Note that for 188-anti the syn-H^7-$H^{5n,6n}$ coupling constant was 2.4 Hz, while for 188-syn the anti-H^7-$H^{5n,6n}$ coupling constant was only 0.5 Hz.

was a weak NOE between $H^{2,3}$ and H^{9} but, surprisingly, none between $H^{2,3}$ and H^{8}. (The methylene hydrogens of the triethylsilyl group are evidently not close enough to the olefinic hydrogens for an interaction to occur.) Unexpectedly, there was a weak NOE between $H^{2,3}$ and H^{7}, perhaps via through-bond interaction. (There is a coupling constant of ca. 0.8 Hz between $H^{2,3}$ and the anti-H^{7} of norbornene derivatives.[28]) There was only a very weak NOE between $H^{5x,6x}$ and H^{7}, probably because of an unfavorable spatial orientation between the two. Lastly, a comparison of the mass spectral data (Table XXVI) for 186 with those for 188-syn and 188-anti strongly supports the syn stereochemistry of 186. The most telling feature in each case is the weaker parent peak (due to retro-Diels-Alder fragmentation) for the syn isomer than for the anti isomer. This greater predominance of retro-Diels-Alder fragmentation in the syn than in the anti isomer was also observed for the trimethylstannyl analogs 189-syn and 189-anti,[103] as shown in Table XXVII.



189-syn



189-anti

Table XXVI. Comparison of some selected 70 eV mass spectral data for 186[a], 187[a], 188-syn[b], and 188-anti[b]

m/e	(Fragment)$^{+\cdot}$	186 %"RIC"	187[c] %"RIC"
208	($Et_3SiC_7H_9$)	0	0.3
179	($Et_2SiC_7H_9$)	4.0	2.3
180	($Et_3SiC_5H_5$) (retro-Diels-Alder)	4.7	2.2
93	(C_7H_9)	2.1	2.3
115	(Et_3Si)	16.7	17.0
87	(Et_2SiH)	13.0	13.3
59	($EtSiH_2$)	10.4	11.6
Sum		50.9	49.0

[a]GC-MS data (Column C).

[b]Taken from reference 103.

[c]A trace of a compound tentatively identified as 187 was detected by GC-MS (Column C). The isomeric ratio of 186 to 187 was 62 to 1.

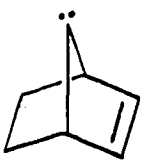
m/e (Fragment)$^{+\cdot}$	188-syn %"Total ion content"	188-anti %"Total ion content"
166 ($Me_3SiC_7H_9$)	0.2	5.8
151 ($Me_2SiC_7H_9$)	4.3	1.0
138 ($Me_3SiC_5H_5$) (retro-Diels-Alder)	20.7	7.0
93 (C_7H_9)	0.5	0.9
73 (Me_3Si)	41.4	41.6
59 (Me_2SiH)	3.7	3.3
45 ($MeSiH_2$)	4.0	3.0
Sum	74.8	62.6

Table XXVII. Comparison of some selected 70 eV mass spectral data for 189-syn[a] and 189-anti[a]

m/e (Fragment)$^{+\cdot}$	189-syn %"Total ion content"	189-anti %"Total ion content"
258 ($Me_3SnC_7H_9$)	0	2.6
230 ($Me_3SnC_5H_5$) (retro-Diels-Alder)	5.9	1.0

[a]From reference 103.

Because of the suspiciously high stereoselectivity of the apparent trapping of carbene 11 by triethylsilane, resulting in product 186, experiments with some other carbene traps were required. Pyrolysis of 35-anti in tetramethylethylene and cyclohexene solutions gave only the usual products, i.e., trimethyltin bromide, spirodiene 29, and



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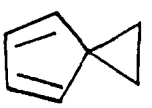

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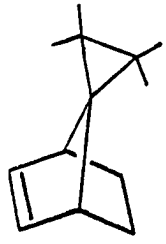
several C_7H_8 oligomers, but no products with the mass spectral data expected for the cyclopropanation products 190 and 191, respectively. Pyrolysis of 35-anti in chloroform solution similarly gave no 192 (from singlet carbene trapping) or 193 (from triplet carbene trapping).



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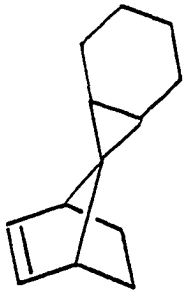

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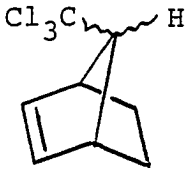

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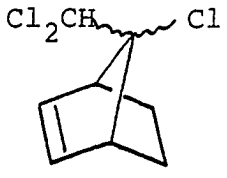
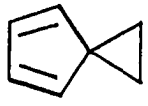


193

Instead, there was obtained, along with trimethyltin bromide and a 37% yield of 29, a 4% yield of 194. Product 194 un-



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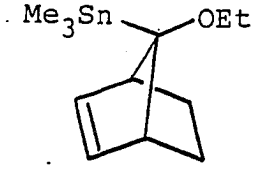

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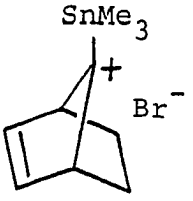
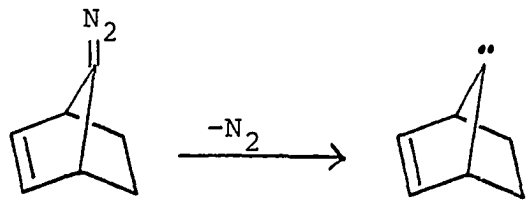


157a

doubtedly arose from a reaction between ion pair 157a and the ethanol stabilizer present in commercial chloroform.

Since 186 was formed so stereoselectively, and neither olefins nor chloroform were able to trap carbene 11, suspicion developed that carbene 11 might not really be involved in the pyrolysis of 35-anti at all. This suspicion was deepened by the fact that, as has already been mentioned a number of times, carbene 11 generated in the gas phase produces the [3.2.0] bicyclic diene 30 to a much greater extent than it produces the spiro-

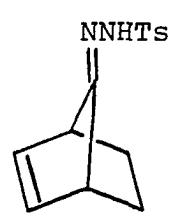
diene 29, whereas 35-anti (in solution) produces 29 as virtually the exclusive product. The only way to resolve the problem was to generate carbene 11 independently, by a less ambiguous method, and to then study its solution chemistry. The diazo compound 28 was chosen for this task.



28 11

3. Solution-phase pyrolysis of the lithium tosylhydrazone salt of bicyclo[2.2.1]hept-2-en-7-one (27a)

The treatment of 195 or 196 with base in methanol solution [66] produced compounds 197, 198, and 199. They



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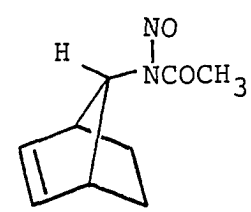

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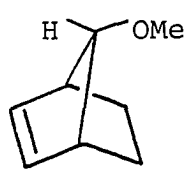
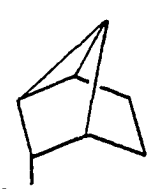
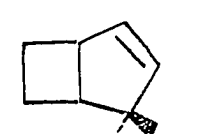


197



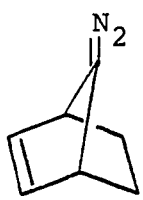
MeO 198



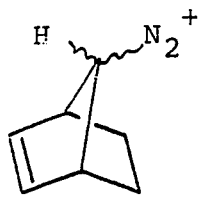
199

were rationalized by protonation of diazo compound 28, to give diazonium salt 200, which then suffered loss of nitrogen

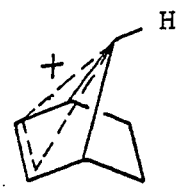
to form the intermediate cations 135 and 183. The trapping of cation 135 by methanol could then lead to 197 and 198,



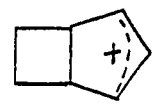
28



200



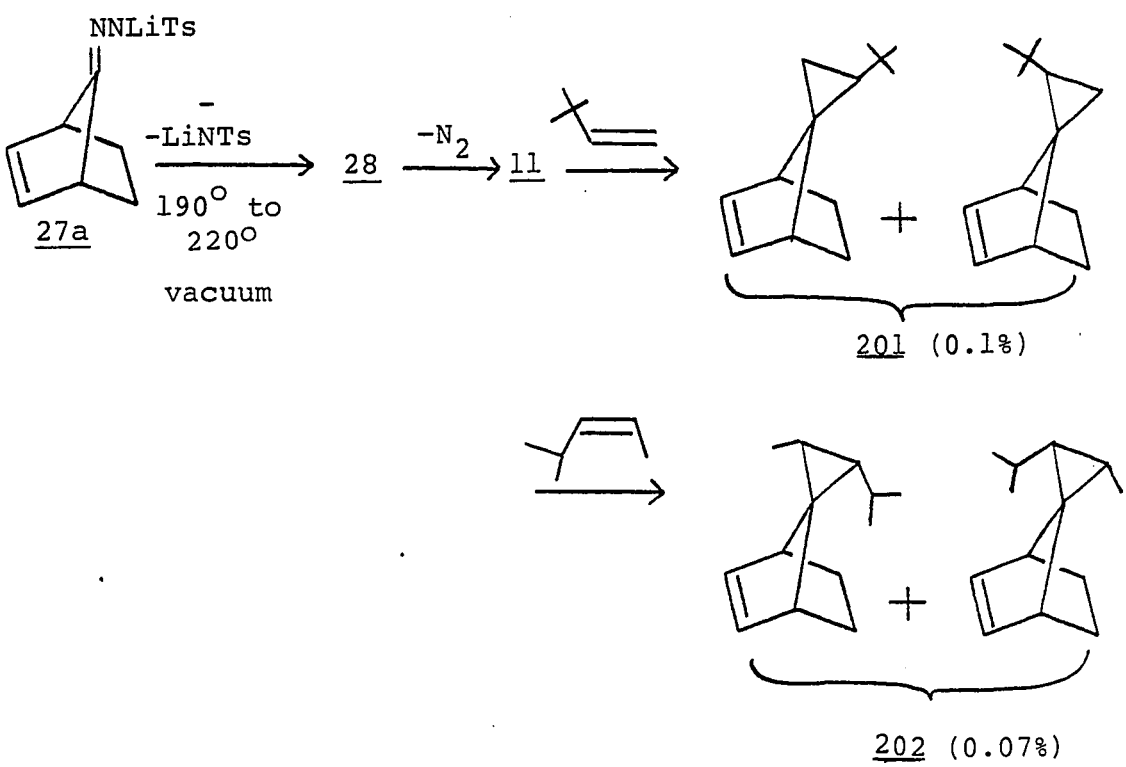
135



183

and trapping of cation 183 could lead to product 199. As is shown in Scheme XXXVII, when the lithium tosylhydrazone salt 27a was pyrolyzed in 3,3-dimethyl-1-butene or in 4-methylpent-2-ene solution, a trace of cyclopropanation product (201 or 202, respectively) was obtained.[23,104]

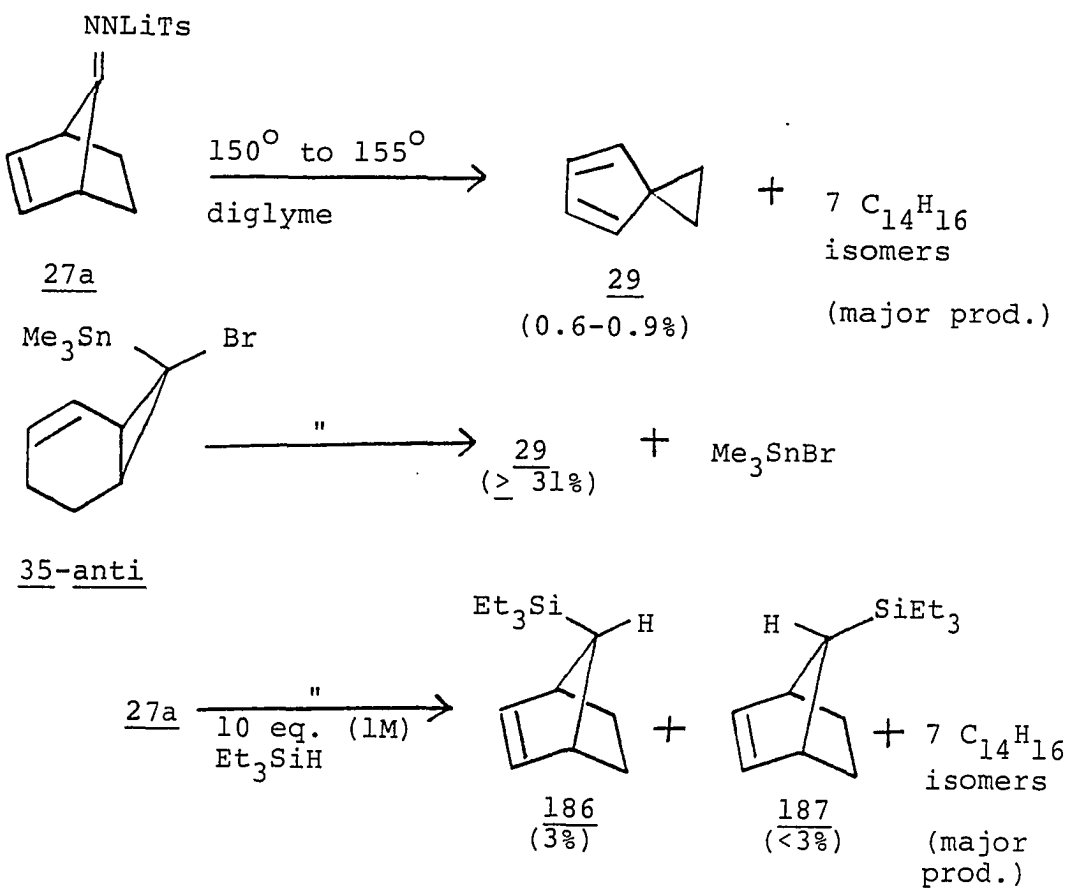
Scheme XXXVII:



However, the intramolecular solution chemistry of carbene 11 had never been studied carefully under aprotic conditions.

As illustrated in Scheme XXXVIII, the pyrolysis of 27a in diglyme solution gave a trace of spirodiene 29, but the major products were a number of C_7H_8 dimers. These results were in sharp contrast to those obtained from a pyrolysis of 35-anti under the same conditions, in which a respectable 31% yield of 29 was obtained. Furthermore, the presence of

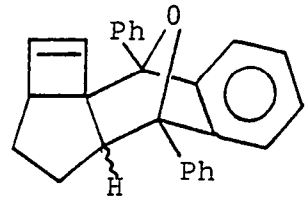
Scheme XXXVIII:



triethylsilane (at a 1 molar concentration) in the pyrolysis of 27a caused only trace amounts of 186 and 187 to be formed. (This is very reminiscent of the trace amounts of carbene trapping products, 201 and 202, obtained in the presence of olefins.[23,104])

Obviously, 27a and 35-anti gave totally different chemistry in solution. In order to verify that the solution pyrolysis of 27a really involved the carbene intermediate 11, some experiments were run with DPIBF, which would be expected to trap diene 30 (the major product from 11 in the gas phase) in the form of Diels-Alder adduct 31. As can be seen in Scheme XXXIX, the use of DPIBF resulted in the formation of

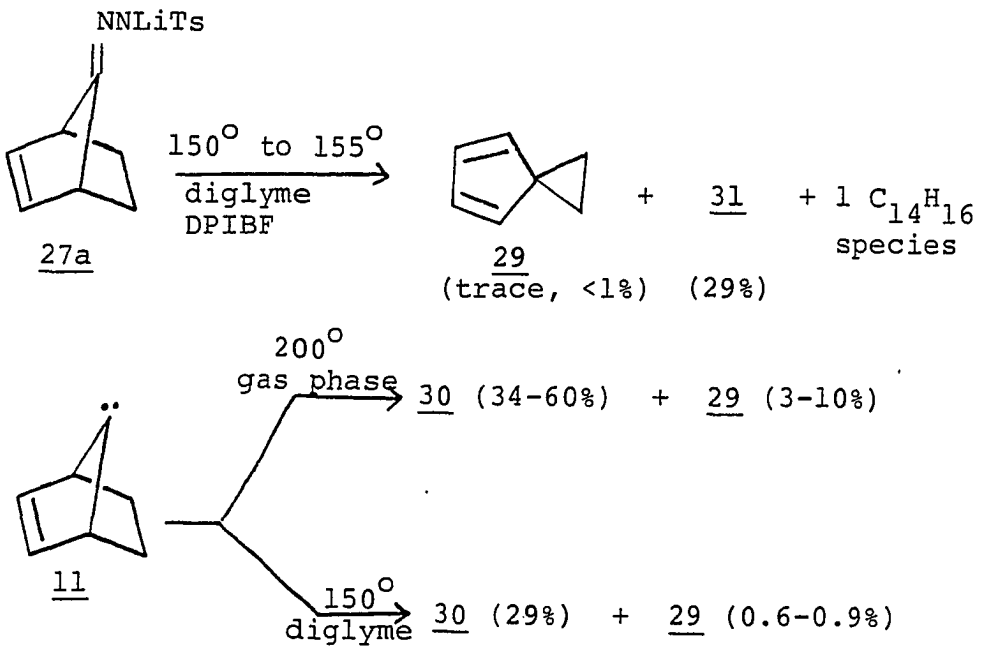
30



31

31 as a major product. One equivalent of DPIBF resulted in a 29% isolated yield of 31, and the use of 2 equivalents led to a 28% yield. Since no unreacted 27a could be recovered, and since the yield of 31 was the same whether 1 or 2 equivalents of DPIBF were employed, one can regard 29% as the maximum yield of diene 30 attainable from carbene 11 in solu-

Scheme XXXIX:

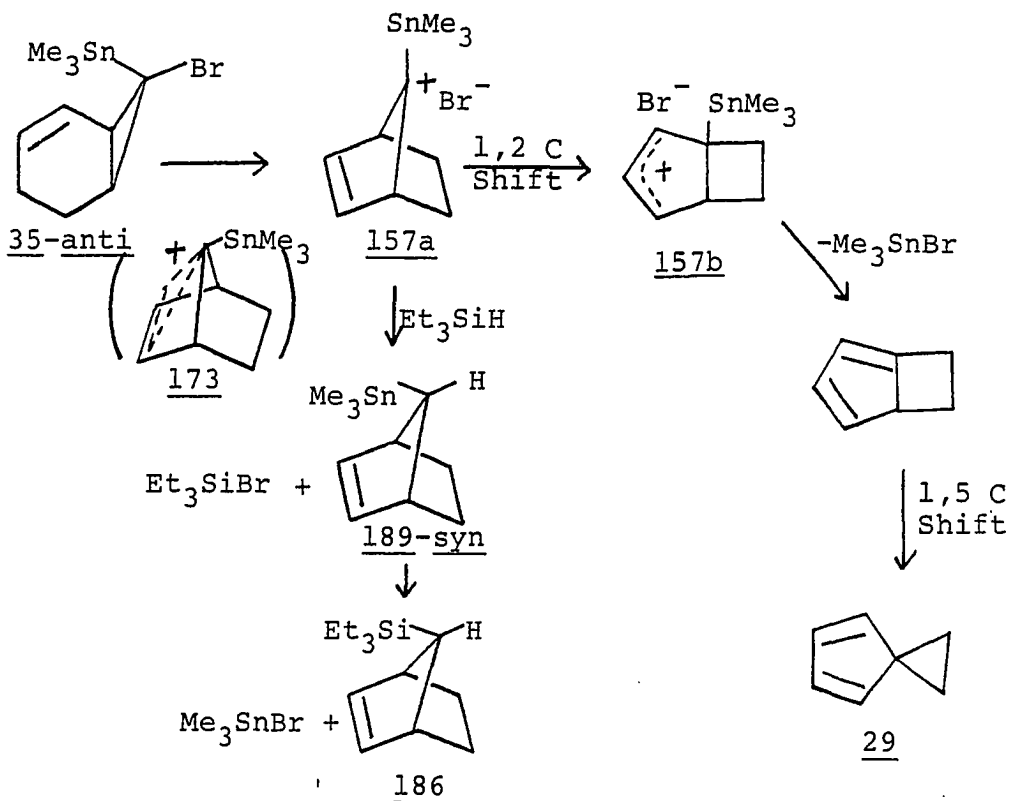


tion, under these conditions. Thus, carbene 11 actually gives very similar chemistry in the gas phase and in solution, as is outlined in Scheme XXXIX. Both of the previously discussed explanations for the differences between the gas-phase chemistry of 27a and the solution-phase chemistry of 35-anti (either solvent effects on the chemistry of carbene 11, or a rearrangement of 30 to 29 in solution) have now been ruled out. One must therefore conclude that the solution pyrolysis reactions of 35-anti (which gave spirodiene 29 as almost the exclusive product in the absence of a trap,

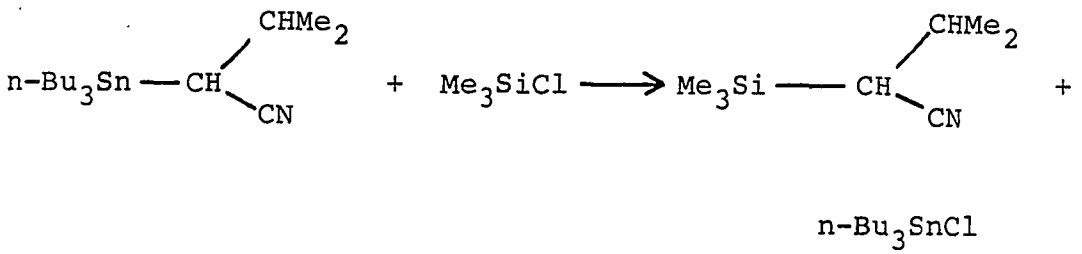
and 186 in 49% yield in the presence of 1 M triethylsilane) do not involve carbene 11!

But then how did compounds 29 and 186 arise from the pyrolysis reactions of 35-anti? The most economical explanation is that offered in Scheme XL. As was already discussed earlier, ion pair 157a is a key intermediate in the pyrolysis of 35-anti. The mechanism shown in Scheme XL for the formation of 29 from 157a is the same as pathway b of Scheme XXXV. Its relative merits have already been dis-

Scheme XL:



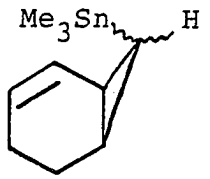
cussed. The mechanism shown for the formation of 186 begins with the reduction of a cation (157a) by triethylsilane, which is a well precedented process.[105-109] (The stereoselective reduction is expected because of the importance of resonance hybrid 173, as was already discussed in entry 2 above.) The silicon-tin redistribution reaction between 189-syn and triethylsilyl bromide also has precedents, the most notable of which is the reaction shown below.[110]



4. Mechanism of formation of syn-7-triethylsilylbicyclo-[2.2.1]hept-2-ene (186)

In order to test for the mechanism proposed in Scheme XL, it was felt that an added tetraalkyltin compound might also undergo a silicon-tin redistribution reaction with the triethylsilyl bromide, thereby "consuming" enough of the triethylsilyl bromide so that some of the 189-syn intermediate might remain unreacted, and thus be observable. Unfortunately, the presence of either 2 equivalents of tetra-n-butyltin, or a huge excess of tetramethyltin (see the Experimental) did not result in any 189-syn or 189-anti. Inter-

estingly though, the tetra-n-butyltin did cause the formation of a small quantity of a product tentatively identified as 163 (the same product as obtained from the tri-n-butyltin hydride reduction of 35-anti, described in entry 2 above). Evidently, the combination of tetra-n-butyltin and tri-



163

ethylsilane at high temperature must have caused a radical chain reaction, which resulted ultimately in the net reduction of the bromine of 35-anti by triethylsilane.

Apparently, either tetra-n-butyltin and tetramethyltin are not reactive enough to compete with 189-syn for the triethylsilyl bromide, or a solvent cage (containing 189-syn and triethylsilyl bromide) does not allow an external tetralkyltin to react with the triethylsilyl bromide. The best experiment to test for the mechanism of Scheme XL is to prepare a benzene solution of 189-syn (and/or 189-anti) plus triethylsilyl bromide, and to then see whether they react to produce 186 plus trimethyltin bromide. Preparation of the necessary samples of 189-syn and 189-anti is currently in progress at the time of writing of this manuscript.

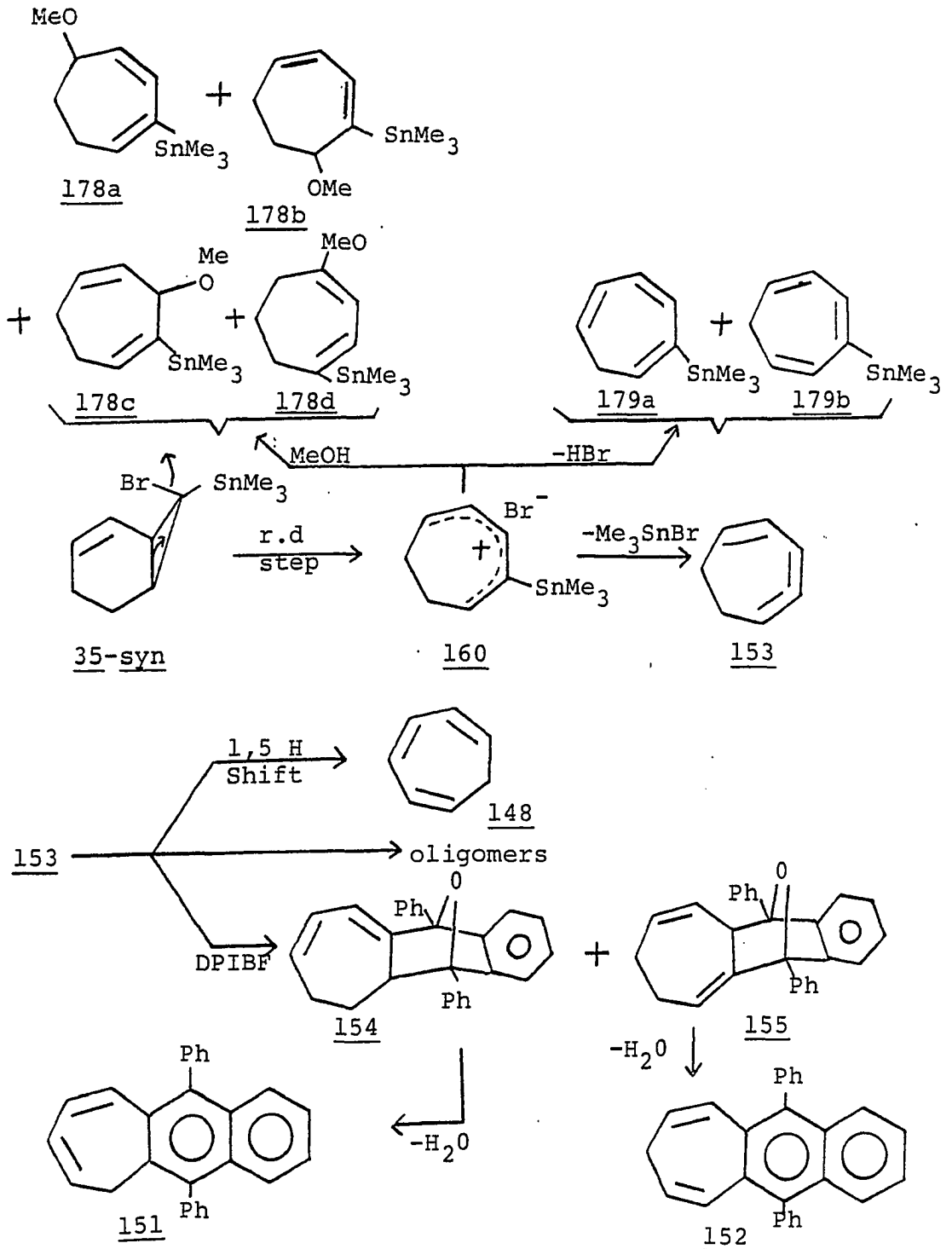
C. Conclusion

The vacuum pyrolysis of 35-anti gave results which were very difficult to decipher. The major products were cyclohepta-1,3,5-triene and toluene. There were a number of other unidentified products formed as well. Only a trace amount of spiro[2,4]hepta-1,6-diene could be detected, and no bicyclo[3.2.0]hepta-1,6-diene (30) could be detected at all.

In their solution pyrolysis reactions, 35-anti and 35-syn displayed entirely different chemistry, and it was found that neither one reacted via a carbene intermediate. The final mechanistic conclusions are illustrated in Scheme XLI. Regarding Mechanism A (the pyrolysis reaction of 35-syn), evidence for ionic intermediate 160 included strong rate acceleration by polar solvents (acetonitrile and diphenyl ether), trapping results with methanol, and a lack of carbene trapping by triethylsilane or methanol. The fact that the stereochemistry of the bromine in 35-syn is suitable for a concerted ionic ring opening to a cis-olefinic ion pair (160) further strengthens the assertion that ion pair 160 is the first intermediate formed. The proposal of allene 153 as the key intermediate was based on the fact that it was trapped by DPIBF, in the form of 151 and 152, whereas it apparently dimerized and trimerized in the absence of DPIBF. Concerning Mechanism B of Scheme XLI (the pyrolysis reaction of 35-anti), evidence that the rate determining step is an

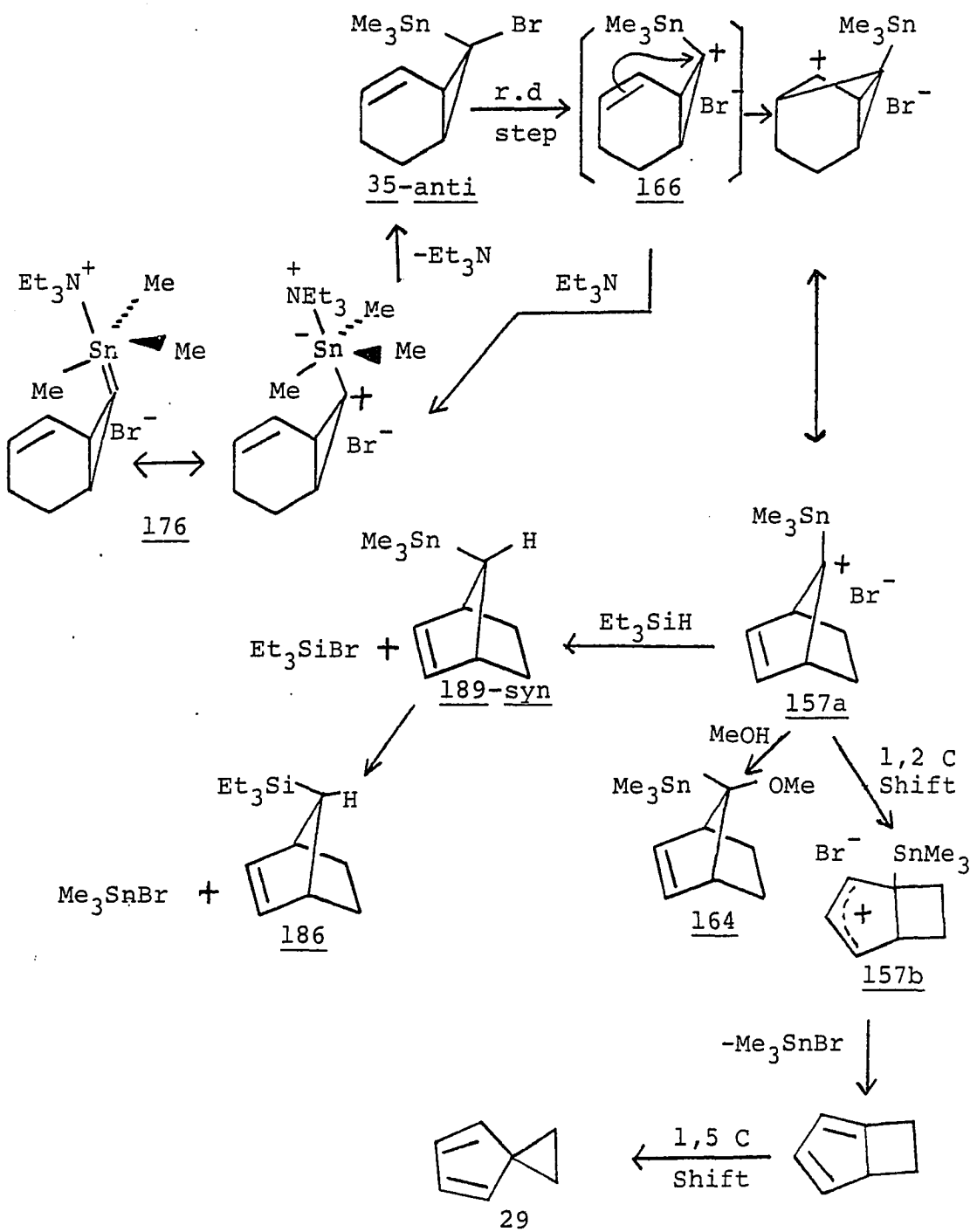
Scheme XLI:

Mechanism A:



Scheme XLI (Continued):

Mechanism B:



initial ionization (resulting ultimately in rearranged ion pair 157a) included acceleration by Lewis acids (tin trichloride and aluminum tetrachloride) and trapping of ion pair 157a by methanol. The unrearranged cyclopropyl cation 166 could not be trapped by methanol, but kinetic evidence was obtained that triethylamine can form a complex (176) by interacting with the tin group of 166. Pyrolysis of 35-anti in tetramethylethylene, cyclohexene, or chloroform solution produced no carbene trapping products. Furthermore, the independent generation of bicyclo[2.2.1]hept-2-en-7-ylidene (11) under the reaction conditions (made from the corresponding lithium tosylhydrazone salt) resulted in only a trace (0.6 to 0.9% yield) of spirodiene 29. The major product (30% yield) from 11 in solution was the same as that obtained in the gas phase, i.e., bicyclo[3.2.0]hepta-1,6-diene (30). The apparent carbene trapping product 186, obtained from the pyrolysis of 35-anti in the presence of triethylsilane, is probably the result of trapping of rearranged ion pair 157a by the hydride of triethylsilane, followed by a silicon-tin redistribution reaction.

Thus, neither the solution pyrolysis reaction of 35-anti nor of 35-syn involves a carbene intermediate. Their gas-phase chemistry is not yet understood.

D. Experimental

1. General considerations

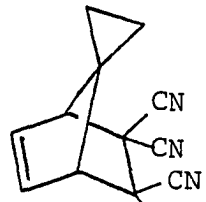
For the general considerations, see the experimental section of Chapter I.

The first order rate constants and their uncertainty levels were calculated via a least squares analysis computer program, provided by Professor J. Espensen, Dept. of Inorganic Chem., Iowa State University ("NLLSQ" program, executed on an Apple II computer). The corresponding correlation factors (r) were calculated on a hand calculator, which had a built in least squares program.

2. Vacuum pyrolysis of anti-7-bromo-syn-7-trimethylstannylbicyclo[4.1.0]hept-2-ene (35-anti), with TCNE contained in the cold trap

A sample (95.3 mg, 0.284 mmol) of 35-anti was placed in a 100 ml round-bottom flask, which was then attached to a pyrex pyrolysis tube (packed with 6 in. of 1/16" glass helices), which had been preheated to 205° to 280°. (The temperature readings were previously calibrated by imbedding a thermometer in the packing material.) A trap was flushed with nitrogen, cooled with liquid nitrogen, and then charged with a solution of 42.1 mg (0.329 mmol) of tetracyanoethylene in 10 ml of dry (freshly distilled from LAH) THF. The trap

was connected to the pyrolysis tube, and the entire system was then evacuated to 0.016 mm pressure. The trap was cooled to liquid nitrogen temperature, and the flask containing the sample of 35-anti was warmed gently with heating tape. After 5 hours, the cold trap was vented to nitrogen, and warmed to -78° (dry ice-acetone bath). The trap was next removed, and its sides were rinsed down with a few ml of dry THF. The trap was then reconnected to the pyrolysis apparatus, and allowed to stand at -78° for 2 hours, followed by standing at room temperature for 16 hours. NMR analysis of the product mixture (acetone-d_6) showed a trace of 147 (ca. 1 to 3% yield), identified by comparison with an authentic sample, along with much larger amounts of unidentified olefinic products. Preparative TLC on silica gel (ether) gave no identifiable products.



147

3. Vaccum pyrolysis of 35-anti, and direct observation of the products by NMR analysis

The desired amount (usually ca. 100 mg) of 35-anti was placed in a 100 ml round-bottom flask, which was then con-

nected to one end of a preheated pyrex pyrolysis tube (packed with the desired amount of either pyrex glass wool or 1/16" glass helices). The other end of the pyrolysis tube was attached to a trap. The entire apparatus was evacuated (high vacuum, ranging from 0.002 to 0.02 mm pressure in different experiments), the trap was cooled with liquid nitrogen, and the flask containing the 35-anti sample was then gently warmed with heating tape. After the length of time required to volatilize the entire sample of 35-anti through the pyrolsis tube, (1/2 to 5 hours), the trap was vented to nitrogen and allowed to warm to -78° (dry ice-acetone bath). The trap was isolated from the system, and rinsed with 0.5 to 1 ml of carbon disulfide. A trace of benzene standard was added, and the resulting carbon disulfide solution was analyzed by lew temperature (-78° to -50°) 100 MHz ^{1}H NMR, room temperature 60 MHz ^{1}H NMR, and, sometimes, also by GC and GC-MS. Along with trimethyltin bromide, variable amounts (depending on the pyrolysis temperature) of cyclohepta-1,3,5-triene (148), toluene, and spiro[2,4]hepta-4,6-diene (29) were identified by comparison of their crude NMR spectra and/or GC retention times, and GC-MS data with those of authentic samples. GC-MS analysis of some of the samples also revealed small amounts of some $C_{14}H_{16}$ species (149). Variable amounts of at least four unknown species (X_1, X_2, X_3 and X_4) were

observed by NMR analysis. 100 MHz ^{1}H NMR of X_1 (CS_2, - 50°): δ 5.8 (t, J = ca. 3 Hz), 5.9 (t, J = ca. 3 Hz) 100 MHz ^{1}H NMR of X_2 (CS_2, -50°): δ 4.7 (m), 4.6 (m). 100 MHz ^{1}H NMR of X_3 (CS_2, -50°): δ 3.2 (br t, J = ca. 8 Hz), 2.6 (br t, J = ca. 8 Hz). 100 MHz ^{1}H NMR of X_4 (CS_2, -50°); δ 2.5 (br s). X_2 is apparently unstable, since its NMR spectrum degraded upon warming to room temperature. Also, X_4 disappeared upon treatment with TCNE, and subsequent evaporation of solvent. Bicyclo[3.2.0]hepta-1,6-diene (30) was not among the products under any of the reaction conditions explored. A qualitative description of the product amounts under the various pyrolysis conditions is provided in Table XXVIII.

4. Vacuum pyrolysis of cyclohepta-1,3,5-triene (148)

Into a 50 ml round-bottom flask were placed 150 µl of cyclohepta-1,3,5-triene. The flask was then connected to a preheated (375° to 430°) pyrolysis tube (packed with 10.5 in. of 1/16" glass helices), which was attached to a trap. The entire apparatus was flushed with nitrogen. The flask was cooled to -78° (dry ice-acetone bath), the apparatus was evacuated to 0.006 to 0.007 mm pressure, and the trap was then cooled with liquid nitrogen. The cyclohepta-1,3,5-triene was allowed to slowly volatilize through the pyrolysis tube over a 35 minute period. The trap was warmed to -78°, vented to nitrogen, and then rinsed with 0.5 ml of carbon disulfide. A trace of benzene standard was

Table XXVIII. Gas-phase pyrolysis of 35-anti

Expt.	Conditions[a]	Initial mg of 35-anti	Amt. recov. 35-anti	Amt. 29
1	265-315°, 0.013mm, 2.5 hr., 6 in. of glass helices	143	>50%	
2	300-375°, 0.016mm, 2 hr., 11in. of glass helices	86	ca. 50%	
3	355-410°, 0.018mm, 1.5 hr., 10 in. of glass helices	80	trace	
4	365-430°, 0.005mm, 11 in. of glass helices	84	ca. 0	
5[e]	225-295°, 0.014mm, 0.5 hr., 12 in. of glass wool	77	ca. 30%	trace[b,c]
6	405-460°, 0.005mm, 12 in. of glass wool	78	ca. 0	trace[b,c]

[a]Temperature readings previously calibrated by imbedding a thermometer in the packing material.

[b]Identified and/or measured by NMR.

[c]Identified by GC (Column H) comparison with an authentic sample, and/or measured by GC (Column H).

[d]Identified by GC-MS (Column A).

[e]NMR analysis showed that the major products were olefinic species other than 29, benzene, toluene, 148, 149, of X_1 through X_4. GC analysis showed that the major products (ca. 12) had retention times much higher than those expected for C_7H_8 species.

Amt. toluene	Amt. 148	Ratio toluene to 148	Amt. benzene	Amt. 149	Amt. X_1	Amt. X_2	Amt. X_3	Amt. X_4
					mi-nor amt.[b]	mi-nor amt.[b]		
b,c,d trace	major amt.[b,c,d]	?	b,c trace	minor amt.[d]	major amt.[b]	major amt.[b]	major amt.[b]	
major amt.[b,c]	major amt.[b,c]	1:3.5[b]						major amt.[b]
major amt.[b,c]	major amt.[b,c]	1:2.9[b]						major amt.[b]
trace[c]	trace[e]	ca. 1:3[c]	b,c trace					
major amt.[b,c,d]	major amt.[b,c,d]	1:3.2	b,c trace	minor amt.[d]				major amt.[b]

added, and the resulting sample was then analyzed by low temperature (-50°) 100 MHz ^{1}H NMR, and by room temperature 60 MHz ^{1}H NMR. Only recovered cyclohepta-1,3,5-triene could be detected.

5. Vacuum pyrolysis of spiro[2,4]hepta-4,6-diene (29)

This vacuum pyrolysis was conducted exactly the same way as that of cyclohepta-1,3-5-triene, described above, except that 200 µl of spiro[2,4]hepta-4,6-diene (29) were used instead of the cyclohepta-1,3-5-triene. Only unreacted 29 could be detected by low temperature (-50°) NMR analysis.

6. Preparation of spiro[2,4]hepta-4,6-diene (29)

A preparation of this compound was described in the literature.[111] In this dissertation work, it was found that following the literature procedure resulted in a mixture (which would be difficult to separate) of 29 and 1,2-dibromoethane. The following procedure (including slight modifications of the literature procedure) provided a pure product.

Approximately 200 ml of ammonia were condensed into a 500 ml 3-neck round-bottom flask, equipped with a dry ice-acetone condenser, an addition funnel, an overhead mechanical stirrer, and a dry ice-acetone cooling bath. Then, 4.35 g (0.189 mole) of sodium (cut into small pieces)

were added, followed by the dropwise addition over a 15 minute period of 20.0 ml (0.242 mole) of cyclopentadiene (freshly cracked from dicyclopentadiene). A blue color, due to unreacted sodium, remained, so another 2.0 ml of cyclopentadiene were added. After the blue color had disappeared, 7 ml (0.0812 mole) of 1,2-dibromoethane (previously distilled at reduced pressure) were added dropwise over a 3 to 4 minute period. The resulting mixture was stirred at -78° for 2 hours. The dry ice-acetone bath was removed from the now green solution, and the stirring was continued for 1 more hour, after which time approximately 1/2 of the ammonia had evaporated. The -78° bath was returned, and the mixture was stirred for another 3 hours. The remaining ammonia was next evaporated by placing a room temperature water bath on the flask. When almost all of the ammonia had evaporated, 150 ml of ether and 75 ml of water were added. The mixture was warmed to room temperature, and transferred to a separatory funnel. The aqueous layer was removed (a large amount of brown polymeric material made separation of the layers difficult) and re-extracted with three 50 ml portions of ether. The ether layers were combined and filtered through diatomacious earth ("Celite 503"), dried (anhydrous sodium sulfate), and filtered. The ether was removed by distillation at atmospheric pressure, leaving 7.83 g of a yellow liquid. Pure 29 (b.p. 71° to

74° at 190 to 200 mm) was collected by distillation at reduced pressure (5 g, 67% yield). 60 MHz ^{1}H NMR of 29 (CCl_4): δ 6.44-6.27 (m, 2H), 6.02-5.85 (m, 2H), 1.54 (s, 4H).

7. Preparation of the Diels-Alder adduct (147) between tetracyanoethylene and spiro[2,4]hepta-4,6-diene (29)

The procedure is that of Murahashi et al.[24] A 50 ml 3-neck round-bottom flask was equipped with a magnetic stirring bar and a nitrogen inlet, and was nitrogen-flushed and dried. It was charged with a solution of 0.693 g (5.41 mmol) of tetracyaneothylene (TCNE) in 20 ml of dry (freshly distilled from LAH) THF. Then, 0.506 g (5.50 mmol) of 29 (prepared as in entry b above) was slowly added, followed by 5 ml of dry THF. There was some brief exothermicity. After the resulting solution had been stirred under nitrogen for 3 hours, only a tiny quantity of crystals had formed, so approximately 10 ml of the THF were flushed off with nitrogen over a 2 hour period. After 5 more minutes of stirring, the mixture was filtered, and the resulting white powder was recrystallized from a mixture of THF (6 ml) and ether (1.5 ml). The first crop (0.39 g) and the second crop (0.24 g) had identical GC traces (Column G). 60 MHz ^{1}H NMR of 147 (acetone-d_6): δ 6.88 (t, 2H, J = 2 Hz), 3.93 (t, 2H, J = 2 Hz), 1.47-0.67 (m, 4H).

8. Pyrolysis of anti-7-bromo-syn-7-trimethylstannylbicyclo[4.1.0]hept-2-ene (35-anti) in benzene

A sample of 35-anti (ranging in amount from 4 to 35 mg) was dissolved in 0.3 ml of benzene or benzene-d_6, and placed in an NMR tube. The sample was then either a) sealed under an atmosphere of air, or b) flushed with nitrogen, and then sealed under nitrogen, or c) degassed (3 freeze-high vacuum-thaw cycles), and then sealed under nitrogen. The particular method used is indicated in the text (section B) for each experiment. The sealed tube was then completely immersed in a preheated oil bath, kept at either 100.5° to 101.5° (thermostatic temperature control), or 160° to 164°. The rate of the reaction was monitored by NMR measurement of the disappearing 35-anti trimethyltin peak and the growing trimethyltin bromide (s, δ 0.1, benzene-d_6). The NMR yield of trimethyltin bromide ranged from 85 to 95%. The major product was spiro[2,4]hepta-4,6-diene identified by comparison of its GC retention time and NMR spectrum with those of an authentic sample. The yield of 29 ranged from 45 to 95%, based on unrecovered 35-anti (either NMR or corrected GC yield), depending upon the particular batch of 35-anti, and upon the particular batch of benzene used. The reaction rate also depended upon the same two variables. It was found that accelerated samples of 35-anti gave higher yields of 29. (Product 29 polymerized slowly during pro-

longed heating periods, as well as during long periods of freezer storage.) Very small amounts of three $C_{14}H_{16}$ species (the same ones as were observed in the pyrolysis of 35-anti, in the presence of DPIBF, vide infra) were identified by GC analysis.

A crude product mixture from such a reaction which was run on a 20 mg sample of 35-anti dissolved in 0.3 ml of benzene was treated with TCNE in the following manner. Approximately 3/4 of the crude benzene solution was placed in a 25 ml 3-neck round-bottom flask, followed by a solution of 8.9 mg of TCNE in 5 ml of dry (freshly distilled from LAH) THF. After the resulting solution had been stirred under nitrogen at room temperature for 26 hours, it was concentrated in vacuo, leaving an oily yellow solid, which was rinsed with 5 ml of ether, and dried. The resulting 4 mg of yellowish solid was identified as the Diels-Alder adduct (147) between TCNE and spirodiene 29, by comparison of its NMR spectrum with that of an authentic sample.

9. Solution-phase pyrolysis of 35-anti in the presence of DPIBF

A solution of 38.7 mg (0.115 mmol) of 35-anti and 31.9 mg (0.118 mmol) of DPIBF in 0.3 ml of benzene-d_6 was placed in an NMR tube, degassed (3 freeze-high vacuum-thaw

cycles), and sealed under nitrogen. The tube was fully immersed in a 155° to 160° oil bath for 20 minutes. NMR analysis showed that virtually no reaction had occurred. Heating (159° to 164°) was continued for 474 more minutes. NMR analysis indicated that the 35-anti was virtually all consumed. Spiro[2,4]hepta-4,6-diene, 29 (identified by comparison of its GC retention time and NMR spectrum with those of an authentic sample), was formed in 38% yield (corrected GC yield). There was also an unidentified trimethylstannyl compound (s, δ 0.1, benzene-d_6) formed in ca. 20% yield (NMR measurement).

A similar reaction run with 23.1 mg of a different batch of 35-anti and 19.1 mg of DPIBF (run for 575 minutes at 158° to 164°) resulted in a 51% yield of 29, and a 10% yield of the unidentified trimethylstannyl compound mentioned above.

Approximately 5 DPIBF Diels-Alder adducts (tentatively identified by GC-MS; some of them with molecular weight 362, which is that expected for an adduct between DPIBF and a C_7H_8 species) were formed in low yield (a combined yield of ca. 2%). Attempted isolation of these adducts (from the combined crude products of several experiments) by preparative TLC on silica gel failed because of their apparent instability on silica gel. GC-MS analysis

of the crude product also indicated very small yields of 3 $C_{14}H_{16}$ species and 1 $C_{21}H_{24}$ compound.

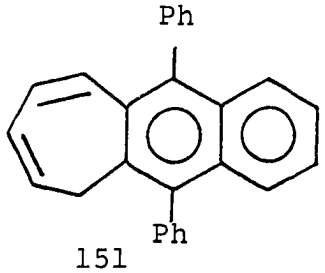
10. Pyrolysis of syn-7-bromo-anti-7-trimethylstannylbicyclo-[4.1.0]hept-2-ene (35-syn)

A sample of 35-syn (ranging in size from 15 to 35 mg) was dissolved in 0.3 ml of either benzene or benzene-d_6, and was placed in an NMR tube. The sample was degassed (3 freeze-high vacuum-thaw cycles) and sealed under nitrogen, and then the tube was fully immersed in an oil bath preheated to 100.5° to 101.5° (thermostatic temperature control), and heated at 100.5° to 101.5°. The progress of the reaction was followed by NMR analysis. Trimethyltin bromide was obtained in 90% yield (NMR yield). The yield of cyclohepta-1,3,5-triene (148), identified by comparison of its GC retention time and NMR spectrum with those of an authentic sample, ranged from 56 to 59% (NMR yield). In contrast to the situation with 35-anti the reaction rate of 35-syn did not depend upon the particular batch of solvent used. Also, identified (by GC-MS) within the product mixture were 4 $C_{14}H_{16}$ species and 3 $C_{21}H_{24}$ species, in low yield.

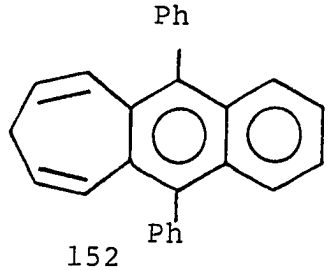
11. Solution-phase pyrolysis of 35-syn in the presence of DPIBF

A solution of 37.9 mg (0.113 mmol) of 35-syn and 33.1 mg (0.122 mmol) of DPIBF in 0.3 ml of benzene-d_6 was

placed in an NMR tube. It was degassed (3 freeze-high vacuum-thaw cycles), sealed under nitrogen, and then heated in an oil bath at 155° to 161° (with the tube fully immersed) for 20 minutes. The 35-syn was completely consumed, according to NMR analysis. Cyclohepta-1,3,5-triene (identified by comparison of its NMR spectrum and GC retention time with those of an authentic sample) was formed in 49% yield (corrected GC yield). Also formed was a 1.5 to 1 mixture of DPIBF trapping compounds 151 and 152. After the solution had been allowed to air oxidize several days (to allow unreacted DPIBF to be converted to o-dibenzolylbenzene), 151 and 152 were isolated by preparative TLC on silica gel (20% ether/80% hex-



151

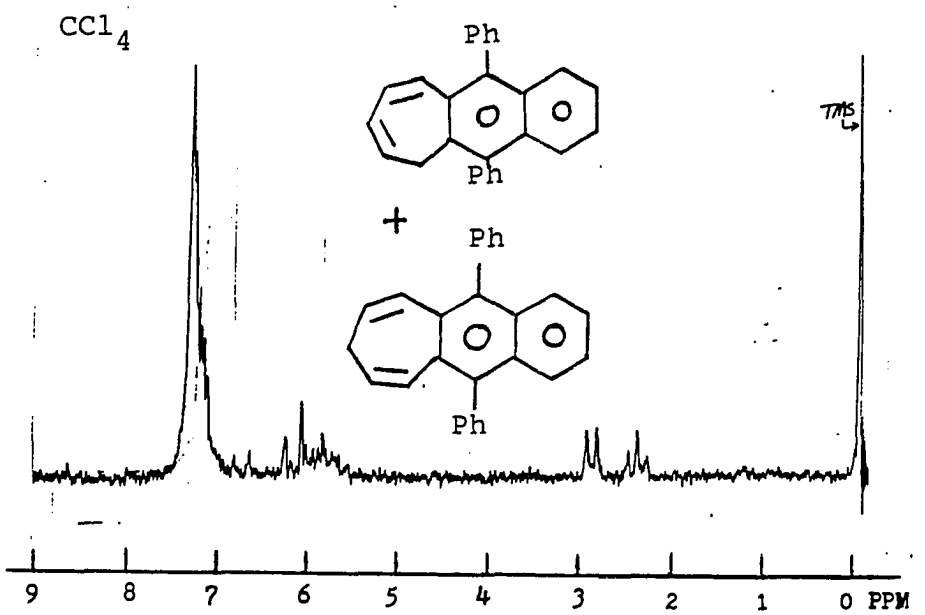


152

ane) in 32% combined yield (rf = 0.71). A similar experiment, run with 38.0 mg of 35-syn and 34.5 mg of DPIBF for 15 minutes at 160° to 165° gave, in 30% isolated yield, a 1.5 to 1 mixture of 151 and 152. The mixture of 151 and 152 was recrystallized from hexane. The first crop consisted of a 1.1 to 1 mixture of 151 and 152 (17% combined yield). Melting

point (Spencer microscope slide apparatus) of the first crop: The crystals sublimed on to the upper microscope slide, resulting in a mixture of needles and plates. The plates melted at 164° to 165.5°, and the needles melted at 168° to 170°. 60 MHz ^{1}H NMR of the first crop (CCl_4): δ 7.28-6.93 (m, 15H); 6.78-6.93 (m) and 6.85 (br s) and 6.5-5.6 (m), combined 4H; 3.00 (d, 1.05 H, J = 6.0 Hz, H^5 of 151); 2.50 (t, 0.95 H, J = 6.0 Hz, H^3 of 152). IR of the first crop (CCl_4): 3070 (s), 3035 (s), 2990 (w), 2960 (sh), 2935 (s), 2890 (w), 2860 (w), 1957 (w), 1812 (w), 1605 (m), 1493 (br m), 1445 (s), 1382 (s), 1375 (sh), 1177 (w), 1088 (w), 1073 (m), 1047 (w), 1035 (sh), 1028 (m), 990 (w), 700 (very s), 683 (s), 653 (m) cm^{-1}. 70 eV MS (Finnegan GC-MS, Column B) of first crop, m/e (%RIC) (151 and 152 had indentical mass spectra): 345 (P+1, 2.44), 344 (P, 9.23), 329 (P-15, 1.02), 267 (4.00), 265 (5.10), 252 (3.42), 169 (1.67), 163 (5.49), 157 (8.58), 151 (3.44), 150 (3.41),143 (2.12), 133 (4.26), 92 (absent), 91 (1.04), 77 (0.95), 51 (0.97). Analysis of the first crop: Calcd. for $C_{27}H_{20}$: 94.15% C, 5.85% H. Found: 93.05% C, 6.03 % H. (Either the product had degraded during transit, or there were some impurities present.) Calcd. for $C_{27}H_{20}$: m/e 344.15650. Found: m/e 344.15526.

The second crop consisted of a 3 to 1 mixture (5% combined yield) of 151 and 152, respectively. 60 MHz ^{1}H NMR



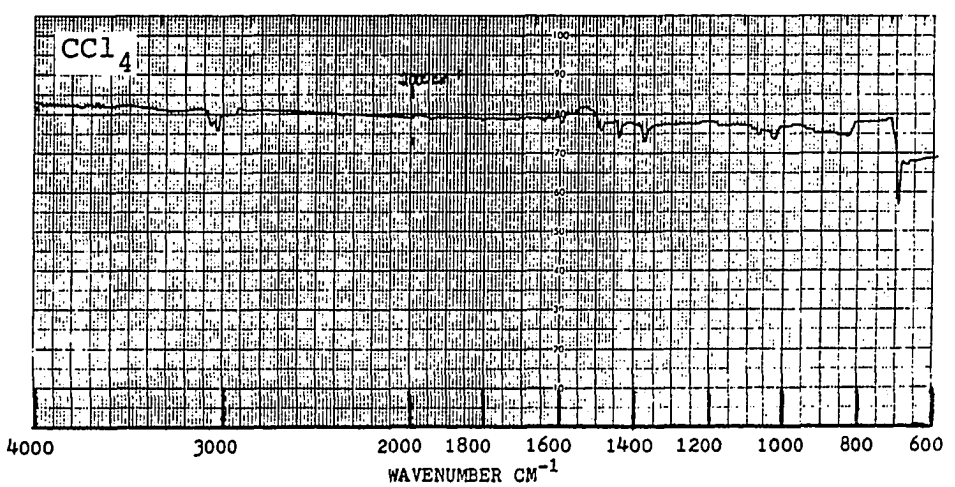


Figure 23. 60 MHz ^{1}H NMR and IR spectra of 151 and 152 (dehydrated DPIBF adducts of 1,2,4-cycloheptatriene), first crop

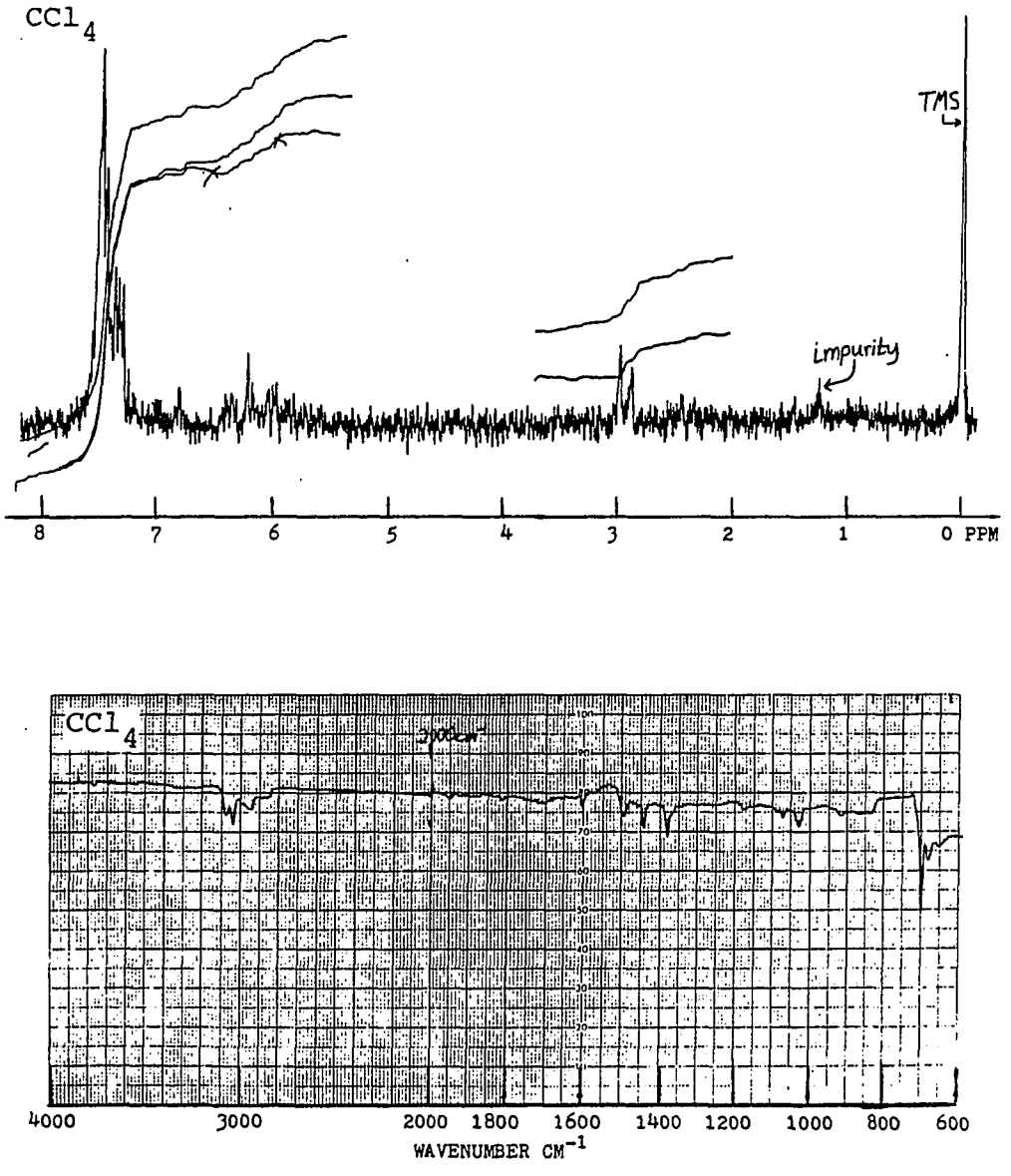


Figure 24. 60 MHz ^{1}H NMR and IR spectra of 151 and 152 (dehydrated DPIBF adducts of 1,2,4-cycloheptatriene), second crop

of the second crop (CCl_4): δ 7.75-6.95 (m, 18H); 6.95-6.7 (m) and 6.8 (br s) and 6.4-5.5 (m), combined 4.5 H; 2.95 (d, 2.0 H, J = 6.0 Hz); 2.50 (t, 0.67 H, J = 6.0 Hz); 1.25 (br s, an impurity). IR of second crop (CCl_4): 3092 (sh), 3075 (s), 3040 (s), 2995 (sh), 2960 (sh), 2935 (s), 2860 (w), 1955 (w), 1815 (w), 1718 (br w), 1607 (m), 1503 (sh), 1496 (m), 1447 (s), 1382 (s), 1177 (w), 1092 (w), 1074 (m), 1037 (sh), 1030 (m), 920 (br w), 700 (very s), 683 (s), 655 (s) cm^{-1}.

12. Solution-phase pyrolysis of cycloheptatriene (148) in the presence of DPIBF

A solution of 11.7 μl (0.113 mmol) of cyclohepta-1,3,5-triene (148) and 34.8 mg (0.129 mmol) of DPIBF in 0.3 ml of benzene-d_6 was placed in an NMR tube. The sample was degassed (3 freeze-high vacuum-thaw cycles), sealed under nitrogen, and heated, fully immersed, in a 166° to 168° oil bath, for 20 minutes. NMR and GC analysis showed no reaction.

13. Pyrolysis of anti-7-bromo-syn-7-trimethylstannylbicyclo-[4.1.0]hept-2-ene (35-anti) in cyclohexane solution

A 46.1 mg sample of 35-anti was dissolved in 0.3 ml of cyclohexane, placed in an NMR tube, degassed (3 freeze-high vacuum-thaw cycles), and then sealed under nitrogen.

The tube was then heated (with 90% of the tube immersed in the oil bath) at 155° to 165° for 37.5 hours. NMR and GC-MS analysis showed that spiro[2,4]hepta-4,6-diene (29) (identified by comparison with an authentic sample) was the major product. Next, the contents of the tube were poured into a stirred solution of 34.4 mg of tetracyanoethylene (TCNE) in 5 ml of dry (freshly distilled from LAH) THF, contained in a 25 ml 3-neck round-bottom flask, under nitrogen. The resulting solution was stirred under nitrogen for 12 hours. Concentration in vacuo left 78 mg of solid material. According to NMR analysis, the major product was the Diels-Alder adduct (147) between TCNE and 29 identified by comparison with an authentic sample). Note: If acetone comes into contact with the crude product mixture, a product between TCNE and acetone forms, with the following 60 MHz NMR (acetone-d_6): δ 2.4 (s), 4.0 (s), 5.95 (s).

14. Solution-phase pyrolysis of 7,7-dibromobicyclo[4.1.0]-hept-2-ene (7) in the presence of tri-n-butyltin hydride

a. With 1.1 equivalents of tri-n-butyltin hydride A 50 ml 3-neck round-bottom flask was equipped with a magnetic stirring bar, an addition funnel, a reflux condenser, and a nitrogen inlet, and was nitrogen-flushed and dried. A

solution of 0.250 ml (0.949 mmol) of tri-n-butyltin hydride in 2 ml of diphenylmethane (previously distilled at aspirator pressure) was placed in the addition funnel, and the flask was charged with a solution of 0.208 g (0.824 mmol) of 7 in 5 ml of diphenylmethane. The flask was immersed in a preheated 162° oil bath, and heated at 162° for 10 minutes. The solution in the addition funnel was then added dropwise over a 1 minute period, and the resulting solution was stirred under nitrogen at 162° to 164° for 1 more hour. GC analysis showed that major amounts of 7-bromobicyclo[4.1.0]hept-2-ene (38-anti and 38-syn) were formed, and that a small amount of cyclohepta-1,3,5-triene (148) was also present in the product mixture.

Distillation of the crude mixture through a short path distillation head (after the addition of 1 ml of carbon tetrachloride) gave a carbon tetrachloride solution of 148 (identified by comparison of its NMR spectrum with that of an authentic sample), with a b.p. of 35° to 40° (pot temperature 80° to 100°). There was no spiro[2,4]hepta-4,6-diene (29) in this carbon tetrachloride solution, but there were traces of toluene and benzene (identified by comparison of their GC retention times with those of authentic samples).

b. With 0.1 equivalent of tri-n-butyltin hydride A 50 ml 3-neck round-bottom flask, equipped with a magnetic

stirring bar, an addition funnel, a reflux condenser, and a nitrogen inlet, was nitrogen-flushed and dried. A solution of 43 μl (0.16 mmol) of tri-n-butyltin hydride in 2 ml of diphenylmethane was placed in the addition funnel, and the flask was charged with a solution of 0.410 g (1.63 mmol) of 7 in 5 ml of diphenylmethane. The flask was next immersed in a preheated oil bath and heated at 163° for 10 minutes. The solution in the addition funnel was added dropwise over a 5 minute period, and the resulting solution was stirred under nitrogen at 163° for 55 more minutes. GC analysis showed that no 29, or 148, or benzene were present in the product mixture. GC-MS analysis (Column A) showed several C_7H_9Br species, and several $C_7H_8Br_2$ species.

15. Solution-phase pyrolysis of 7 (without tri-n-butyltin hydride or DPIBF)

A 50 ml 3-neck round-bottom flask, equipped with a magnetic stirring bar, a reflux condenser, and a nitrogen inlet, was nitrogen-flushed and dried. It was charged with a solution of 0.232 g of 7 in 4 ml of diphenylmethane (previously distilled at aspirator pressure), and immersed in a preheated 165° oil bath, and then heated at 157° to 165° for 70 minutes. The GC trace was virtually identical to that obtained from the experiment which was run with

0.1 equivalent of tri-n-butyltin hydride, described above in entry 14b.

16. Solution-phase pyrolysis of anti-7-bromo-syn-7-trimethylstannylbicyclo[4.1.0]hept-2-ene (35-anti) in the presence of tri-n-butyltin hydride

A 25 ml 3-neck round-bottom flask, equipped with a magnetic stirring bar, an addition funnel, a reflux condenser, and a nitrogen inlet, was nitrogen-flushed and dried prior to being charged with a solution of 31.9 mg (0.0950 mmol) of 35-anti in 2 ml of mesitylene (previously distilled at 45 mm; b.p. 70°). A solution of 5.0 µl (0.019 mmol) of tri-n-butyltin hydride in 1.5 ml of mesitylene was then placed in the addition funnel, and the flask was immersed in a preheated 135° to 136° oil bath (thermostatic temperature control). After 5 minutes, the solution in the addition funnel was added dropwise over a 15 minute period. After 20 hours of heating at 135° to 136°, GC analysis showed that virtually no spiro[2,4]hepta-4,6-diene (29) or trimethyltin bromide were generated. The 35-anti remained virtually unreacted. However, a trace of a product tentatively identified by GC-MS as 7-trimethylstannylbicyclo[4.1.0]hept-2-ene (163) was formed within the first 15 minutes after the tri-n-butyltin hydride addition. 70 eV MS (Finnegan GC-MS,

Column A) of 163, m/e (%RIC): FPTC (first peak of a $Sn^{120,118,116}$ isotope cluster) at 243 ($P^{Sn,120}$-15, 0.31), FPTC at 211 (0.08), 185 (0.04), 169 (1.54), 167 (1.54), FPTC at 165 ($P^{Sn,120}$-93, 8.73), 151 (0.46), FPTC at 150 (1.10), 148 (0.80), 147 (0.57), 145 (0.15), FPTC at 135 (2.23), 121 (0.81), 118 (0.68), 94 (0.66), 93 ($P^{Sn,120}$-165, 8.14), 91 (7.35), 79 (1.57), 78 (1.32), 77 (6.10), 66 (0.38), 65 (3.09), 53 (1.31), 51 (2.11). (The mass spectra of the two epimers of 7-trimethylstannylbicyclo[2.2.1]hept-2-ene, 189-syn and 189-anti, described in entry 31 below were very different from that of 163.)

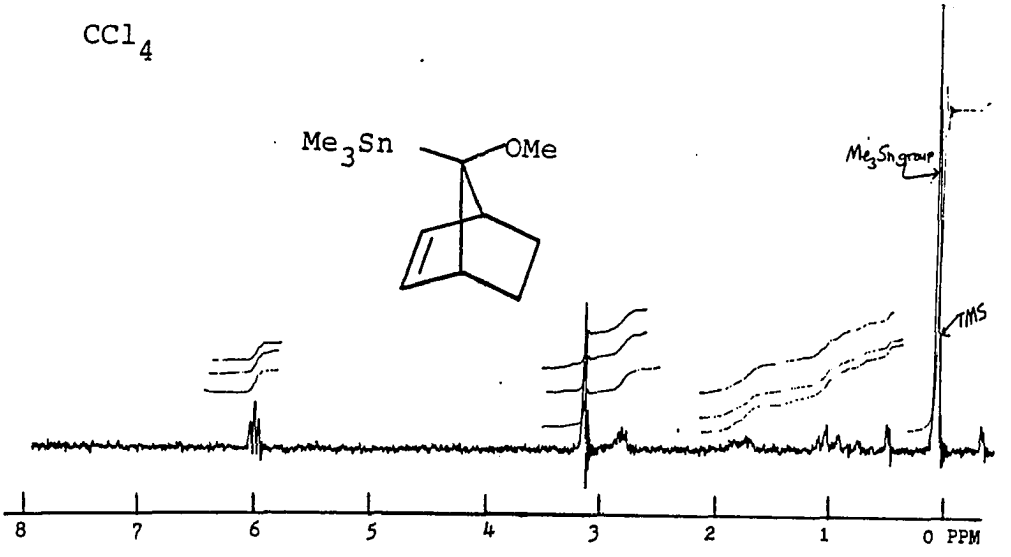
17. Pyrolysis of 35-anti in methanol solution

A solution of 30.5 mg of 35-anti in 0.3 ml of dry (freshly distilled from calcium oxide) methanol was placed in an NMR tube, flushed with nitrogen, and sealed under an atmosphere of nitrogen. The tube was fully immersed in a preheated oil bath which was then maintained at 162° to 167° for 83 minutes. NMR analysis indicated approximately complete consumption of the 35-anti. Along with trimethyltin bromide (24% NMR yield), were obtained a 28% NMR yield of anti-7-methoxy-syn-7-trimethylstannylbicyclo[2.2.1]hept-2-ene (164) and a 44% NMR yield of a product tentatively identified by NMR and GC-MS analysis as anti-7-methoxy-syn-

7-bromodimethylstannybicyclo[2.2.1]hept-2-ene (165). Also observed was a major amount (20% corrected GC yield) of anti-7-bromobicyclo[4.1.0]hept-2-ene (38-anti), identified by comparison of its GC retention time and GC-MS with those of an authentic sample. The 38-anti most likely arose from cleavage of the trimethyltin group of 35-anti by the hydrogen bromide which was generated when 164 and 165 were formed, and when methanol reacted with trimethyltin bromide. Products 164 and 165 were isolated by preparative GC on a 12' x 6 mm, 3% OV-1 glass column (column temperature 110° to 130°, carrier gas flow rate 46 ml/minute). The retention time of 38-anti was 7.5 minutes. The GC retention time of 164 was 17 minutes. 60 MHz ^{1}H NMR of 164 ($CDCl_3$): δ 5.92 (br t, 2H, J = 2 Hz), 3.15 (s, 3H), 2.78 (m, 2H), 1.9-1.6 (m, ca. 2H), 1.15-0.8 (m, ca. 2H), 0.03 (s, with $Sn^{117,119}$ satellites, 9H, $J_{HCSn}^{117,119}$ = 49,52 Hz); (CCl_4): δ 5.92 (br t, 2H, J = 2 Hz), 3.09 (s, 3H), 2.77 (m, 2H), 1.84-1.61 (m, ca. 2H), 1.13-0.68 (m, ca. 2H), 0.03 (s, with $Sn^{117,119}$ satellites 9H) $J_{HCSn}^{117,119}$ = 49,51.5 Hz). 300 MHz ^{1}H NMR, Nicolet NT-300 (C_6D_6): 5.680 (t, 2H, J = 2.2 Hz), 2.939 (s, 3H), 2.66 (m, 2H), 1.87 (m, 2H, $H^{5,6}$ exo), 0.98 (m, 2H, $H^{5,6}$ endo), 0.157 (s, with $Sn^{117,119}$ satellites, 9H). A 2D-NOE 300 MHz ^{1} NMR study showed a weak NOE between the vinyl and the trimethyltin protons, but none between the exo-ethano bridge protons and the trimethyltin protons.

(Unfortunately, there was no NOE between the methoxy and the exo-ethano bridge protons.) IR (C_6D_6): 3030 (w), 2970 (s), 2940 (s), 2860 (w), 2820 (w), 1465 (sh), 1445 (br m), 1265 (m), 1250 (sh), 1210 (sh), 1195 (w), 1180 (sh), 1135 (sh), 1123 (m), 1097 (s), 1060 (m), 1030 (w), 983 (m), 960 (w), 870 (w), 838 (w), 790 (br sh), 760 (br, s), 720 (s) cm^{-1}. ^{13}C NMR, Jeol FX-90Q ($CDCl_3$): δ 135.676 (rel. intens. 822), 54.144 (364), 48.022 (957), 22.127 (991), -7.340 (683); Bruker 300 MHz, dilute sample (C_6D_6): δ 135.5797 (rel. intens. 6.038), 53.6582 (1.535), 48.1429 (5.000), 22.2806 (5.47), -7.5282 (2.066). 70 eV MS (Finnegan GC-MS, Column C), m/e (%RIC): FPTC (first peak of a $Sn^{120,118,116}$ cluster) at 288 ($P^{Sn,120}$, ca. 0.10), FPTC at 273 ($P^{Sn,120}$-15, 0.39), FPTC at 260 ($P^{Sn,120}$-28, 0.24), FPTC at 165 ($P^{Sn,120}$-123, 5.32), 123 ($P^{Sn,120}$-165, 23.55), 95 (4.40), 91 (5.07), 79 (2.70), 77 (2.12), 65 (1.32), 53 (3.50), 52 (6.04), 51 (4.21). Analysis: Calcd. for $C_{10}H_{17}OSn$ (P-15), m/e 273.03014. Found: m/e 273.03041. (Parent present, but too weak to measure accurately.)

The retention time of 165 (tentatively identified as such), on the above described preparative GC column, was 45 minutes. 60 MHz ^1H NMR of 165 ($CDCl_3$): δ 6.06 (br t, 2H, J = 2 Hz), 3.41 (s, v. small, impurity), 3.36 (s, 3H), 3.02 (m, 2H), 2.02-1.65 (m, ca. 2H), 1.37-1.0 (m, ca. 2H), 0.67 (s,



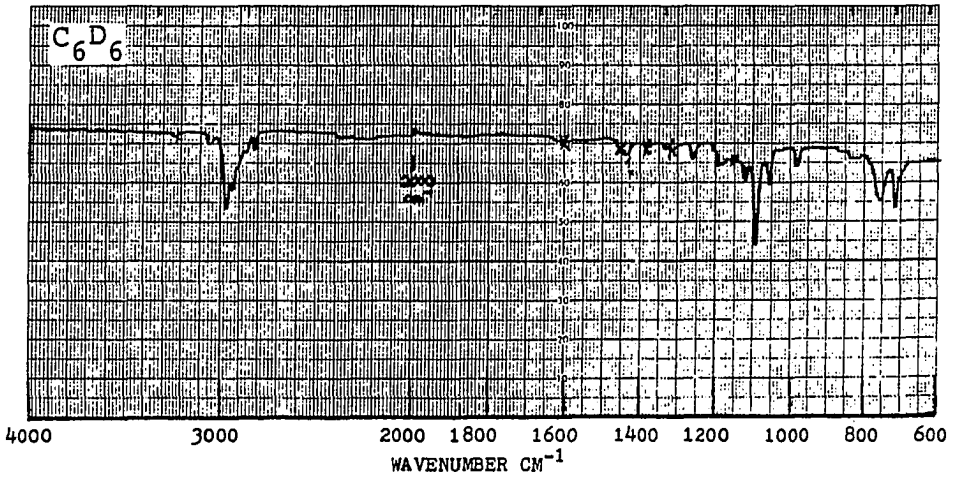
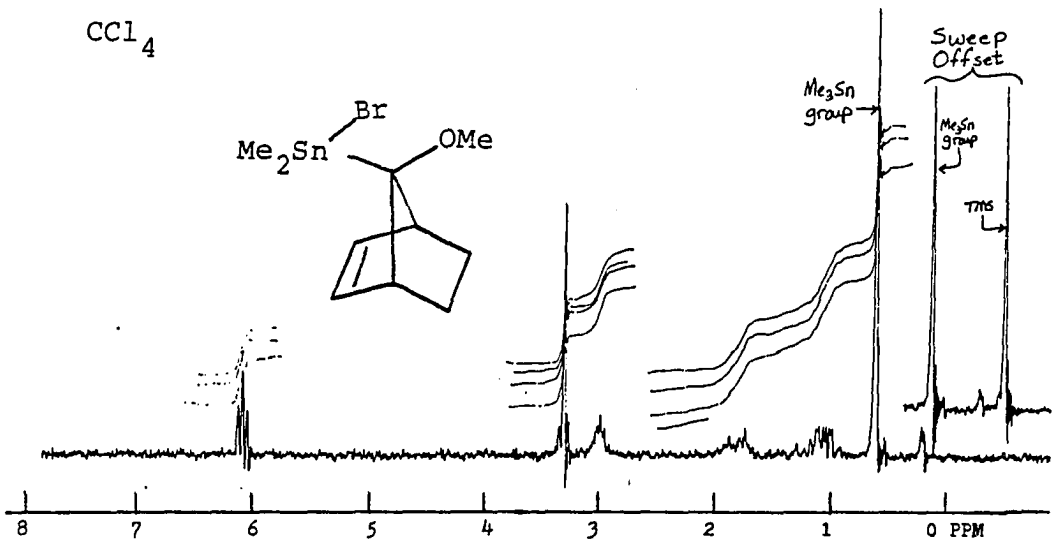


Figure 25. 60 MHz ^{1}H NMR and IR spectra of 164 (anti-7-methoxy-syn-7-trimethylstannylbicyclo[2.2.1]-hept-2-ene)



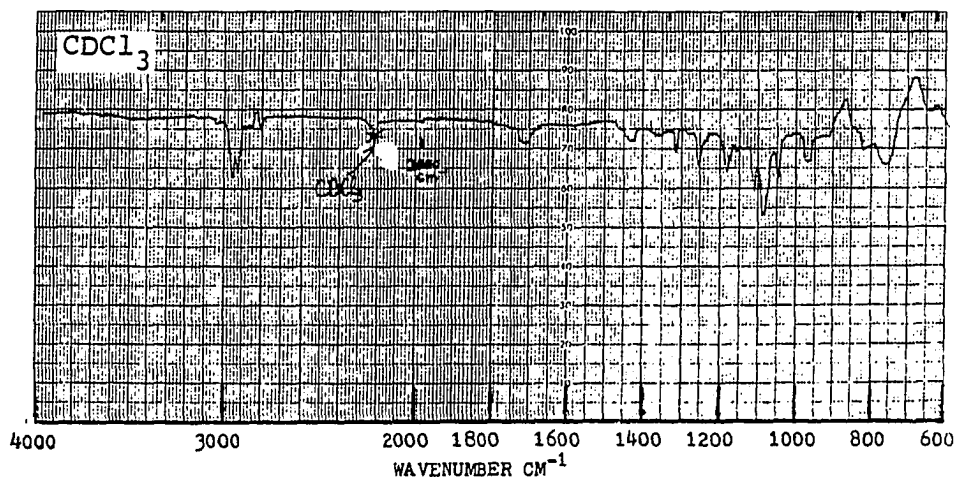


Figure 26. 60 MHz ^{1}H NMR and IR spectra of 165 (anti-7-methoxy-syn-7-bromodimethylstannylbicyclo-[2.2.1]hept-2-ene)

with $Sn^{117,119}$ satellites, 6H, $J_{HCSn}^{117,119}$ = 49.5,52 Hz); ($\underline{CCl_4}$): δ 6.07 (br t, 2H, J = 2 Hz), 3.38 (s, v. small, impurity), 3.33 (s, 3H), 3.01 (m, 2H), 2.06-1.69 (m, ca. 2H), 1.26-1.04 (m, ca. 2H), 0.64 (s, with $Sn^{117,119}$ satellites, 6H, $J_{HCSn}^{117,119}$ = 49,52 Hz). IR ($CDCl_3$): 3065 (w), 2980 (s), 2950 (s), 2870 (w), 2833 (w), 1770 (br, w), 1735 (br, m), 1450 (br, m), 1332 (m), 1300 (w), 1270 (m), 1255 (sh), 1197 (m), 1190 (sh), 1174 (w), 1160 (w), 1130 (m), 1105 (br, s), 1065 (m), 990 (br, m), 985 (sh), 840 (m), 825 (w), 770 (br, m) cm^{-1}. ^{13}C NMR, Jeol FX-90Q ($CDCl_3$): δ 136.976 (rel. intens. 1614), 102.034 (385), 55.066 (483), 48.076 (1051), 22.127 (1264), 1.273 (517). 70 eV MS (Finnegan GC-MS, Column C), m/e (%RIC): FPTC (first peak of a $Sn^{120,118,116}$ cluster) at 231 ($P^{Sn,120}$+ 2-123, 0.09), 229 ($P^{Sn,120}$-123, 0.17), 123 ($P^{Sn,120}$-229, 35.99), 95 (9.21), 91 (7.99), 79 (4.62), 77 (3.39), 65 (2.21), 53 (1.38), 52 (2.59), 51 (1.95). (The parent peak was not visible.)

18. Pyrolysis of syn-7-bromo-anti-7-trimethylstannyl-bicyclo[4.1.0]hept-2-ene (35-syn) in the presence of methanol

A 5.1 mg sample of 35-syn was dissolved in 0.35 ml of 71% methanol/29% benzene-d_6 (measured by volume), placed in an NMR tube, briefly flushed with nitrogen, and sealed under

nitrogen. The tube was then fully immersed in a preheated oil bath, which was then maintained at 100.5° to 101.5° (thermostatic temperature control) for 35 minutes. Analysis by NMR indicated 100% consumption of the starting material. Analysis by GC-MS showed, in addition to trimethyltin bromide, a trace amount of cyclohepta-1,3,5-triene, and traces (ca. 3% yield, each) of 6 compounds tentatively identified as 178a (5-methoxy-2-trimethylstannylcyclohepta-1,3-diene), 178b (7-methoxy-1-trimethylstannylcyclohepta-1,3-diene), 178c (3-methoxy-2-trimethylstannylcyclohepta-1,4-diene), 178d (4-methoxy-1-trimethylstannylcyclophepta-1,3-diene), 179a (2-trimethylstannylcyclohepta-1,3,5-triene), and 179b (3-trimethylstannylcyclohepta-1,3,5-triene), respectively. Representative 70 eV MS (Finnegan GC-MS, Column E) for 178a through 178d, m/e (%RIC): FPTC (first peak of a $Sn^{120,118,116}$ isotope cluster) at 288 ($P^{Sn,120}$, 0.07), FPTC at 273 ($P^{Sn,120}$-15, 0.30), FPTC at 229 (1.24), FPTC at 199 (0.64), FPTC at 165 ($P^{Sn,120}$-123, 5.49), FPTC at 150 (0.65), FPTC at 135 (1.49), 124 (4.74), 123 ($P^{Sn,120}$-165, 3.49), 109 (6.60), 92 (2.96), 91 (17.03), 79 (2.14), 77 (2.18), 65 (2.08), 53 (1.32), 51 (0.86). Representative 70 eV MS (Finnegan GC-MS, Column E) for 179a and 179b, m/e (%RIC): FPTC (first peak of a $Sn^{120,118,116}$ isotope cluster) at 256 ($P^{Sn,120}$, 0.39), FPTC at 241 ($P^{Sn,120}$-15, 2.42), FPTC at 211 (1.15), FPTC at 165 ($P^{Sn,120}$-91, 5.67), FPTC at 135 (2.37), FPTC at 120

(Sn^{120}, 1.64), 92 (3.55), 91 ($P^{Sn,120}$-165, 37.79), 77 (0.66), 65 (2.11), 51 (0.39).

19. Pyrolysis of anti-7-bromo-syn-7-trimethylstannyl-bicyclo[4.1.0]hept-2-ene (35-anti) in triethylsilane solution

A solution of 25.2 mg of 35-anti in 0.3 ml of triethylsilane was placed in an NMR tube, flushed with nitrogen, and sealed under a nitrogen atmosphere. The tube was fully immersed in a preheated oil bath, which was then maintained at 163° to 167° for 122 minutes. Along with approximately the normal amount of trimethyltin bromide (judged by the GC trace), was obtained a 74% NMR yield of syn-7-triethylsilyl-bicyclo[2.2.1]hept-2-ene (186). There was no spiro[2,4]-hepta-4,6-diene (29) formed (determined by NMR and GC analysis). There was a small amount (ca. 10% yield) of a product tentatively identified as either bicyclo[4.1.0]hept-2-ene. Preparative TLC on silica gel (hexane) gave a pure sample of 186. 60 MHz ^{1}H NMR of 186 (CCl_4): δ 5.81 (t, 2.0H, J = 2 Hz), 2.92 (m, 2.0H), 1.9-0.2 (complex m, 23H, possibly included impurities); (C_6D_6): δ 5.75 (t, 2.0H, J = 2 Hz), 2.86 (m, 2.0H), 1.75-0.2 (complex m, 23H, possibly included impurities). Irradiation of the δ 2.86 multiplet caused the δ 5.75 triplet to collapse to a singlet ($w_{1/2}$ = 5.7 Hz).

300 MHz ^{1}H NMR, (C_6D_6): δ 5.782 (t, 2.0H, J = 1.95 Hz), 2.865 (m, 2.0H), 1.552 (d of m, 2.0H, J = 7.2, 1 Hz, $H^{5,6\,exo}$), 1.026 (dd, 2.4H, J = 7.2, 3.9 Hz, $H^{5,6\,endo}$), 0.974 (t, 9.2H, J = 7.8 Hz, methyl of triethylsily group), 0.724 (sl. broadened s, 1.0H, $w_{1/2}$ = 2.7 Hz, $H^{7\,anti}$), 0.509 (q, 6.6H, J = 7.8 Hz, methylene of triethylsilyl group). A 2D-NOE experiment was described in the Results and Discussion section. The chemical shifts of $H^{5,6\,exo}$ and $H^{5,6\,endo}$ were assigned by their relative chemical shifts, by comparison with numerous known examples of bicyclo[2.2.1]hept-2-ene derivatives.[28,102] IR (CCl_4): 3070 (w), 2960 (s), 2942 (sh), 2915 (m), 2880 (s), 2860 (sh), 2810 (sh), 1467 (sh), 1462 (m), 1445 (sh), 1417 (m), 1377 (w), 1331 (m), 1303 (w), 1254 (w), 1240 (m), 1183 (m), 1147 (w), 1117 (m), 1087 (w), 1075 (w, br), 1015 (s), 1005 (sh), 972 (w), 950 (w), 932 (w), 907 (w), 871 (m), 860 (w), 847 (sh), 839 (w), 705 (s), 682 (sh), 655 (br, sh) cm^{-1}; ^{13}C NMR, Jeol FX-90Q (C_6D_6): δ 134.517 (rel. intens. 1302), 48.058 (668), 44.754 (1574), 26.982 (1636), 7.641 (2154), 4.614 (2363). Note that a similar ^{13}C NMR spectrum run on a crude sample of 186 showed no evidence of any of its stereoisomer, to within the limits of detection of NMR. 70 eV MS (Finnegan GC-MS, Column C), m/e (%RIC): 208 (P, absent), 180 (P-28, 4.70), 179 (P-29, 4.00), 151 (P-57, 6.17), 123 (2.90), 115 (P-93, 16.68), 113 (3.59), 95 (2.65), 93

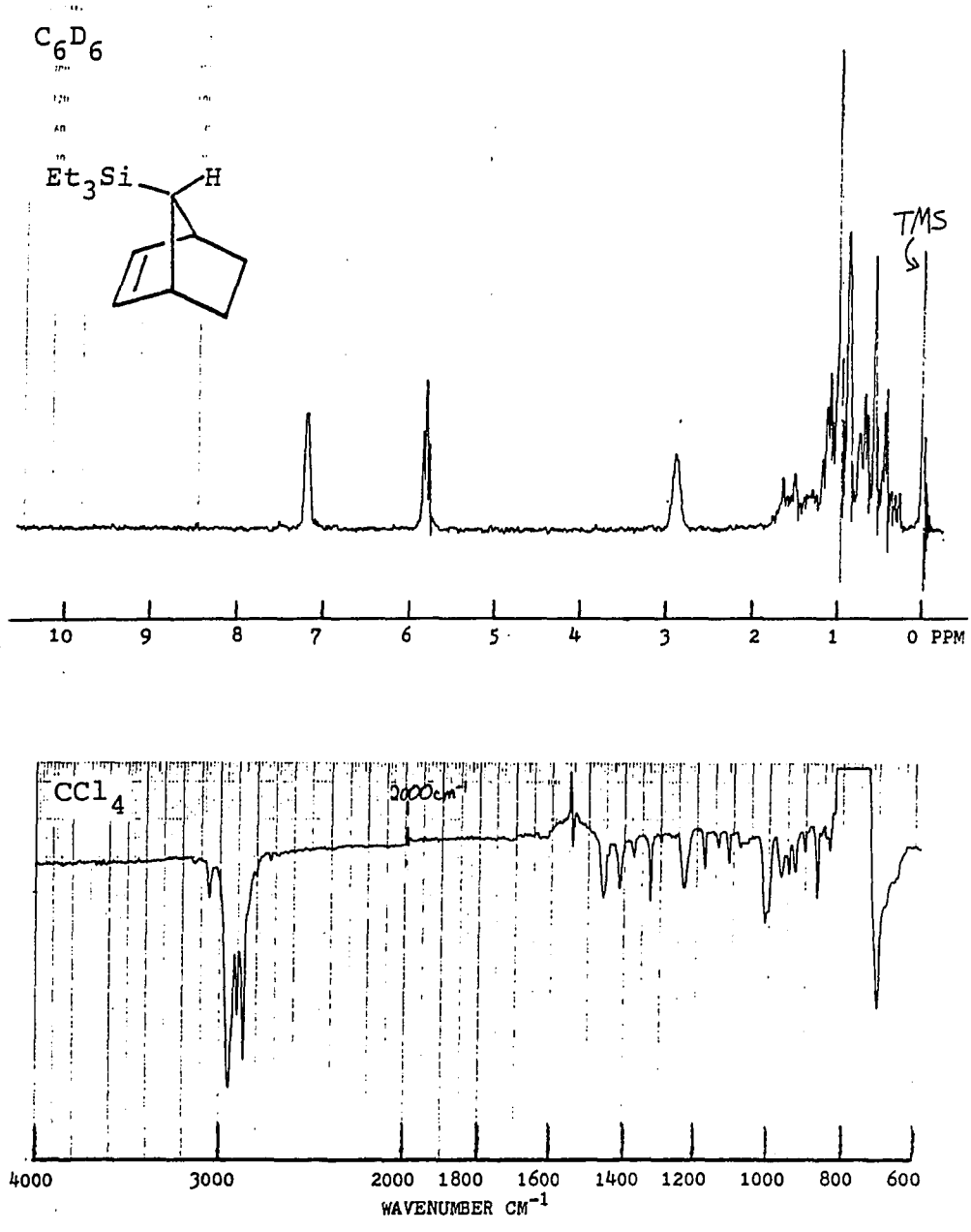


Figure 27. 60 MHz ^{1}H NMR and IR spectra of 186 (syn-7-triethylsilylbicyclo[2.2.1]hept-2-ene)

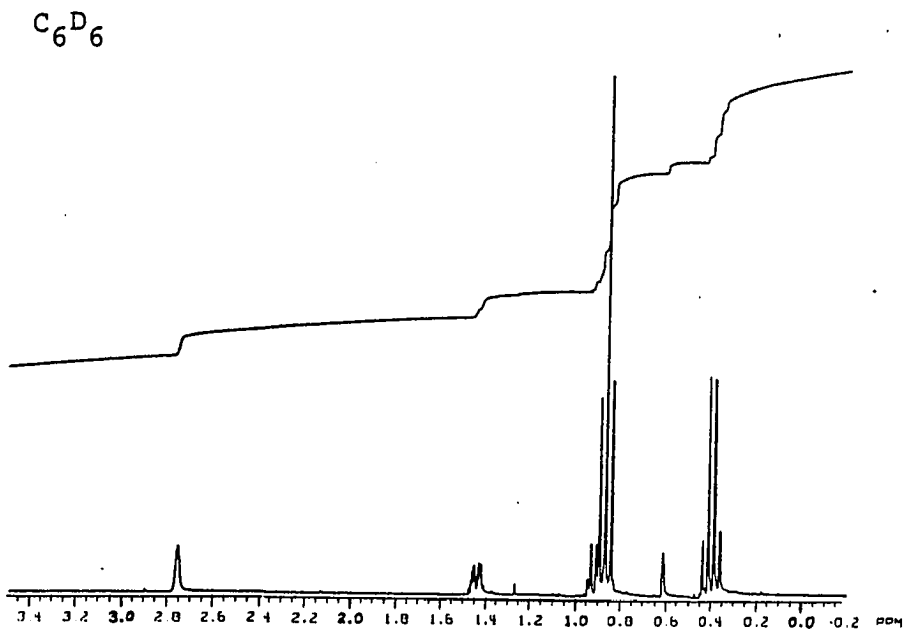


Figure 28. 300 MHz ^{1}H NMR of 186 (syn-7-triethylsilyl-bicyclo[2.2.1]hept-2-ene)

(P-115, 2.05), 87 (12.92), 85 (2.79), 59 (10.37), 57 (2.73). Analysis: Calcd. for $C_{11}H_{19}Si$ (P-29): m/e 179.12560. Found: m/e 179.12612. (The parent peak was absent.)

Also observed by GC-MS analysis, on Column C, of the product mixture was a trace (ca. 1% yield) of a compound which could be anti-7-triethylsilylbicyclo[2.2.1]hept-2-ene (187) or 7-triethylsilylbicyclo[4.1.0]hept-2-ene. 70 eV MS (Finnegan GC-MS, Column C): 208 (P, 0.25), 180 (P-28, 2.23), 179 (P-29, 2.28), 151 (P-57, 8.05), 123 (4.75), 115 (P-93, 17.04), 113 (1.64), 95 (2.77), 93 (P-115, 2.30), 91 (2.27), 87 (13.31), 85 (1.72), 59 (11.63), 57 (2.55).

20. Pyrolysis of 35-anti in tetramethylethylene solution

A 30.7 mg sample of 35-anti was dissolved in 0.3 ml of tetramethylethylene, placed in an NMR tube, thoroughly flushed with nitrogen, and then sealed under nitrogen. The tube was then 90% immersed in a preheated oil bath, and heated at 155° to 165° for 5 hours. NMR and GC-MS analysis showed that spiro[2,4]hepta-4,6-diene (29), identified by comparison with an authentic sample, was the major product. GC-MS analysis also showed the presence of several $C_{14}H_{16}$ species, which were also present in the product mixtures from the benzene pyrolyses of 35-anti, (vide supra), but there was none of the cyclopropanation product 190.

21. Pyrolysis of 35-anti in cyclohexene solution

A solution of 32.3 mg of 35-anti in 0.3 ml of cyclohexene (distilled prior to use) was placed in an NMR tube, flushed with nitrogen, and sealed under an atmosphere of nitrogen. The tube was then completely immersed in a preheated oil bath, and heated at 160° to 165° for 398 minutes. NMR analysis indicated that the starting material was approximately 100% consumed. Trimethyltin bromide was obtained in ca. quantitative yield (NMR yield), and spiro-[2,4]hepta-4,6-diene (29) was produced in ca. 80% yield (NMR yield). GC-MS analysis revealed the presence of five $C_{14}H_{16}$ species (in very low yield), but none of the cyclopropanation product 191.

22. Pyrolysis of 35-anti in chloroform solution

A solution of 30.3 mg of 35-anti in 0.3 ml of chloroform (stabilized with 0.75% ethanol) was placed in an NMR tube, flushed with nitrogen, and sealed under an atmosphere of nitrogen. The tube was then completely immersed in a preheated oil bath, which was then kept at 162° to 167° for 83 minutes. NMR analysis showed complete consumption of 35-anti. Trimethyltin bromide was obtained approximately quantitatively (NMR yield), and the NMR yield of spiro[2,4]-hepta-4,6-diene (29) was 37%. Also observed by NMR (after

evaporation of the solvent) and GC-MS was a product tentatively identified as anti-7-ethoxy-syn-7-trimethylstannylbicyclo[2.2.1]hept-2-ene (194), in 4.1% yield (NMR yield). 60 MHz ^{1}H NMR of 194 ($CDCl_3$): δ 6.01 (t, 2H, J = 2.5 Hz), 3.40 (q, ca. 4H, J = 7 Hz), 1.28 (t, ca. 6H, J = 7 Hz), 0.04 (s, with $Sn^{117,119}$ satellites, 9H). 70 eV MS (Finnegan GC-MS, Column C): FPTC (first peak of a $Sn^{120,118,116}$ cluster) at 302 ($P^{Sn,120}$, ca. 0.015), FPTC at 287 ($P^{Sn,120}$-15, 0.10), FPTC at 274 ($P^{Sn,120}$-28, 0.13), FPTC at 273 ($P^{Sn,120}$-29, 0.21), FPTC at 165 ($P^{Sn,120}$-137, 6.13), 137 ($P^{Sn,120}$-165, 22.42), 109 (8.19), 81 (6.61), 53 (1.37), GC-MS analysis showed none of the carbene trapping products 192 and 193.

23. Preparation of 7,7-dimethoxy-1,2,3,4-tetrachlorobicyclo[2.2.1]hept-2-ene (203)

Compound 203 was prepared from 5,5-dimethoxy-1,2,3,4-tetrachlorocyclopenta-1,3-diene according to the procedure of Gassman and Marshall.[112] Because, in the present work, it was to be prepared on a much smaller scale than in the literature preparation, a somewhat different reaction apparatus was required. It consisted of a 10 x 2.7 cm test tube (with a female standard taper joint), which was equipped with a Claisen adaptor. The Claisen adaptor had a large reflux condenser (with a drying tube) attached to one of its necks. The fritted glass portion of a coarse gas dispersion

tube was inserted down into the bottom of the reaction tube, with its open end extending out through a rubber septum (which had been installed in the second neck of the Claisen adaptor). In this way, it was easy to make sure that the fritted glass portion of the bubbler was completely immersed in the reaction mixture.

A 15 g sample of 5,5-dimethoxy-1,2,3,4-tetrachlorocyclopenta-1,3-diene[113] was placed in the test tube of the above apparatus, and heated at 180° to 190° (oil bath) while a slow bleed of a mixture of nitrogen and ethylene gases (somewhat richer in ethylene than in nitrogen) was passed through the bubbler. The level of liquid was ca. 1/4 inch above the top of the fritted glass. Approximately 1/2 inch of froth was maintained on the top of the solution. After 11 hours, NMR analysis indicated that the reaction was 96% complete. The pressure inside the ethylene tank (a 4.5 lb. tank) had dropped only 50 psi during the course of the reaction. (If the apparatus is not designed to use the ethylene very efficiently, the ethylene will be used much more rapidly than this.)

The above crude product was combined with a similar one (prepared from 16.5 g of 5,5-dimethoxy-1,2,3,4-cyclopenta-1,3-diene), and distilled through a 13 cm distillation head at 0.02 to 0.05 mm. During the initial pump-down (up

to a pot temperature of 50°), some volatile material tended to get into the pump trap, and thereby reduce the vacuum. The trap had to be cleaned out at this stage, in order to assure a constant pressure throughout the distillation, so that the progress of the distillation could be minitored. It was found that when the distillate became nearly colorless, pure product was being collected.

Fraction 1: b.p. 36-43°, 0.02-0.05 mm, pot temp. 100°; o.6 g of yellow oil. NMR analysis showed it to be mostly starting material (methoxy group singlet at δ 3.30) plus an unidentified impurity, X (methoxy group singlet at δ 3.39).

Fraction 2: b.p. 43-46°, 0.02-0.05 mm, pot temp. 100°; 3.0 g of yellow oil. NMR analysis showed it to be a mixture of 203 (ca. 50%), starting material (ca. 25%), and impurity X (ca. 25%).

Fraction 3: b.p. 46-52°, 0.02-0.05 mm, pot temp. 100°; 2.75 g of yellow oil. NMR analysis showed that it was mostly 203, but contained substantial amounts of starting material and impurity X.

Fraction 4: b.p. 52-55°, 0.02-0.05 mm, pot temp. 100°; 2.96 g of yellow oil. NMR analysis showed the presence of 203, plut starting material (ca. 6%) and impurity X (ca. 8%).

Fraction 5: b.p. 54-59°, 0.02-0.05 mm, pot temp. 110°; 6.11 g of slightly yellow oil. NMR analysis showed that it

contained 203, plus starting material (ca. 1.5%), and impurity X (ca. 2%).

Fraction 6: b.p. 59-62°, 0.02-0.05 mm, pot temp. 110° to 135°; 15 g of colorless oil. NMR analysis showed that it consisted of pure 203. 60 MHz ^{1}H NMR of 203 (CCl_4): δ 3.49 (s, 3H), 3.42 (s, 3H), 2.4-1.5 (complex m, 4H).

Fractions 4,5, and 6 were combined to give 24.1 g (72% yield) of 97% pure (by NMR) 203 (b.p. 52-62°, 0.02-0.05 mm).

24. Preparation of 7,7-dimethoxybicyclo[2.2.1]hept-2-ene (204)

The procedure used was that of Gassman and Marshall.[112] A 500 ml 3-neck round-bottom flask, was equipped with a reflux condenser, a 75 ml addition funnel, and an overhead mechanical stirrer (nichrome wire paddle). The apparatus was thoroughly flushed with nitrogen. Then 18.3 g (0.796 g-atom) of sodium (cut into small pieces) were added to the flask, followed by a 5 minute nitrogen flush. Next, 210 ml of dry (freshly distilled from LAH) THF and 26 ml of dry (freshly distilled from calcium hydride) tert-butyl alcohol were added. A solution of 14.7 g (0.0503 mole) of 203 in 10 ml of dry THF was placed in the addition funnel, and the flask contents were vigorously stirred, and brought to a gentle reflux. The 203/THF solution was added dropwise over a

2 hour period. (The heating had to be decreased somewhat in order to keep the reaction under control.) The reaction mixture was stirred and heated to reflux for 10 hours, after which time the pieces of sodium had become fused into a single large chunk, so the reaction was probably already finished. After 1 more hour, the heating and stirring were discontinued, and the mixture was allowed to cool to room temperature, and then filtered, with the aid of a 20 ml ether rinse, through a 4 x 4 inch wire screen, and then re-filtered, via suction filtration, through "Celite 503" diatomaceous earth. (Note that this filtration takes a very long time. It has been suggested[112] that it can be replaced by a careful quench with methanol.) The filter was rinsed with two 30 ml portions of ether, which were then added to the main filtrate. The filtrate was poured into a beaker containing 300 ml of chopped ice and 35 ml of ether. After the ice had been allowed to melt, the mixture was transferred to a separatory funnel and shaken. The organic layer was withdrawn and washed with three 20 ml portions of saturated sodium chloride solution, dried (anhydrous magnesium sulfate), filtered, and concentrated via atmospheric pressure distillation (employing a 17 cm distillation head), with a pot temperature of 60° to 95°. The residue was then distilled at aspirator pressure through a 6 inch vigreaux

column. After a brief forerun had been collected, a 57% yield of product 204 (a light yellow liquid) was collected at 68° to 71°, at aspirator pressure (pot temperature 80° to 110°). 60 MHz ^{1}H NMR of 204 (CCl_4): δ 5.92 (t, 2H, J = 2 Hz), 3.12 (s, 3H), 3.05 (s, 3H), 2.65 (m, 2H), 2.05-0.65 (complex m, 4H).

25. Preparation of bicyclo[2.2.1]hept-2-en-7-one (52)

The procedure used was that of Gassman and Marshall,[114a] and Gassman and Pape.[114b] A 10 ml round-bottom flask was charged with a magnetic stirring bar, 1.97 g of 204, and 3 ml of 5% aqueous sulfuric acid. The mixture was vigorously stirred at 27° to 37° (oil bath) for 22 hours, after which time it was cooled to room temperature and extracted with 3 x 5 ml of distilled pentane. The pentane extracts were combined and dried (anhydrous magensium sulfate), filtered, and concentrated via atmospheric pressure distillation, using a 6 inch vigreaux column (pot temperature 45° to 65°). The residue was further concentrated at 80 mm (room temperature), and then distilled through the 6 inch vigreaux column. An 89% yield of product 52 (colorless liquid) was obtained (b.p. 75° to 77° at 80 mm, pot temperature 110° to 120°). (A heat gun had to be applied to the distillation apparatus in order to get out the last half of the product.) NMR

analysis showed that it consisted of a 12 to 88 (weight ratio) mixture of 204 and 52, respectively. The product was stored in a freezer in a glass stoppered flask. (Gassman and Marshall[114] made a special note about the volatility of 52.) 60 MHz ^{1}H NMR of 52 (CCl_4): δ 6.52 (t, 2H, J = 2 Hz), 2.75 (m, 2H), 2.25-0.75 (complex m, 4H).

26. Preparation of bicyclo[2.2.1]hept-2-en-7-one tosylhydrazone (195)

The procedure used was basically that of Murahashi et al.,[24] but it was found that the rate of product formation was strongly dependent upon whether an acid catalyst was present. Murahashi et al. evidently had a substantial amount of sufuric acid impurity in their sample of 52 (see below), which caused 195 to form quite rapidly when the 52 was treated with p-toluenesulfonylhydrazine (tosylhydrazine).

a. Without adding an acid catalyst To a solution of 0.91 g (4.9 mmol) of tosylhydrazine in 15 ml of absolute methanol was added 0.60 g (4.9 mmol) of 52 (the above prepared 88% pure product). The resulting solution was stirred at room temperature for 3 hours, and was then allowed to stand at room temperature overnight (stoppered flask). The solution turned slightly yellow, and only a very small quantity of crystals precipitated out. The volume of the

solution was reduced to one half, via a nitrogen flush, and it was then refrigerated for 3 hours, and filtered, yielding 0.80 g (59% crude yield) of small white crystals. Recrystallization from 6 ml of hot methanol, plus 10 drops of water, yielded a 0.44 g first crop of white crystals, and a 0.07 g second crop of yellow crystals. The first and second crops had identical IR spectra. The first and second crops were combined, to give a 38% yield of 195. 60 MHz ^{1}H NMR of 195 (K_2CO_3-dried CD_2Cl_2): δ 7.81-7.20 (AB quartet, 5H, spacings= 26, 8 Hz; the most unfield peak of the AB quartet became sharper and smaller upon the addition of D_2O, because it included the N-H proton, and the AB quartet integrated to 4H in the presence of D_2O), 6.40-6.21 (ddd, 1H, spacings = 3, 1, 0.5 Hz), 6.21-6.02 (ddd, 1H, spacings = 3, 1, 0.5 Hz), 3.37 (m, 1H), 2.97 (m, 1H), 2.42 (s, 3H), 1.92-0.97 (complex m, 4H). Irradiation at δ 2.97 caused the δ 6.40-6.21 ddd to collapse to a broad perturbed doublet (J = 3 Hz), and the δ 6.21-6.02 ddd to collapse to a perturbed dd (spacings = 3, 1 Hz), and the low-field half of the δ 1.92-0.97 multiplet to become somewhat less complex. Irradiation at δ 3.37 caused the δ 6.21-6.02 ddd to become a broad, perturbed doublet (J = 3 Hz), and the δ 6.40-6.21 ddd to become a perturbed dd (spacings = 3, 1 Hz), and the low-field half of the δ 1.92-0.97 multiplet to become less complex.

IR (nujol mull): 3220 (s), 1930 (w), 1810 (w), 1720 (sh), 1708 (m), 1690 (sh), 1595 (m), 1582 (sh), 1493 (w), 1403 (m), 1335 (s), 1290 (w), 1163 (s), 1135 (w), 1120 (m), 1090 (m), 1015 (br m), 930 (br m), 875 (w), 860 (w), 812 (m), 785 (w), 727 (m), 709 (m), 660 (br m) cm^{-1}. This IR spectrum agreed very well with that reported in the literature.[24]

b. With an added acid catalyst To a stirred solution of 0.153 (0.819 mmol) of p-toluenesulfonyl hydrazine and 1.6 mg of p-toluenesulfonic acid in 1.5 ml of dry (freshly distilled from calcium oxide) methanol was added (over a one minute period, via pipet) a solution of 0.100 g (0.817 mmol) of 88% pure 52 in 0.5 ml of dry methanol. The resulting solution (in a tightly stoppered flask) was stirred at room temperature for 40 minutes, after which time a large quantity of white solid suddenly began precipitating out. After a total of 2 hours of stirring, the solid was filtered and dried under high vacuum for 30 minutes, resulting in 0.11 g (49% yield) of a fluffy white powder, whose NMR and IR spectra were identical to those of product 195, described above in procedure a.

When a crude sample of 195 was dissolved in acetone-d_6, the 195 gradually disappeared (according to NMR analysis), and was replaced by bicyclo[2.2.1]hept-2-en-7-one (52),

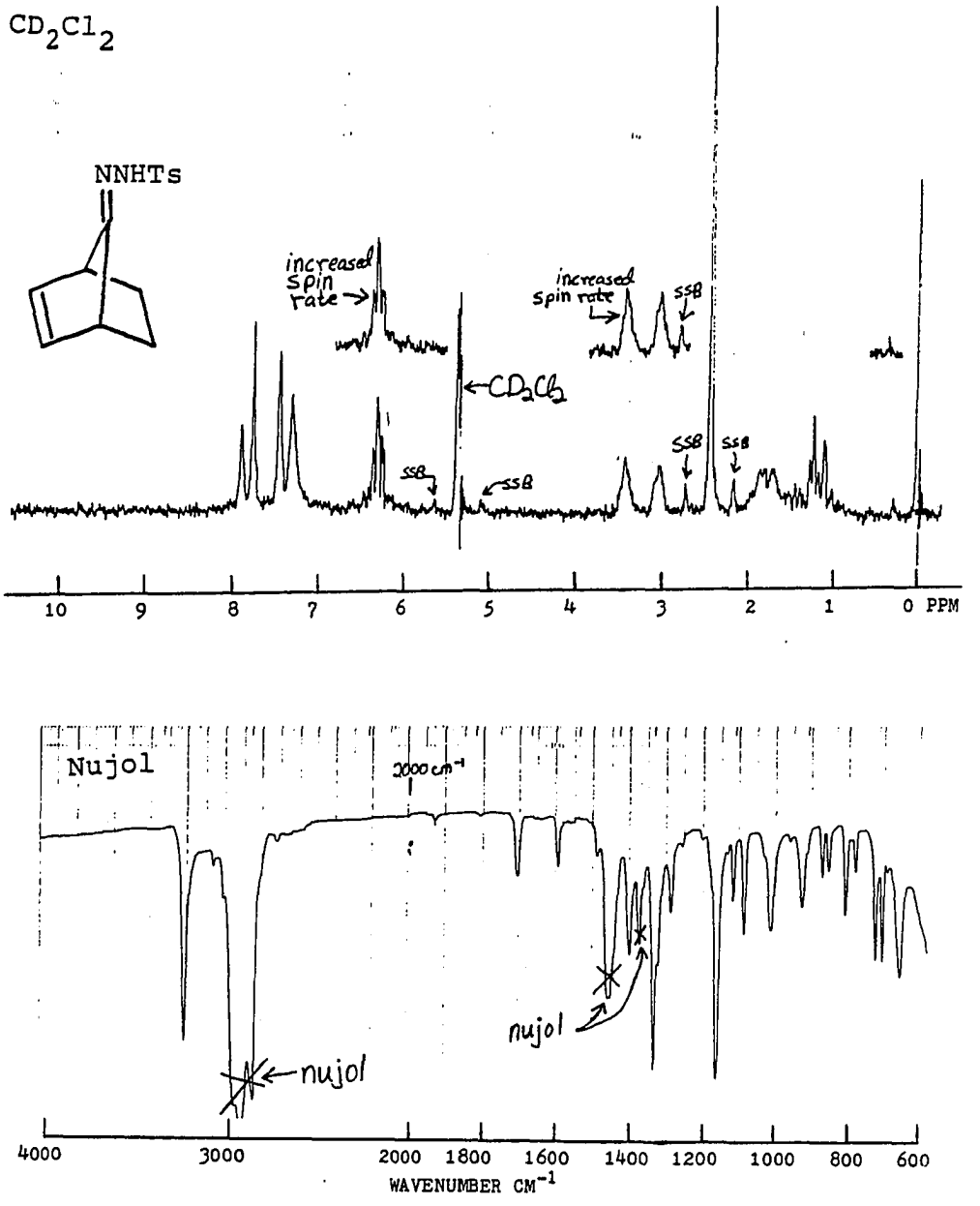


Figure 29. 60 MHz ^1H NMR and IR spectra of 195 (bicyclo-[2.2.1]hept-2-en-7-one tosylhydrazone)

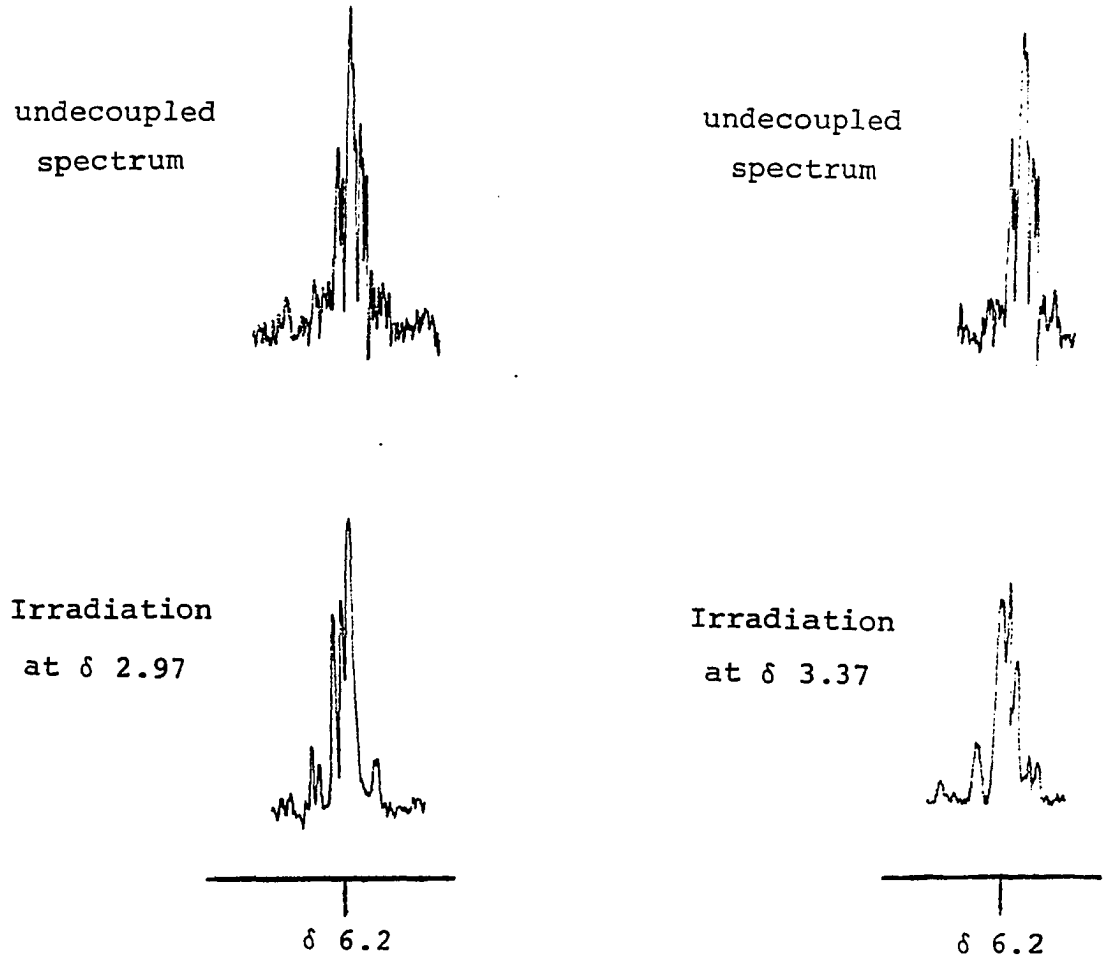


Figure 30. 60 MHz ^{1}H NMR decoupling study of 195 (bicyclo-[2.2.1]hept-2-en-7-one tosylhydrazone)

identified by its NMR spectrum, and by the fact that it vaporized away upon being subjected to high vacuum at room temperature for 30 minutes. The tosylhydrazone of acetone-d_6 was presumably also formed. It took 30 minutes for 50% conversion of the 195 to occur, and ca. 2 hours for complete conversion. This acid-catalyzed conversion of 195 and 52 (whose rate is, of course, dependent upon the acid concentration) in acetone-d_6 solution readily explains why Murahashi and co-workers[24] mistakenly reported the NMR spectrum of 52 as being that of 195. A recrystallized sample of 195 was converted much more slowly (overnight) to 52. A recrystallized sample of 195, which had been dried over potassium carbonate (as a benzene solution) beforehand, remained stable as an acetone-d_6 solution, even after D_2O had been added, and it had been allowed to stand overnight. When a recrystallized sample of 195, which contained traces of p-toluenesulfonic acid, was dissolved in methylene chloride-d_2, 52 was again slowly generated, if water was present, along with a new product (t, δ 5.9), tentatively identified as the hydrate of 52, i.e., 7,7-dihydroxybicyclo[2.2.1]hept-2-ene.

27. Pyrolysis of anti-7-bromo-syn-7-trimethylstannylbicyclo[4.1.0]hept-2-ene (35-anti) in diglyme solution

The diglyme was first freed of peroxides by passing it through a 1 x 27 cm alumina column, and was then dried

(i.e., stirred over sodium, under nitrogen, at room temperature overnight, and then heated to reflux over sodium at 50° to 65°, at aspirator pressure, for two hours). The diglyme was distilled at aspirator pressure, and then a few pieces of sodium were added to the distillate, and the storage flask was wrapped with aluminum foil, thoroughly flushed with argon, and kept in a refrigerator.

A 27.3 mg sample of 35-anti was placed in a base-washed NMR tube, which was then capped with a rubber septum, and flushed with argon. Dry diglyme (0.4 ml) was syringed in under argon. The tube (vented to an argon line at atmospheric pressure) was then dipped into a preheated oil bath. Heating at 150° to 153° for one hour resulted in no reaction. Heating at 145° to 155° for another 13.5 hours resulted in 59% conversion (measured by NMR integration vs. an internal standard) of the starting material. The NMR yield of spiro-[2.4]hepta-4,6-diene (29) was 31%, based on unrecovered starting material. After another 8 hours of heating, the conversion of starting material was 76%, but the yield of 29, based on unrecovered starting material, was only 19%. The 29 was obviously being lost during prolonged heating, probably due to its volatility, and to its polymerizability. (It was already mentioned earlier in this chapter that prolonged periods of heating of 35-anti in benzene solution

resulted in lower yields of 29. Furthermore, 29 polymerized even during prolonged periods of freezer storage in benzene solution.) Therefore, the measured 31% yield of 29 represents a lower limit to the actual yield.

28. Pyrolysis of the lithium salt of bicyclo[2.2.1]hept-2-en-7-one tosylhydrazone (27a)

a. Pyrolysis in an NMR tube Into a base-washed NMR tube were placed 20.1 mg (0.0728 mmol) of bicyclo[2.2.1]hept-2-en-7-one tosylhydrazone (195). The tube was thoroughly flushed with argon, and capped with a rubber septum. Next, 0.4 ml of dry diglyme (prepared as described in entry 27 above) was then syringed in under argon, followed by a trace of tetramethylsilane. The NMR spectrum was recorded. Next, 43 µl (0.080 mmol) of a 1.87 M n-butyllithium/hexane solution was syringed in under argon. The top part of the solution turned brown and became warm. When the mixture was agitated, its color became light yellow, and a whitish precipitate gradually settled out. The exothermicity and precipitation seemed to be complete within ca. 5 minutes.

After 15 more minutes of standing (under argon), the mixture was agitated, to give a suspension, and the bottom part of the tube was then immersed in a preheated 100° oil bath. The temperature of the bath was increased to 150° over a 20 minute period, and then maintained at 150°

to 155° for 49 more minutes. The resulting mixture was cooled to ambient temperature, and filtered through "Celite 503" diatomaceous earth, in a tissue paper-disposable Pasteur pipet filter. Approximately 0.15 ml of dry diglyme was used as a rinse.

In an attempt to recover and identify any unreacted 27a (in the form of 195), the solids were shaken with 0.5 ml of methylene chloride-d_2 plus 0.1 ml of D_2O. NMR analysis of the resulting methylene chloride-d_2 solution showed no material other than water. The NMR spectrum of the diglyme filtrate showed some poorly defined olefinic absorptions, but there was clearly not a major amount of spiro[2,4]hepta-4,6-diene (29). GC and GC-MS analyses revealed a trace (<1% yield) of 29, identified by comparison with an authentic sample. GC-MS analysis further showed an even smaller amount of a second, unidentified, C_7H_8 species, plus major amounts of at least 2 $C_{14}H_{16}$ species. (The GC trace was probably not continued long enough to pick up all of the $C_{14}H_{16}$ species which were detected in entry 29 below.)

b. Pyrolysis in a flask The diglyme, which had been prepared as described in entry 27 above, was re-dried by distillation from sodium benzophenone ketyl at aspirator pressure, and was stored over sodium, with the flask wrapped in aluminum foil, under argon, in a refrigerator.

A 5 ml round-bottom flask, equipped with a magnetic stirring bar, was charged with 20.8 mg (0.0754 mmol) of 195. The flask was thoroughly flushed with argon, and 1 ml of dry diglyme was then syringed in under argon. The 195 required a few minutes of stirring to dissolve. The flask was next cooled with a cold tap water bath, while 45 µl (0.0842 mmol) of a 1.87 M n-butyllithium/hexane solution were syringed in under argon, over a 10 second period, accompanied by the vigorous stirring of the reaction mixture. The mixture very quickly turned yellow, and a whitish precipitate gradually formed. Stirring at room temperature under argon was continued for 30 minutes.

The flask was then fitted with an argon-purged reflux condenser, and dipped into a preheated 100° oil bath. While the reaction mixture was being stirred under argon, the temperature of the bath was increased to 150° over a 15 minute period, and then maintained at 150° to 156° for 76 minutes. The suspension gradually became light brownish yellow, and some boiling was evident. The mixture was then cooled to room temperature. The neck of the flask was rinsed with 0.3 ml of dry diglyme, and the resulting mixture was filtered through "Celite 503" diatomaceous earth, in a tissue paper-disposable Pasteur pipet filter.

The solids were stirred with a solution of 3 µl of acetic acid in 1 ml of methylene chloride for 1 hour, and

then re-filtered. The filtrate was concentrated, and re-dissolved in methylene chloride-d_2. NMR analysis of this solution showed no 195, but did indicate the presence of a p-toluene group-containing compound, tentatively identified as p-toluenesulfinic acid.

The NMR spectrum of the diglyme filtrate was very similar to that obtained in section a above. GC and GC-MS studies showed that a 0.9% corrected GC yield of 29 (identified by comparison with an authentic sample) had been obtained, but none of the second C_7H_8 species which was mentioned above in section a. The GC-MS analysis also revealed the presence of major amounts of at least 5 $C_{14}H_{16}$ isomers, along with several other unidentified products. (The GC trace was probably not continued long enough to pick up all of the $C_{14}H_{16}$ species which were detected in entry 29 below.)

c. Pyrolysis in a sealed tube The diglyme was purified as in part b above. The reaction apparatus consisted of a flat-bottom 15 mm (ID) x 17.3 cm tube which contained a constriction (for sealing) 4.7 cm below the top of the tube. The tube was equipped with a magnetic stirring bar and a rubber septum. It was thoroughly argon-flushed and dried, and then charged with a solution of 30.3 mg (0.110 mmol) of 195 in 0.8 ml of dry diglyme. It was again flushed with argon. While the vigorously stirred diglyme

solution of 195 was being cooled with a room temperature bath, 70.0 µl (0.131 mmol) of a 1.87 M n-butyllithium/hexane solution was syringed in over a 1.5 minute period. The solution quickly turned orange, and then gradually became reddish brown, and a precipitate formed. The solution was stirred for 40 minutes at room temperature, under argon.

The tube was then sealed under argon. The color of the mixture became lighter immediately after the tube had been sealed. It was stirred for 5 minutes at room temperature. Then, the tube was 80% immersed in a preheated 104° oil bath, with stirring of the reaction mixture. The temperature of the bath was increased to 150° over an 18 minute period, and then maintained at 150° to 154° for two hours. Vapor formation and condensation were evident at the very top of the tube, and the suspension gradually turned brown. The heat source was then turned off, and the tube was allowed to slowly cool to 45° over a 1/2 hour period. Then, the tube was cooled to room temperature, and opened. The reaction mixture was filtered through "Celite 503" diatomaceous earth in a tissue paper-disposable Pasteur pipet filter (with pressure being applied by a pinch clamp on a connected piece of Tygon tubing).

The solids were stirred with a solution of 6 µl of acetic acid in 1 ml of methylene chloride for three hours,

and then re-filtered. The filtrate was concentrated and re-dissolved in methylene chloride-d_2. NMR analysis showed a product tentatively identified as p-toluenesulfinic acid, but no 195.

The NMR spectrum of the diglyme filtrate was very similar to those obtained in parts a and b above. GC analysis revealed a 0.6% corrected GC yield of 29 (identified by comparison with an authentic sample), along with the same $C_{14}H_{16}$ species as were obtained in section b above.

A second, similar sealed tube reaction was conducted, using the following quantities of reagents: 29.4 mg (0.107 mmol) of 195, 0.8 ml of dry diglyme, and 60.0 µl (0.112 mmol) of a 1.87 M n-butyllithium/hexane solution. The n-butyllithium was added one drop per minute, over a 6 minute period. The reaction mixture became slightly yellowish, and then white, instead of reddish brown as it had in procedure b above.

GC analysis of the diglyme filtrate again showed 29, in 0.6% yield (corrected GC yield).

29. Pyrolysis of 27a in the presence of triethylsilane

This experiment was run the same way as in part c of entry 28, except that triethylsilane was added to the diglyme solution of bicyclo[2.2.1]hept-2-en-7-one tosylhydrazone (195)

prior to the n-butyllithium addition. Also, the sealed tube was completely immersed in the oil bath, to avoid allowing the triethylsilane to volatilize out of the solution. The following amounts of reagents were used: 29.4 mg (0.107 mmol) of 195, 0.160 ml (1.00 mmol) of triethylsilane, 0.8 ml of dry diglyme, 60.0 µl (0.112 mmol) of a 1.87 M n-butyllithium/hexane solution.

The NMR spectrum of the diglyme filtrate was very similar to those of parts a, b, and c of entry 28 above. GC-MS analysis revealed the presence of a trace (<1% yield) of spiro[2,4]hepta-4,6-diene (29), identified by comparison with an authentic sample, and major amounts of n-butyltriethylsilane and 7 $C_{14}H_{16}$ isomers, along with a number of other unidentified products. Syn-7-triethylsilylbicyclo-[2.2.1]hept-2-ene (186), identified by comparison of its GC retention time and GC-MS with those of an authentic sample, was present, but only in ca. 3% yield. The GC-MS further indicated that an isomer of 186, possibly anti-7-triethylsilylbicyclo[2.2.1]hept-2-ene (187) or 7-triethylsilylbicyclo[4.1.0]hept-2-ene was also present, in an amount even smaller than that of 186.

30. Pyrolysis of 27a in the presence of DPIBF

a. With 1.1 equivalents of DPIBF The procedure used was the same as in part b of entry 28 above, except the DPIBF

was added to the flask, along with bicyclo[2.2.1]hept-2-en-7-one tosylhyrazone (195). The following quantities of reagents were used: 29.6 mg (0.107 mmol) of 195, 32.1 mg (0.119 mmol) of DPIBF, 0.8 ml of dry diglyme, and 60.0 µl (0.112 mmol) of a 1.87 M n-butyllithium/hexane solution. The n-butyllithium was added one drop/minute, over a 7 minute period. Each drop caused the formation of an orange-brown color, which then slowly faded. A precipitate also gradually formed during the n-butyllithium addition. The addition of the last drop of n-butylithium caused a very dark brown color to form, which then slowly faded to yellow during a 45 minute period of stirring at room temperature, under argon. After the flask had been dipped into a preheated 100° oil bath, its temperature was increased to 150° over an 11 minute period, and then kept at 150° to 154° for two hours. There was hardly any refluxing at all! After the heating period, the mixture had become brownish.

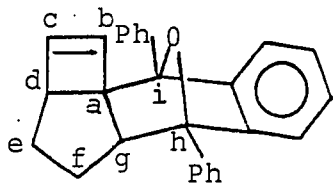
GC analysis of the filtered diglyme solution revealed a trace (≤1% yield) of 29 (identified by comparison of its retention time with that of an authentic sample) and major amounts of the two diasteromers of the Diels-Alder adduct (31) between bicyclo[3.2.0]hepta-1,6-diene (30) and DPIBF. GC-MS analysis verified that 31 had the expected molecular weight, and also showed that only one of the

7 $C_{14}H_{16}$ isomers described in the above two procedures (entries 28 and 29) was present in this product mixture. Several other unidentified products were also detected.

After the product mixture had been freed of diglyme by concentration under high vacuum, and air-oxidized (in order to transform the unreacted DPIBF to the very polar, and easily separable, 1,2-dibenzoylbenzene), product 31 was isolated (29% yield) by preparative TLC (rf = 0.76) on silica gel (20% ether/80% hexane). It was an extremely viscous colorless oil. Its spectral data are presented in part b below. The $C_{14}H_{16}$ compound could not be detected anywhere on the TLC plate.

b. With 2.1 equivalents of DPIBF This experiment was run the same way as part a above, with the following quantities of reagents: 30.2 mg (0.109 mmol) of 195, 62.7 mg (0.232 mmol) of DPIBF, 0.8 ml of dry diglyme, and 60.0 µl (0.112 mmol) of a 1.87 M n-butyllithium/hexane solution. Product 31 was isolated in 28% yield. 60 MHz ^{1}H NMR of the two diastereomers of 31 (CCl_4): δ 7.78-7.15 (complex m, 10H), 6.98 (br s, 4H), 6.11 (d, 0.65H, J = ca. 3 Hz), 6.03 (d, 0.38H, J = ca. 3 Hz), 5.87 (two closely spaced doublets, 0.97H, J = ca. 3 Hz), 3.09-0.73 (complex m, 7.5H--possibly included some impurities). Hence, the steoisomeric ratio was 0.65 to 0.31 (=1.7:1). IR (CCl_4): 3115 (sh), 3100 (sh),

3072 (s), 3042 (s), 2950 (sh), 2935 (s), 2905 (sh), 2865 (m), 1965 (w), 1953 (w), 1940 (w), 1908 (br w), 1885 (br w), 1825 (br w), 1812 (w), 1645 (br w), 1605 (m), 1500 (s), 1458 (s), 1449 (s), 1440 (sh), 1380 (w), 1358 (sh), 1348 (m), 1312 (s), 1305 (sh), 1280 (br m), 1245 (w), 1210 (br w), 1178 (w), 1155 (w), 1133 (w), 1070 (br w), 1050 (w), 1040 (w), 1015 (br sh), 998 (s), 983 (s), 965 (sh), 937 (sh), 915 (w), 882 (w), 875 (sh), 858 (w), 840 (w), 692 (s), 678 (sh), 665 (br w), 650 (sh), 630 (br w) cm^{-1}. $\underline{^{13}C\ NMR}$ (CCl_4): δ 149.624 (rel. intens. 839), 148.270 (576), 146.428 (552), 146.103 (781), 141.877 (1632), 140.252 (1215), 138.952 (537), 137.922 (1924), 137.651 (722), 137.435 (928), 136.134 (1350), 127.954 (7607), 127.683 (5695), 127.033 (5196), 126.491 (1952), 126.275 (3834), 126.112 (5093), 125.950 (3379), 125.570 (2933), 125.191 (509), 124.920 (3583), 120.532 (1254), 119.449 (1811), 118.907 (1394), 118.040 (1902), 90.249 (755), 89.274 (679), 89.165 (693), 88.245 (413), 74.051 (639), 72.967 (977), 53.466 (1362), 53.033 (1226), 52.545 (1760), 51.732 (1921), 32.502 (1865), 28.222 (1848), 26.868 (1194), 26.543 (1188). The carbon signals were assigned to the positions designated in the below structure



31

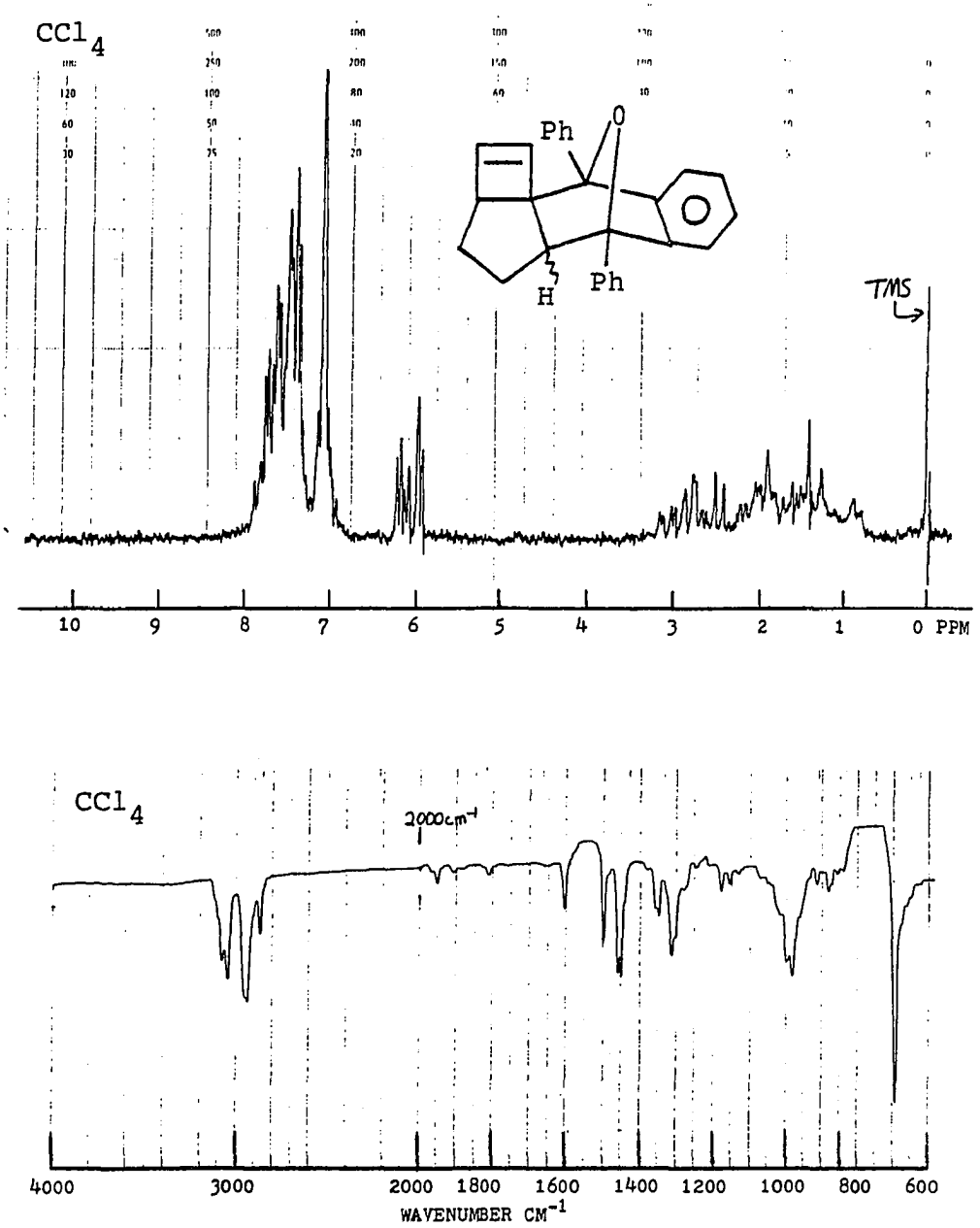


Figure 31. 60 MHz ^{1}H NMR and IR spectra of 31 (the Diels-Alder adduct between bicyclo[3.2.0]hepta-1,6-diene, 30, and DPIBF)

by means of an off resonance decoupling experiment. The 4 peaks from δ 90.249 to 88.245 (carbons h and i) remained singlets (only slightly broadened). The two peaks at δ 74.051 and 72.967 (carbon a) were split into doublets of doublets. (The spacings were very small, i.e., 23 Hz). The 4 peaks from δ 53.466 to 51.732 (carbons d and g) were split into doublets (spacing = 87 Hz) with finer couplings superimposed. (A gated decoupling experiment resulted in a spacing of 130 Hz instead of 87 Hz.) The 4 peaks from δ 32.502 to 26.543 (carbons e and f) were split into triplets. (This latter change was much more obvious in a gated decoupling experiment. Each triplet had a spacing of 124 Hz in the gated decoupling experiment.) The 4 peaks from δ 120.532 to 118.040 (carbons b and c) were split, but the resulting multiplets partially overlapped with the aromatic absorbances. Note that the spacings given above are not the residual C-H coupling constants, since they depend upon the strength of the second applied rf field.[115] The two diastereomers of 31 had identical 70 eV mass spectra (Finnegan GC-MS, Column D), m/e (%RIC): 362 (P, 0.99), 344 (P-18, ca. 0.1), 271 (2.43), 270 (P-92, 12.39), 257 (0.63), 241 (2.45), 239 (1.78), 229 (1.61), 228 (0.70), 226 (0.67), 215 (0.89), 202 (1.02), 193 (1.17), 189 (0.65), 179 (1.51), 178 (1.16), 166 (0.81), 165 (5.01), 164 (0.89), 163 (0.80), 152 (0.92), 139 (0.64), 135 (0.85), 133 (0.76), 128 (0.74), 126 (0.68), 119 (0.70), 115 (1.28),

113 (0.90), 108 (0.75), 106 (0.67), 105 (7.78), 101 (0.69), 92 (P-270, 0.53), 91 (5.40), 78 (1.07), 77 (12.90), 65 (1.51), 63 (0.69), 51 (2.08), Analysis: Calcd. for $C_{27}H_{22}O$: m/e 362.16707. Found: m/e 362.16742.

31. Pyrolysis of anti-7-bromo-syn-7-trimethylstannyl-bicyclo[4.1.0]hept-2-ene (35-anti) in triethylsilane, in the presence of tetraalkyltin species

a. With 2 equivalents of tetrabutyltin in triethylsilane solvent A solution of 10.2 mg (0.0304 mmol) of 35-anti and 20 µl (0.061 mmol) of tetra-n-butyltin in 0.30 ml of triethylsilane was placed in an NMR tube, and flushed with argon. The tube was sealed under nitrogen, and then fully immersed in a preheated oil bath, and heated at 160° to 164° for 251 minutes. NMR and GC analyses showed that syn-7-triethylsilylbicyclo[2.2.1]hept-2-ene (186) was the major product. GC-MS analysis also revealed a very small amount (6% of the amount of 186) of a product tentatively identified as 7-trimethylstannylbicyclo[4.1.0]hept-2-ene (163). The same compound was obtained from the tri-n-butyltin hydride treatment of 35-anti (entry 16 above). 70 eV MS of 163 (Finnegan GC-MS, Column E), m/e (%RIC): 243 ($P^{Sn,120}$-15, 0.35), 241 ($P^{Sn,118}$-15, 0.35), 239 ($P^{Sn,116}$-15, 0.18), 230 (absent), 215 (0.03), FPTC (first peak of a $Sn^{120,118,116}$ isotope cluster) at 211 (0.08), 185 (0.06), 178 (absent)

169 (2.48), 167 (2.09), FPTC at 165 ($P^{Sn,120}$-93, 15.13), 151 (0.69), 150 (1.43), 148 (1.07), 147 (0.74), 145 (0.17), FPTC at 135 (2.45), 121 (0.68), FPTC at 120 (Sn^{120}, 0.85), 94 (0.83), 93 ($P^{Sn,120}$-165, 11.13), 92 (absent), 91 (8.24), 79 (0.72), 78 (0.90), 77 (5.12), 66 (0.29), 65 (2.29), 53 (0.76), 51 (0.96). No n-butyltriethylsilane could be detected by GC-MS.

For comparison purposes, the mass spectra of 189-syn (syn-7-trimethylstannylbicyclo[2.2.1]hept-2-ene) and 189-anti (anti-7-trimethylstannylbicyclo[2.2.1]hept-2-ene) are of interest. 70 eV MS of 189-syn (Chemistry Dept., Iowa State University MS Library), m/e (%RIC): 243 (2.84), 230 (5.98), 215 (7.60), 185 (17.87), 165 (36.91), 151 (0.37), 150 (4.95), 147 (0.55), 135 (6.94), 121 (1.77), 120 (4.87), 93 (0.96), 92 (0.30), 91 (1.18), 83 (0.44), 79 (0.74), 77 (1.33), 66 (0.89), 65 (1.22), 41 (0.92), 39 (1.37). 70 eV MS of 189-anti (Chemistry Dept. Iowa State University MS library), m/e (%RIC): 258 (2.74), 243 (16.19), 230 (0.90), 215 (3.40), 185 (2.84), 178 (0.41), 165 (0.12), 151 (0.62), 150 (1.93), 145 (0.47), 135 (4.93), 121 (0.94), 120 (1.93), 94 (2.31), 93 (31.19), 91 (6.92), 78 (0.53), 77 (5.55), 66 (1.40), 41 (1.15), 39 (1.22).

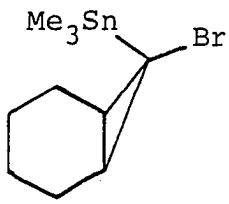
b. In 1:1 tetramethyltin-triethylsilane solvent A solution of 11.5 mg (0.0343 mmol) of 35-anti in 0.19 ml of tetramethyltin plus 0.21 ml of triethylsilane was placed in

an NMR tube, which was then sealed under nitrogen. It was next fully immersed in a preheated oil bath, and heated at 158° to 163° for 178 minutes. NMR and GC analyses showed that syn-7-triethylsilylbicyclo[2.2.1]hept-2-ene (186) was the major product. There was no evidence for any 7-trimethylstannylbicyclo[4.1.0]hept-2-ene (163), syn-7-trimethylstannylbicyclo[2.2.1]hept-2-ene (189-syn), or anti-7-trimethylstannylbicyclo[2.2.1]hept-2-ene (189-anti).

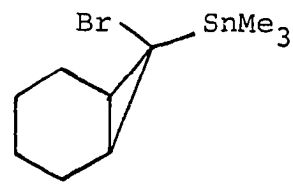
IV. 7-BROMO-7-TRIMETHYLSTANNYL-BICYCLO[4.1.0]HEPTANE

A. Introduction

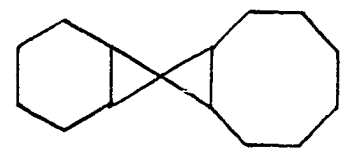
The results of Chapter III made it very clear that neither the solution pyrolysis reaction of anti-7-bromo-syn-7-trimethylstannylbicyclo[4.1.0]hept-2-ene (35-anti), nor of its C^7-epimer (35-syn) involved a carbene intermediate. It was therefore decided to reexamine the thermolysis of their simpler, saturated analogs, 205-anti and 205-syn, respectively. Seyferth and Lambert[65] pyrolyzed 205-anti and 205-syn



205-anti



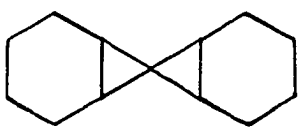
205-syn



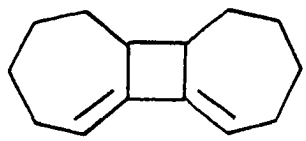
206

separately in refluxing cyclooctene solution, and obtained the cyclopropanation product 206 from each. The yields, however, were very different from the two starting materials, with the former giving a 76% yield of 206, and the latter a 40% yield. Since a longer heating period was required for the reaction of 205-syn, it is not clear, a priori, whether this yield difference is a real difference in the chemistry of 205-anti and 205-syn, or simply the result of the thermal

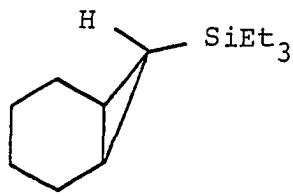
instability of product 206. Seyferth and Lambert [65] also studied the pyrolysis of a 4 to 1 mixture of 205-anti and 205-syn in cyclohexene solution at 170°. They obtained a 33% isolated yield of cyclopropanation product 98, and a 5 to 12% yield of allene dimer 207. When a 4 to 1 mixture of 205-anti and 205-syn was pyrolyzed in chlorobenzene solution (at



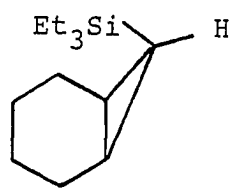
98



207



127-anti



127-syn

125° to 128°) in the presence of 3 equivalents (2 molar concentration) of triethylsilane, the Si-H insertion products 127-anti and 127-syn, and the allene dimer 207 were obtained in 24%, 25%, and 12% isolated yields, respectively. Seyferth and Lambert[65] suggested that a carbene intermediate might be responsible for these divalent carbon transfer reactions, but at the same time admitted that they had no basis for making a conclusive statement about the mechanism.

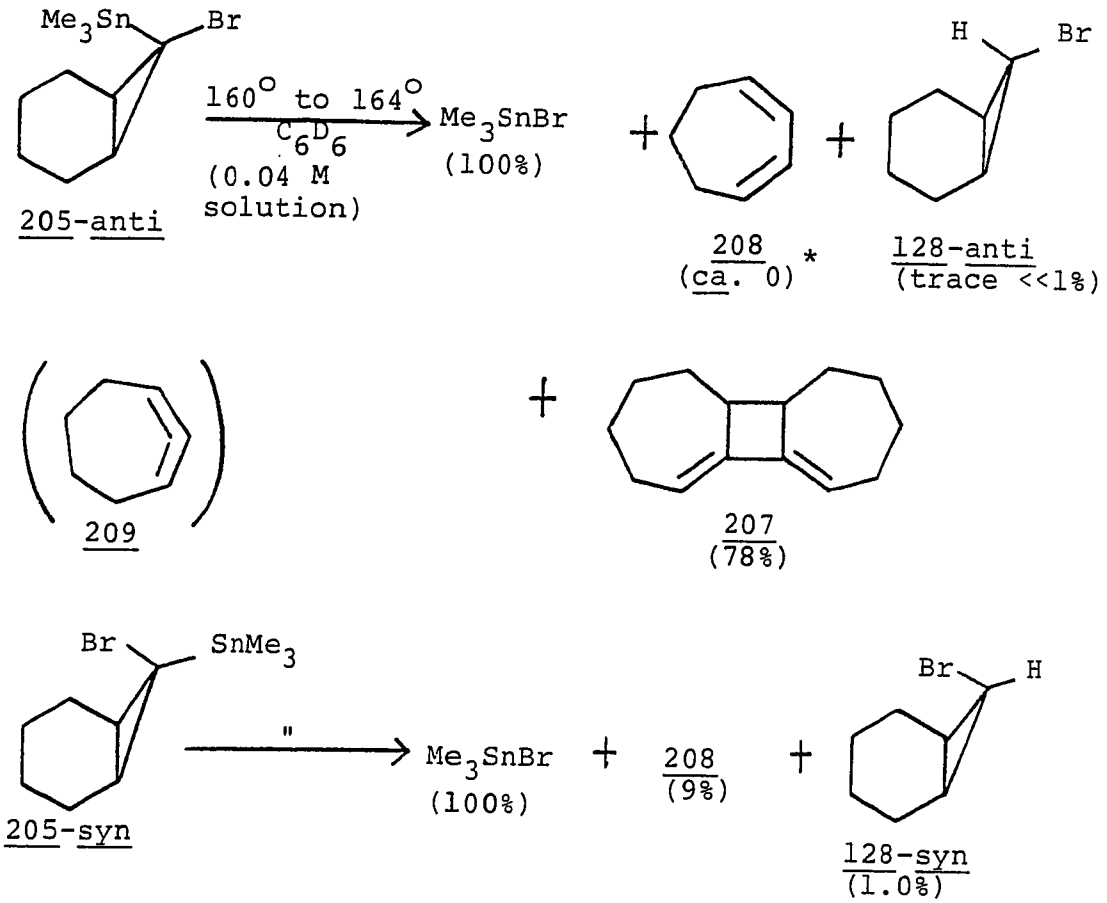
B. Results and Discussion

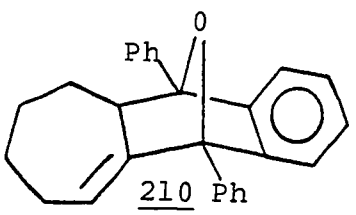
1. Product studies

As is illustrated in Scheme XLII, the pyrolysis of a 0.04 M benzene solution of either 205-anti or 205-syn at 160° gave 207 as the major product. In the case of 205-syn, a small amount (9% corrected GC yield) of 1,3-cycloheptadiene (208) was also formed, but in the case of 205-anti, there was virtually no 208. The reason for this dichotomy will become apparent later in this chapter. Product 207 likely arose from allene 209. (The yields of trimethyltin bromide given in Scheme XLII were NMR yields, and the yields of the other products were corrected GC yields, all based on unrecovered starting material.) Note that pyrolyzing a 0.6 M benzene solution of a mixture of 205-anti and 205-syn gave, in place of some of the 207, a substantial amount of 6 C_7H_{10} trimers, tentatively identified as such by GC-MS analysis (see the Experimental).

As might be expected, the pyrolysis of a 0.3 M benzene solution of either 205-anti or 205-syn, containing 1 equivalent of DPIBF, gave a 30% isolated yield of product 210 (from the Diels-Alder trapping of allene intermediate 209). The two diastereomers of 210 were formed in a 1 to 6 ratio (see the Experimental). The relatively low yield of 210 was prob-

Scheme XLII:

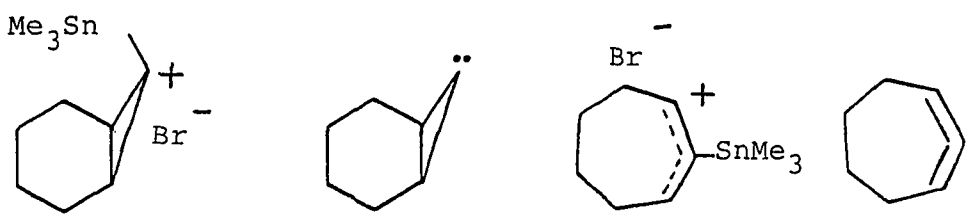




*See reference 116.

ably a result of the workup procedure used (air-oxidation overnight, followed by preparative TLC isolation). Very importantly, dimer 207, and the C_7H_{10} trimers, which had been formed in the absence of DPIBF, were not formed in its presence. This latter result verifies that products 207, 210, and the C_7H_{10} trimers must have all originated from a common intermediate, namely allene 209.

Studies were next conducted with cyclohexene and methanol as traps for possible carbene and carbocation intermediates. The story which is about to unfold in the following pages centers around a deep-seated difference between the chemistry of 205-anti and 205-syn. Compound 205-anti produces mainly compounds arising from the trapping of either ion pair 211 or cyclopropylidene 96, but 205-syn produces mostly compounds



211 96 212 209

from the trapping of either ion pair 212 or allene 209. (The NMR yield of trimethyltin bromide was again 100%.)

First of all, as is shown in Table XXIX, it was observed that 205-anti and 205-syn gave very different product distributions in cyclohexene solution. These re-

sults indicate that, as is illustrated in Scheme XLIII, 205-anti probably reacts by first generating carbene 96 (perhaps via loss of trimethyltin bromide from ion pair 211). Carbene 96 is then either trapped by cyclohexene, thus generating cyclopropanation product 98, or ring-opens to form allene 209, which in turn forms dimer 207. The partitioning yields shown in Scheme XLIII are based on the simplifying assumption that 205-anti reacts entirely via carbene 96. As will be seen later, some results with methanol trapping suggest that this assumption is a valid one. (It is indicated in Scheme XLIII that the 4% yield of cyclohepta-1,3-diene (208) from 205-syn arose from ion pair 212 via some alternate mechanism. This alternate mechanism, which will be discussed shortly, involves deprotonation of 212, to form a diene, followed by acid cleavage of the trimethyltin group. This mechanism probably also accounts for the 9% yield of 208 from 205-syn in benzene solution, shown in Scheme XLIII.) Because of the much greater proportion of ring opening in the case of 205-syn than in 205-anti, a working hypothesis naturally developed that an initial C-Br bond heterolysis must be very important. (According to Woodward-Hoffmann rules, the bromine in 205-syn has the proper stereochemistry for a facile concerted ionic ring opening to produce a cis-cycloheptenyl cation, i.e., 212.)

Scheme XLIII:

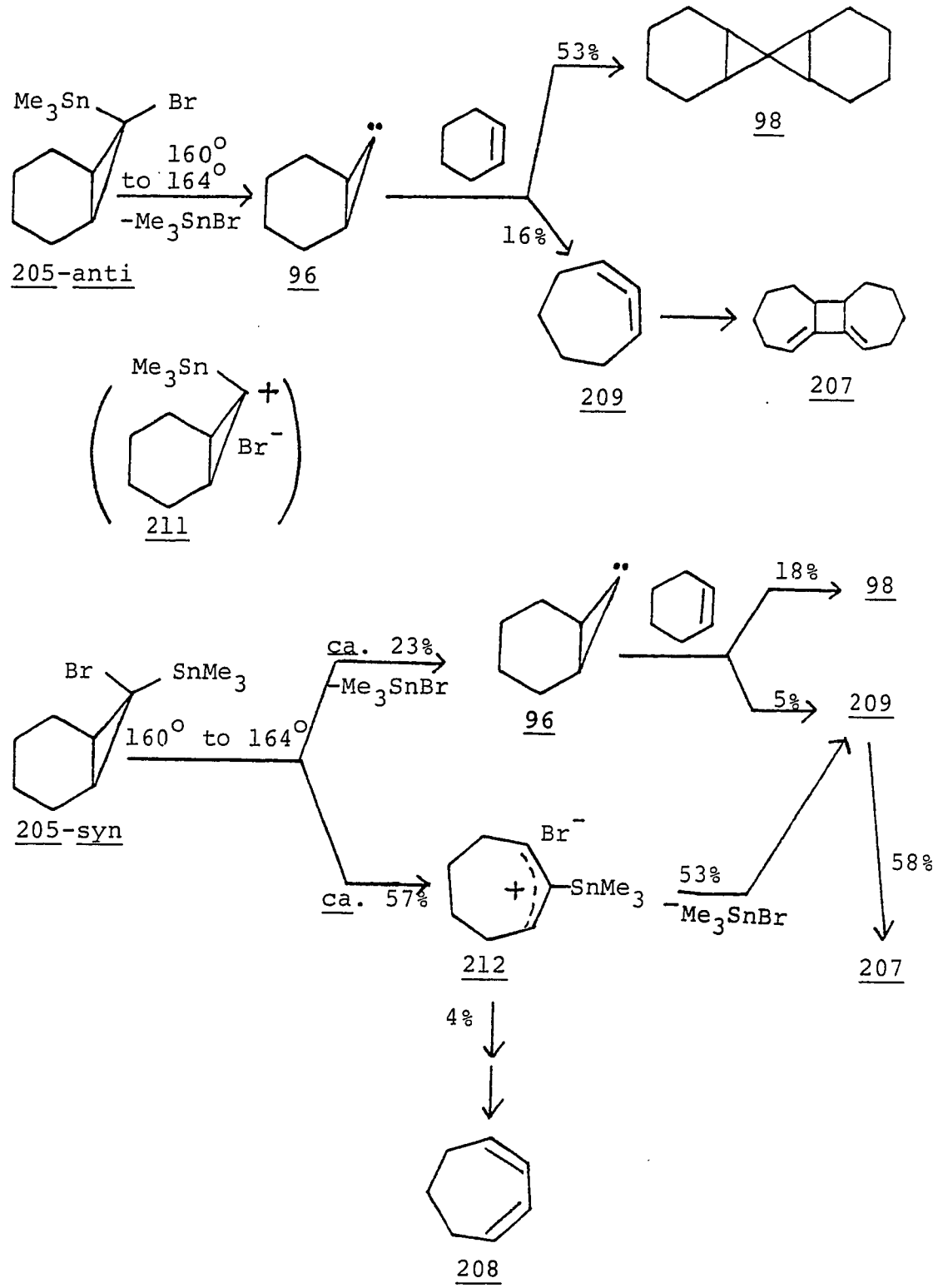


Table XXIX. Pyrolyses of 205-anti and 205-syn in cyclohexene solution[a] at 160° to 164°

Expt.	SM	Amt. of SM (mg)	%Yield[b] 208	%Yield[b] 98	%Yield[b] 207
1(X-66)[c]	205-anti	5.4	ca. 0[d]	53	16
2(X-69)[c]	205-syn	4.2	4	18	58

[a]Base-washed glassware. Cyclohexene purified by distillation from sodium benzophenone ketyl, and then stored over sodium, under argon, in a refrigerator. Each sample of starting material was dissolved in 0.26 ml of cyclohexene, flushed with N_2, and sealed under N_2 in an NMR tube.

[b]Yield meas. by GC integration vs. internal std., with correction factors, based on unrecov. starting material.

[c]Notebook number, followed by page number.

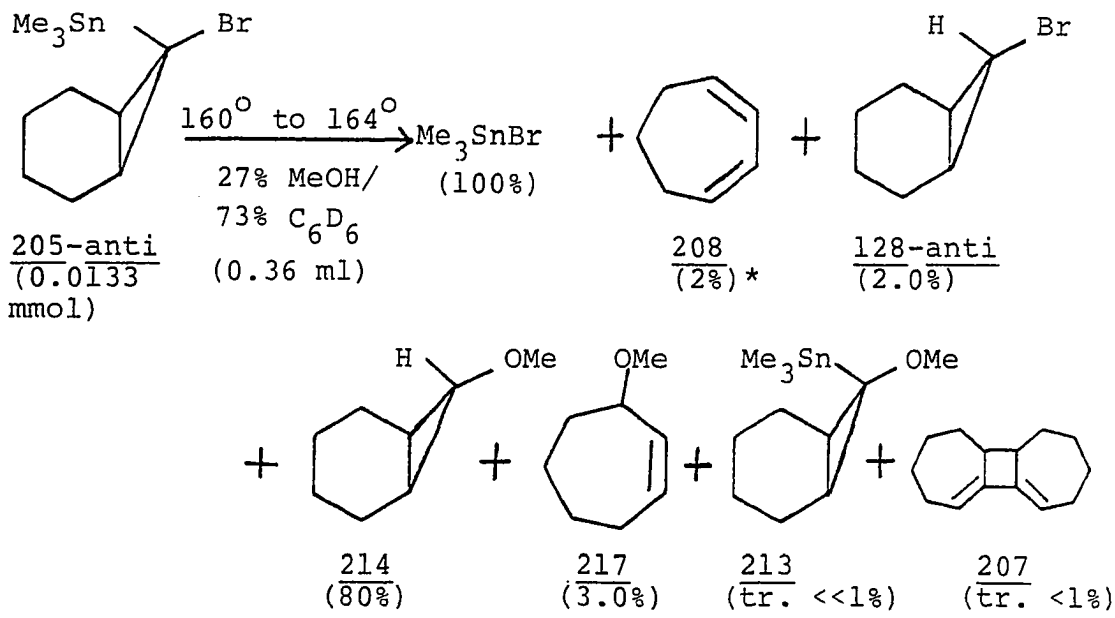
[d]See reference 116.

It should be pointed out that there is some uncertainty with respect to whether or not carbene 96 is formed from 205-syn (in ca. 18% yield in order to account for the amount of 98 formed in experiment 2, Table XXIX). If it is, then it is probably formed by synchronous loss of trimethyltin bromide (in order to avoid a cyclopropyl cation which should ring-open with no activation barrier; should such a cyclopropyl cation have a lifetime, then 98 could form from it via reaction with cyclohexene). Such synchronous loss of tri-

methyltin bromide has not been otherwise observed. Another possibility is that 98 forms directly from 205-syn plus cyclohexene, via a carbenoid mechanism, which could be probed kinetically. This has not been done.

Could the proposed ionic intermediates 211 and 212 be trapped by methanol? The answer is an emphatic "yes," as long as the proper reaction conditions are chosen. Initially, experiments were conducted with benzene/methanol solvent mixtures. The product distribution obtained from the pyrolysis of 205-anti in a 27% methanol/73% benzene (measured by volume) solution is shown in Scheme XLIV. (The yields were corrected GC yields, based on unrecovered starting material.) Product 213 must have resulted from the trapping of ion pair 211. Although 214 appears to have been the result of the insertion of carbene 96 into the O-H bond of methanol, it could equally well have originated from the acid cleavage of the trimethyltin group of 213, a well precedented process.[89] To test for the latter possibility, 205-anti was also pyrolyzed with 1 equivalent of triethylamine present as an acid scavenger. As shown in the second equation of Scheme XLIV, a very substantial amount (15% yield) of cation-trapping product 213 was formed, at the expense of carbene-trapping product 214. The yield of 214 under these conditions was only 58%, implying that approximately 25% of the

Scheme XLIV:



205-anti (0.0133 mmol)

208 (2%)*

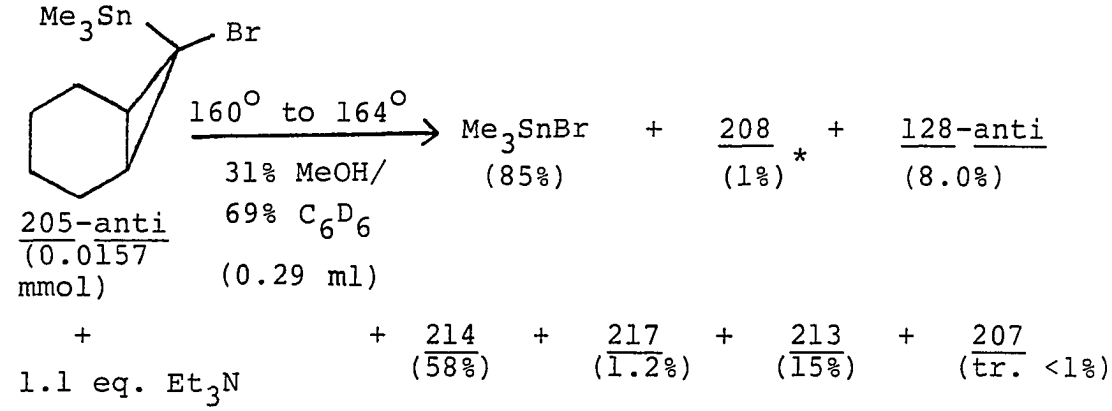
128-anti (2.0%)

214 (80%)

217 (3.0%)

213 (tr. <<1%)

207 (tr. <1%)



205-anti (0.0157 mmol)

*See reference 116.

214 formed in the first equation (in the absence of triethylamine) was due to acid-cleavage of the tin group of 213. Experiments with varied amounts of triethylamine needed to be conducted, in order to determine whether the remaining 214 (58% yield) had resulted from the trapping of carbene 96, or simply from a less than unit efficiency of acid deactivation by the triethylamine. The results of a series of such experiments are listed in Table XXX. It is easy to see from those results that 1 equivalent of the amine had already resulted in the maximum possible yield (15% to 18%) of 213. Therefore, the portion of 214 formed under such conditions (58% yield) must be regarded as arising from the trapping of carbene 96 by methanol. The stereoselectivity observed for the formation of product 214 is interesting. A similar stereoselectivity was observed by Kirmse and Jendralla[94] in a study of the diazo precursor of carbene 96. In order to understand this stereoselectivity, one must consider the three possible mechanisms of carbene trapping by alcohols[88b]: a) one-step insertion into the O-H bond, b) protonation of the carbene to give a carbocation (or ion pair), followed by nucleophilic attack of methanol or methoxide ion, and c) electrophilic attack of the carbene at the oxygen of methanol, followed by a 1,2-proton transfer. The nucleophilic vs. electrophilic character of the carbene

Table XXX. Effect of amine concentration on the methanolic benzene-d_6 solution[a] pyrolysis of 205-anti at 160° to 164°

Expt.	Mmol of 205-anti	Amine	Mmol of amine	Vol. ratio (MeOH:C_6D_6)	Soln. vol. (ml)
1(XI-2)[c]	0.0157	Et_3N	0.0172	31:69	0.29
2(XI-9)[c]	0.0124	Et_3N	0.0395	29:71	0.35
3(XI-8)[c]	0.0148	proton[e] sponge	0.0154	32:68	0.31

[a]Base-washed glassware. Each sample of 205-anti was dissolved in the solvent, flushed with nitrogen, and sealed under nitrogen, in an NMR tube.

[b]Yield measured by GC integration vs. an internal standard, with correction factors, based on unrecovered starting material.

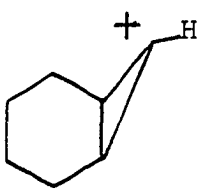
[c]Notebook number, followed by page number.

[d]See reference 116.

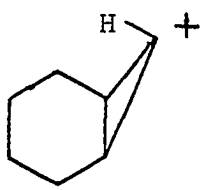
[e]N,N,N',N'-tetramethyl-1,8-diaminonaphthalene.

%Yield[b] 208	%Yield[b] 128-anti	%Yield[b] 214	%Yield[b] 213
1[d]	8.0	58	15
ca. 0[d]	4.1	65	14
ca. 0[d]	5.2	57	18

should play a major role in selecting the proper mechanism (verified by a recent study by Kirmse et al.[88b] of cyclopentadienylidene and cycloheptatrienylidene). Mechanism (a) does not explain the stereoselective formation of 214, because one would expect a stereoisomeric mixture of 214 and its C^7-epimer. Mechanism (b) does not explain the results very well either, since one expects, on the basis of steric considerations, that ion 215a should be formed in preference to ion 215b.[91] Ion 215a would have virtually no barrier to



215a

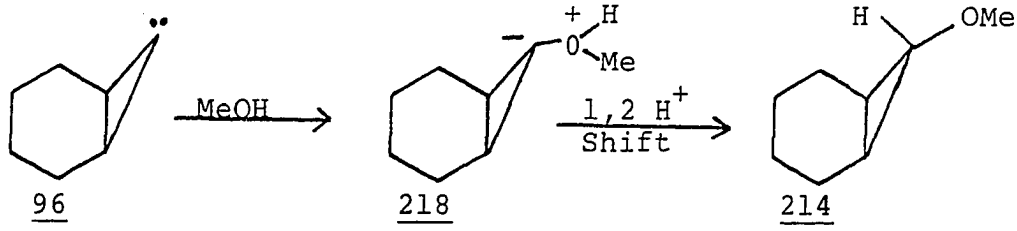


215b

216

a concerted ring opening to cation 216. Thus, if mechanism (b) were operative, compounds derived from the ring-opened cation 216 should make up the majority of the product distribution, which clearly did not happen in practice. Furthermore, there is no reason to expect carbene 96 to be particularly nucleophilic, which is a requirement for mechanism (b) to be operative.[88b] (The 1 to 3% yield of methoxy product 217, shown in Scheme XLIV, probably arose through mechanism

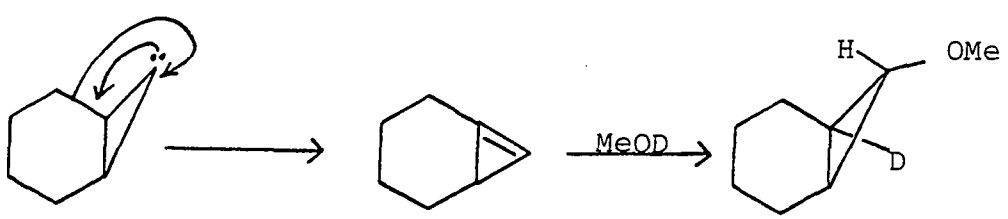
(b), via cyclopropyl cation 215a and ring-opened cation 216. The source of the 1 to 2% yield of diene 208 is unclear at present. It may be derived from methoxy compound 217 under the polar reaction conditions. Since none of it was formed in non-polar solvents, i.e., cyclohexene and benzene, it was probably not derived directly from allene 209.) By the process of deduction, then, one must conclude that product 214 is formed via mechanism (c), as is diagrammed below. Furthermore, it is reasonable to expect carbene 96 to be electrophilic, and, due to steric restrictions, the methanol would



be expected to attack preferentially from the less hindered side, thus giving rise to intermediate 218 stereoselectively, which would then form methoxy compound 214 via a 1,2-proton shift. (The stereoselectivity of the methanol attack on 96 is probably enhanced by the known importance of clustering effects in reactions of methanol with carbenes.[88a]) A major difference between mechanisms (a), (b), and (c) is that the first two might display primary deuterium isotope effects

(in a medium containing both methanol and methanol-O-d), whereas the third should apparently display a secondary deuterium isotope effect. Therefore, in order to further probe the mechanism of formation of carbene-trapping product 214, the pyrolysis of 205-anti was conducted in a solution containing both methanol and methanol-O-d.

First of all, an experiment was run with 29% methanol-O-d/71% benzene-d_6 to make sure that the following precedented[117] trapping mechanism, involving compounds 219 and 220, was not operative. NMR analysis revealed that, to

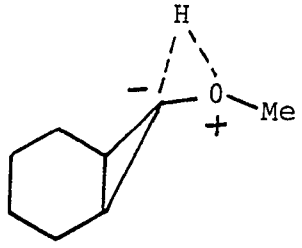


96 219 220

within the limits of NMR detection, H^7 was completely replaced by deuterium. The above cyclopropene mechanism for the formation of 214 was thus ruled out.

When 205-anti was pyrolyzed in a 29% methanol/71% benzene-d_6 solvent system, prepared with a 0.98 to 1.0 mixture of methanol-O-d and methanol, respectively, mass spectral analysis revealed that the carbene-trapping product 214 was formed with 29% deuterium incorporation. (See the Experimental for more details.) From these data, the

deuterium isotope effect (k_H/k_D) was determined to be 2.4. This primary deuterium isotope effect would seem to indicate a significant amount of O-H bond breaking during the rate-determining step, as diagrammed below. There are, however,



at least two reasonable alternative explanations. One is that at the high temperature of the pyrolysis (160° to 164°), there is a significant amount of intermolecular protonation of intermediate 218 by other molecules of methanol, thus affording a primary deuterium isotope effect. The second explanation is that a small fraction of product 214 may arise through acid cleavage of the cation trapping product, 213 even in the presence of triethylamine. (A large amount of such cleavage was previously ruled out by the control experiments in Table XXX, but such cleavage would be expected to display a large primary deuterium isotope effect.) At the time of preparation of this manuscript, experiments are in progress to better understand the measured deuterium isotope effect of 2.4.

Since pyrolysis of 205-anti in methanolic benzene solution (Scheme XLIV) gave 213 via trapping of a cationic intermediate (211), and 214 via trapping of a carbene intermediate (96), varying the methanol concentration might be expected to change the product distribution. The results in Table XXXI show this expectation to be correct.

Figure 32 shows the linear relationship between the yields of trapping products 213 and 214, and the methanol concentration, a result which is entirely consistent with the proposal that ion pair 211 gives rise both to the cation-trapping product 213, and to carbene 96.

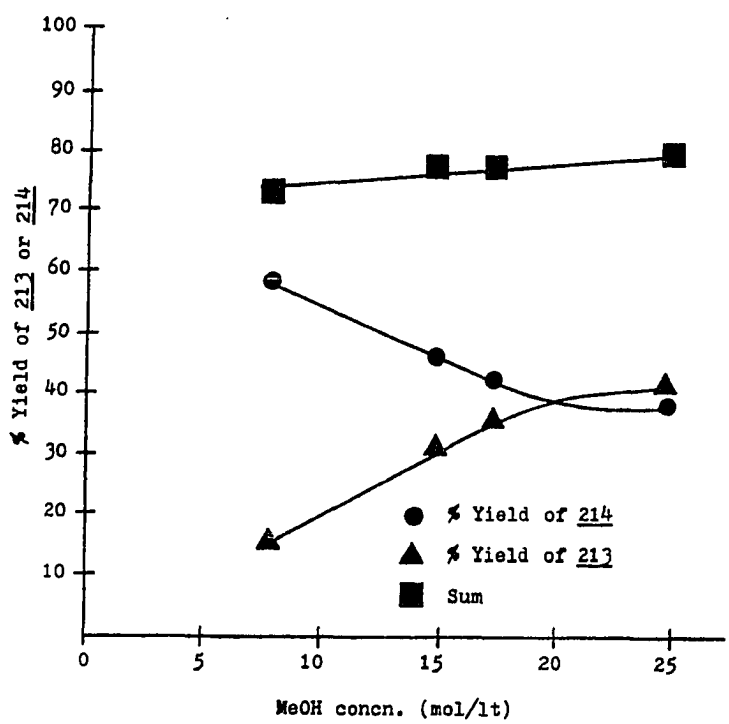


Figure 32. Relationship between methanol concentration and the yields of the cation-trapping product 213 and of carbene trapping product 214

Table XXXI. Effect of methanol concentration on the pyrolysis of 205-anti in methanolic benzene-d_6 solution[a] in the presence of triethylamine at 160° to 164°

Expt.	Mmol of 205-anti	Mmol of Et_3N	Vol. ratio (MeOH:C_6D_6)	Soln. vol. (ml)
1(XI-2)[c]	0.0157	0.0172	31:69	0.29
2(XI-16)[c]	0.0151	0.0151	60:40	0.33
3(XI-14)[c]	0.0136	0.0151	70:30	0.33
4(XI-15)[c]	0.0107	0.0115	100:0	0.33

[a]Base-washed glassware. Each sample of 205-anti was dissolved in the solvent, flushed with nitrogen, and sealed under nitrogen, in an NMR tube.

[b]Yield measured by GC integration vs. an internal standard, with correction factors, based on unrecovered starting material.

[c]Notebook number, followed by page number.

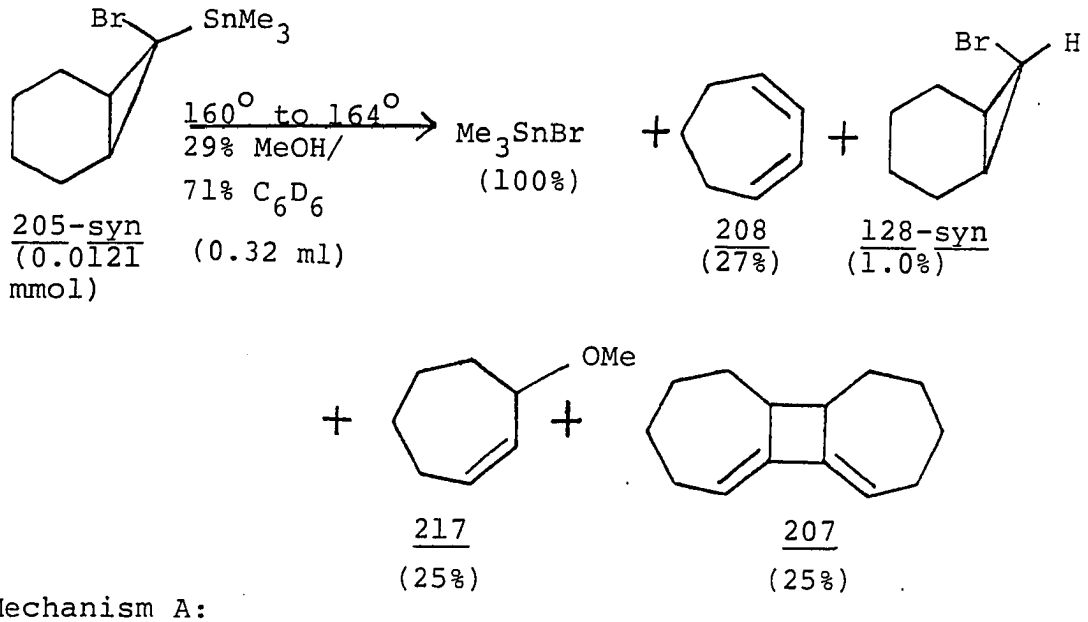
[d]See reference 116.

%Yield[b] 208	%Yield[b] 128-anti	%Yield[b] 214	%Yield[b] 213
1[d]	8.0	58	15
ca. 0[d]	3.6	46	31
ca. 0[d]	1.6	42	35
ca. 0[d]	1.3	38	41

It was hoped that an amine, such as diethylamine, might also be able to trap ion pair 211, and thus provide further proof for the involvement of that intermediate. Unfortunately, however, pyrolysis of 205-anti (0.0139 mmol) in benzene-d_6 solution (0.25 ml) containing 3 equivalents of diethylamine (experiment X-75) for 90 minutes (after which time 205-anti, in the absence of diethylamine, would have undergone 81% conversion) resulted in the quantitative recovery of starting material. An explanation for this result is an amine inhibition mechanism similar to that discussed in Chapter III for the effect of triethylamine on the thermolysis of anti-7-bromo-syn-7-trimethylstannylbicyclo[4.1.0]hept-2-ene (35-anti).

Attention was next turned toward the pyrolysis of 205-syn in methanolic benzene solution. The product distribution obtained from a pyrolysis in 29% methanol/71% benzene (measured by volume) solution is shown in Scheme XLV. (The yields were corrected GC yields, and were based on unrecovered starting material.) It is highly significant that no methanol insertion product (214) was formed, indicating that 205-syn does not generate a cyclopropylidene under these reaction conditions. All of the observed products (except for a trace, i.e., a 1% yield, of 128-syn) resulted from a ring-opened intermediate, presumably ion pair 212.

Scheme XLV :



205-syn (0.0121 mmol)

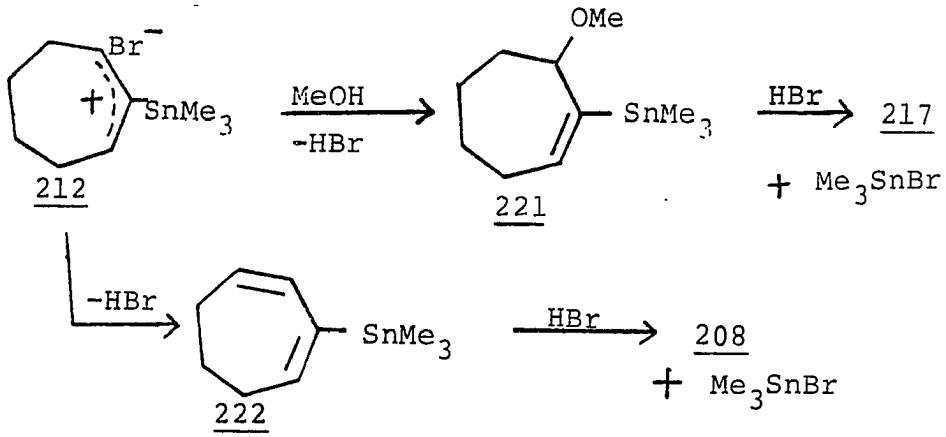
208 (27%)

128-syn (1.0%)

217 (25%)

207 (25%)

Mechanism A:

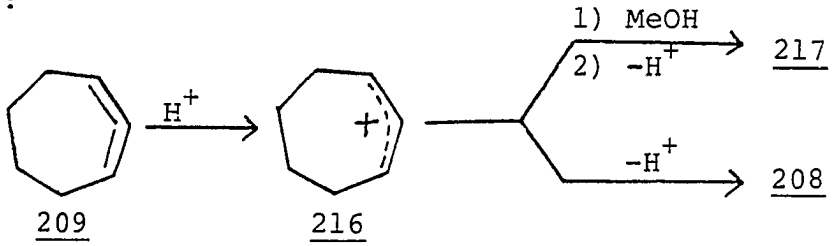


212

221

222

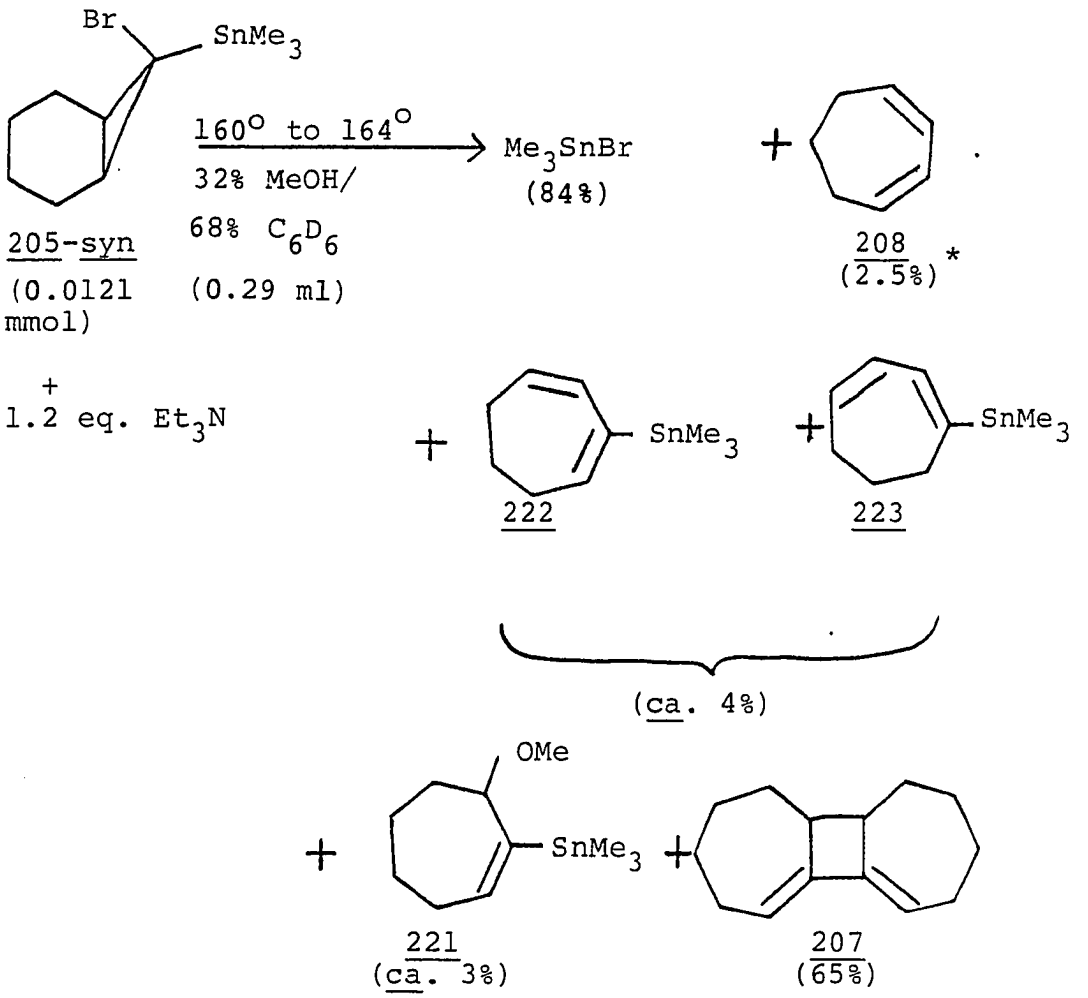
Mechanism B:



209

216

Scheme XLV (Continued):



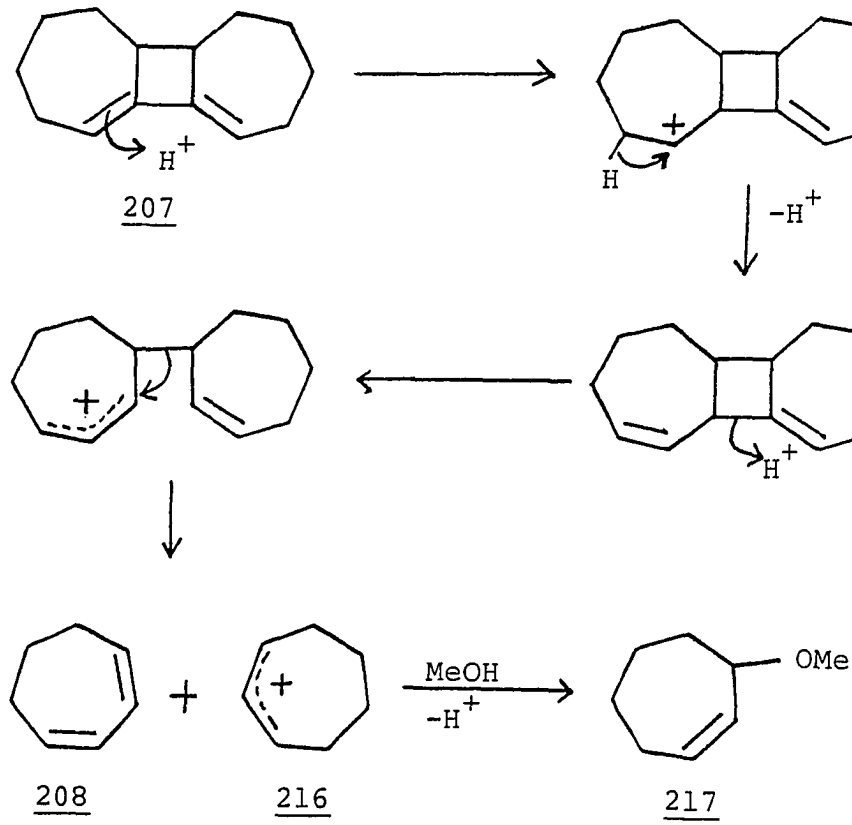
*See reference 116.

It was unclear whether Mechanism A or Mechanism B of Scheme XLV might account for the formation of diene 208 and methoxy compound 217. In order to find out, 205-syn was pyrolyzed in 32% methanol/68% benzene solution, in the presence of 1 equivalent of triethylamine as a buffer. As is shown in Scheme XLV, now there was no 217 formed, and the yield of 207 had been increased greatly (from 25% to 65%), and there were three new products detected, i.e., 221, 222, and 223 (all tentatively identified by GC-MS). Obviously, compound 221 must have resulted from methanol trapping of ionic intermediate 212. Product 222 must have resulted from deprotonation of 212, and 223 most likely arose from a 1,5-hydrogen shift reaction of 222.

But what of the exact mechanisms for the formation of diene 208 and methoxy compound 217 in the experiment without triethylamine (Scheme XLV)? Three reasonable mechanisms can be advanced, Mechanisms A and B of Scheme XLV, and the one shown below in Scheme XLVIa.

Two experiments were conducted in order to rule out the mechanism of Scheme XLVIa. The first one involved pyrolyzing 205-syn in methanolic benzene (in the absence of triethylamine) for two different time periods. If the mechanism of Scheme XLVIa were operative, the yields of 208 and 217 would increase with time at the expense of 207.

Scheme XLVIa:



207 208 216 217

As is shown in Table XXXII, the yield of 207 did decrease to a small extent, but the yields of 208 and 217 also decreased slightly. These decreases were probably due to decomposition and polymerization of the products during the extended heating period. Since the amounts of 208 and 217 did not increase with time, this experiment constitutes strong evidence against the mechanism of Scheme XLVIa.

The second experiment which ruled out the mechanism of Scheme XLVIa consisted of pyrolyzing a sample of 207 in a

Table XXXII. Pyrolysis of 205-syn in methanolic benzene-d_6 solution[a] for two different time periods at 160° to 164°

Expt.	Mmol of 205-syn	Vol. ratio (MeOH:C_6D_6)	Soln. vol. (ml)	Total Time heated (min.)
1(X-73-2)[d]	0.0121	29:71	0.32	30
2(X-74)[d]	0.0121	29:71	0.33	90

[a]Base-washed glassware. Each sample of 205-syn was dissolved in the solvent, briefly flushed with nitrogen, and sealed under nitrogen, in an NMR tube.

[b]Yield meas. by NMR integration vs. an internal std.

[c]Yield meas. by GC integration vs. internal std., with correction factors, based on unrecovered starting material.

[d]Notebook number, followed by page number.

%Recov.[b] SM	%Yield[c] 208	%Yield[c] 128-syn	%Yield[c] 217	%Yield[c] 207
6	28	1.0	29	35
0	27	ca. 0	25	25

30% methanol/70% benzene-d_6 solution, which contained 0.1 equivalent of hydrogen bromide. The amount of 207 was decreased by ca. 35%, and there was some evidence of its isomerization (see the Experimental), but no 208 or 217 appeared.

Mechanism B of Scheme XLV might at first seem unlikely, because it requires the proton to add to the central carbon atom of the allene moiety of 209, whereas electrophiles most often prefer to add to one of the outer carbon atoms of an allene.[118] However, the unusual geometry and electronic nature of allene 209[119] might very well cause the unusual transformation of 209 to 216 to occur.

Based on the available data, a combination of Mechanisms A and B could account for products 208 and 217. (Mechanism A alone cannot account for them because the yields of 221, 222, and 223, which were formed in the presence of triethylamine, are much too small.) It has been suggested that the analysis shown in Scheme XLVIb might explain the results of the buffered and unbuffered thermolysis reactions of 205-syn in methanolic benzene solution. (In Scheme XLVIb, it is suggested that, in the buffered reaction, the 2.5% yield of 208 arose from protic cleavage of the tin groups of 222 and 223. It was assumed that the buffered reaction involved no protonation of allene 209, since protic C-Sn cleavage is expected to be more facile than allene protonation.)

Scheme XLVIb:

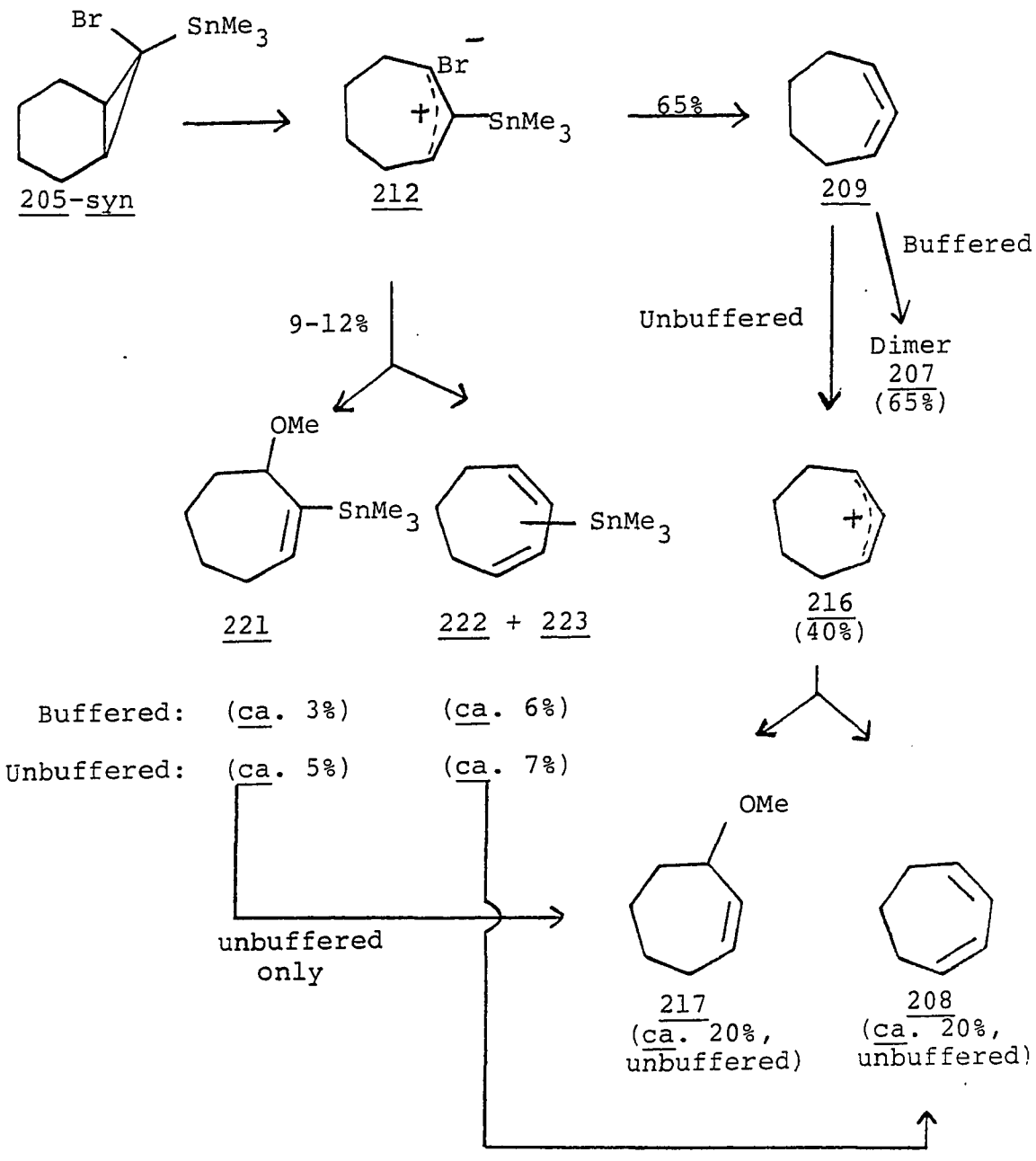


Table XXXIII. Effect of amine concentration of the pyrolysis of 205-syn in methanolic benzene-d_6 solution[a] at 160° to 164°

Expt.	Mmol of 205-syn	Amine	Mmol of amine	Vol. ratio (MeOH:C_6D_6)	Soln. vol. (ml)
1(XI-1)[d]	0.0121	Et_3N	0.0143	32:68	0.29
2(XI-11)[d]	0.00918	Et_2NH	0.242	30:70	0.32

[a]Base-washed glassware. Each sample of 205-syn was dissolved in the solvent, briefly flushed with nitrogen, and sealed under nitrogen, in an NMR tube.

[b]Yield meas. by NMR integration vs. an internal std.

[c]Yield meas. by GC integration vs. internal std., with correction factors, based on unrecovered starting material.

[d]Notebook number, followed by page number.

[e]See reference 116.

[f]See the Experimental for a discussion of the GC correction factors for these yields.

Total time heated (min.)	%Recov.[b] SM	%Yield[c] 208	%Yield[c] 222 + 223	%Yield[c] 221	%Yield[c] 207
12	17	2.5[e]	4.4[f]	3.2[f]	65
30	2	1[e]	4.4[f]	3.6[f]	64

Increasing the amine concentration might be expected to increase the proportion of deprotonation of intermediate 212, and thereby increase the yields of products 222 and 223 at the expense of 221. Such a result would help support the proposed involvement of intermediate 212. The pyrolysis of 205-syn was therefore conducted with one equivalent of triethylamine and with 26 equivalents of diethylamine (whose base strength is approximately the same as that of triethylamine in methanolic benzene solution[120]). The results are given in Table XXXIII. The lack of any increase in the yields of 222 and 223 with increased base concentration is at first perplexing. Upon more careful consideration, however, it becomes apparent that products 207 and (most of) 208 must be derived from a different intermediate than are 222 and 223! The most reasonable proposal would seem to be the one diagrammed in Scheme XLVII, which suggests that allene 209 and product 221 can origninate from either tight ion pair 212 or solvent-separated ion pair 224, while products 222 and 223 can be derived only from 224.

According to the mechanism of Scheme XLVII, if the methanol concentration were increased, one might expect the yields of 222 and 223 to increase, because an increased amount of solvent-separated ion pair 224 would be expected to be present. Furthermore, the yield of 221 might also be

Scheme XLVII:

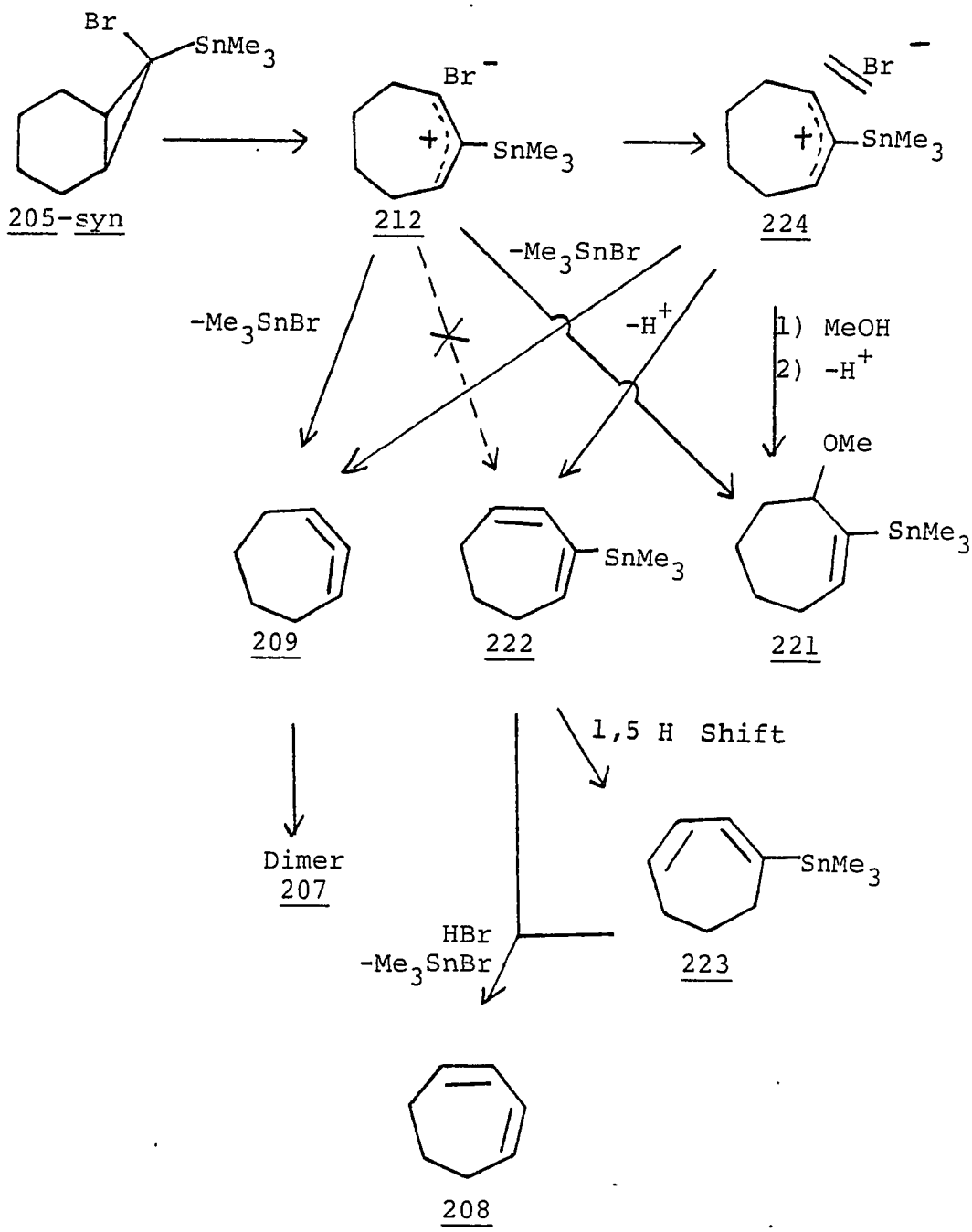


Table XXXIV. Effect of methanol on the pyrolysis of 205-syn in methanolic benzene-d_6 solution[a] in the presence of triethylamine at 160° to 164°

Expt.	Mmol of 205-syn	Mmol of Et_3N	Vol. ratio ($MeOH:C_6D_6$)	Soln. vol. (ml)
1(XI-33)[c]	0.0136	0.0151	14:86	0.36
2(XI-1)[c]	0.0121	0.0143	32:68	0.29
3(XI-32)[c]	0.0145	0.0158	50:50	0.36
4(XI-31)[c]	0.0136	0.0151	71:29	0.35

[a]Base-washed glassware. Each sample of 205-anti was dissolved in the solvent, flushed with nitrogen, and sealed under nitrogen, in an NMR tube.

[b]Yield measured by GC integration vs. an internal standard, with correction factors, based on unrecovered starting material.

[c]Notebook number, followed by page number.

[d]See the Experimental for a discussion of the GC correction factors for these yields.

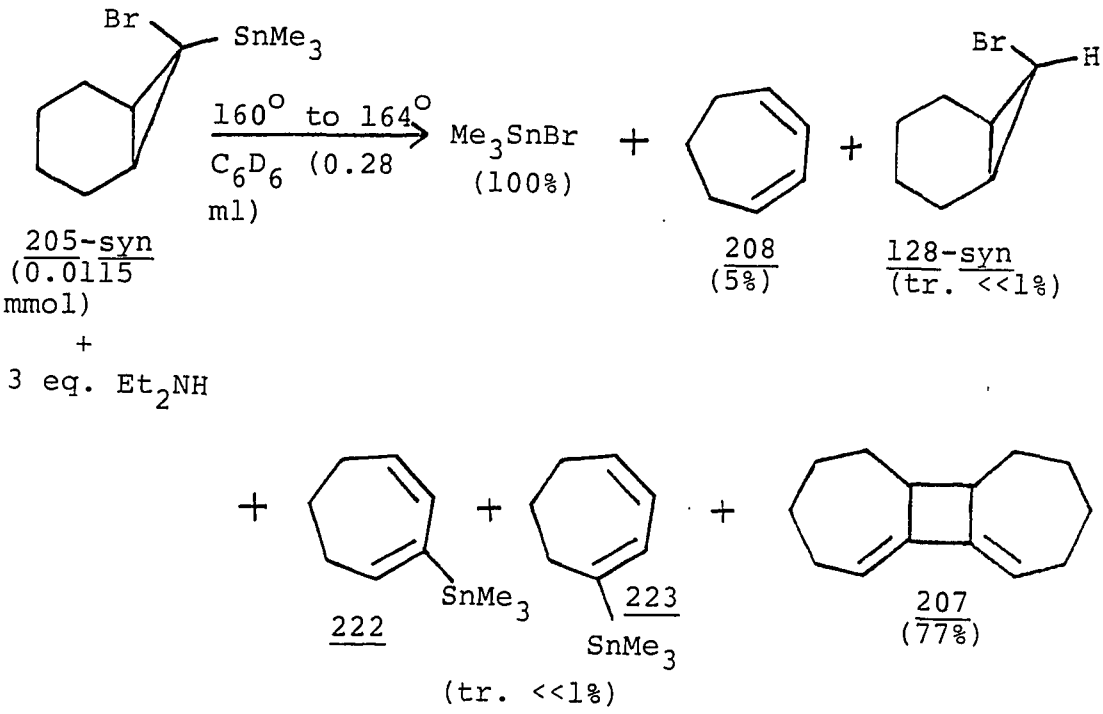
[e]See reference 116.

%Yield[b] 208	%Yield[b] 222 + 223	%Yield[b] 221	%Yield[b] 207	Ratio (222+223+221) : 207
9.0	1.5[d]	1.5[d]	71	0.011
2.5[e]	4[d]	3[d]	65	0.031
2[e]	1.5[d]	3[d]	70	0.016
ca. 0[e]	0.5[d]	1.5[d]	75	0.007

increased for two reasons: a) the larger proportion of 224 present, and b) the more efficient trapping of 212 because of the higher concentration of methanol present. The results of a series of methanol concentration studies are detailed in Table XXXIV. The yields of 221, 222, and 223 reached their maximum values in the 32% methanol/68% benzene experiment (experiment 2 of Table XXXIV), and then dropped off as the methanol concentration was increased further. These data clearly did not meet with the expectations just discussed, but the mechanism diagrammed in Scheme XLVII may be adequate as is, given the complex effects which solvent variation could have upon all the different rate constants. For simplicity sake, the mechanism of Scheme XLVII will be included in the Conclusion.

It was hoped that an amine, such as diethylamine, might be able to trap the ring-opened ion pair 212 more efficiently than methanol had. Unfortunately, when a benzene solution of 205-syn plus 3 equivalents of diethylamine was pyrolyzed (Scheme XLVIII), no cation trapping products could be detected by GC-MS analysis. (The yields in Scheme XLVIII were corrected GC yields, and were based on unrecovered starting material.) Note that also in experiment 2 of Table XXXIII, in which 205-syn was pyrolized in the presence of 26 equivalents of diethylamine in

Scheme XLVIII:



methanolic benzene solution, there were no cation-trapping products observed.

2. Kinetics studies

Efforts were next directed toward further clarification of the pyrolysis mechanisms of 205-anti and 205-syn through kinetics studies.

The benzene-d_6 solution pyrolysis reactions of 205-anti and 205-syn were both first order in starting material, as shown by the rate plots in Figure 33. (The sample prepara-

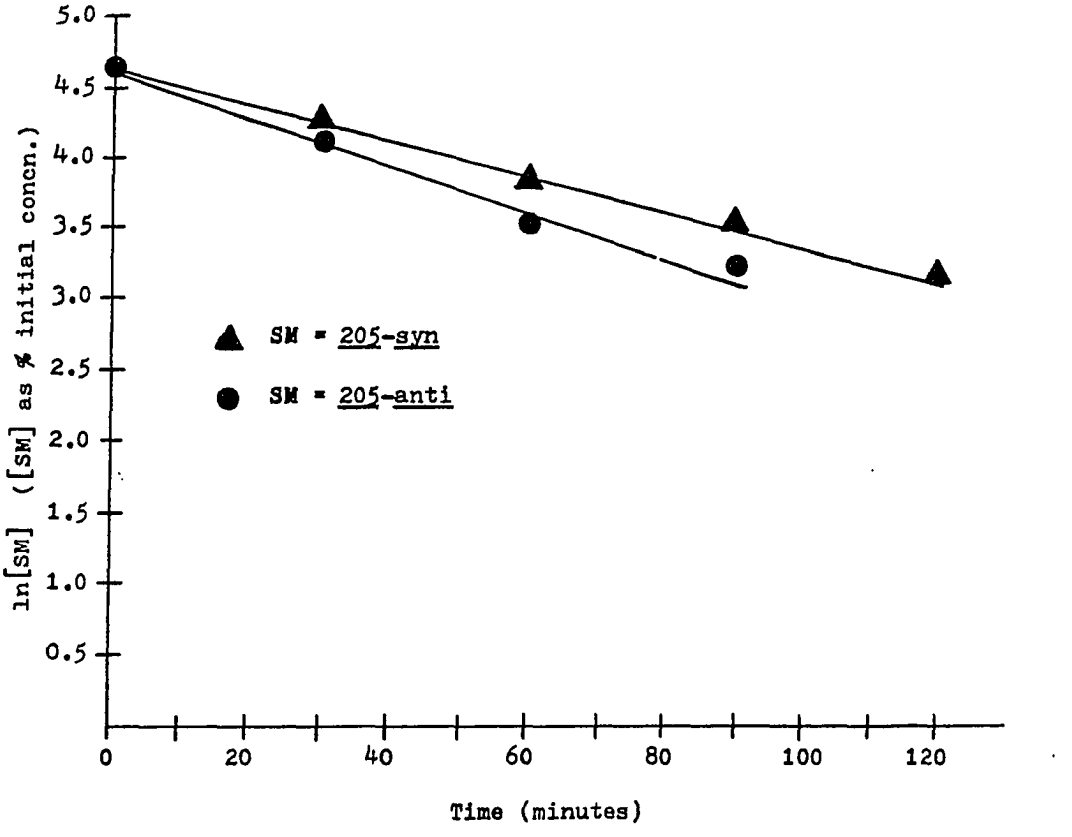


Figure 33. Rate plots of the pyrolysis reactions of 205-anti and 205-syn in benzene-d_6 solution at 160° to 164°

tion is described in the Experimental.) The rate constant at 160° to 164° for 205-anti was 28 ± 1 x 10^{-5} sec^{-1}, and that for 205-syn was 20.6 ± 0.2 x 10^{-5} sec^{-1} (according to least squares analyses, as described in entry 1 of the Experimental).

The cyclohexene solution pyrolysis reactions of 205-anti and 205-syn were also both first order in starting material, as shown by the rate plots of Figure 34. Their rate constants at 160° to 164° were 96 ± 4 x 10^{-5} sec^{-1}, and 4.73 ± 0.08 x 10^{-5} sec^{-1}, respectively (according to least squares analyses, as described in entry 1 of the Experimental).

Note that, in both benzene and cyclohexene solution, 205-anti reacted faster than 205-syn. This same qualitative difference was observed by Seyferth and Lambert[65] for a mixture of 205-anti and 205-syn heated in refluxing cyclohexene solution (83°). The rate difference was rationalized[65] by the greater relief of steric strain expected for the loss of trimethyltin bromide from 205-anti than for that from 205-syn. However, because it is now known from the earlier results of this chapter that the first step in the reaction of 205-anti is C-Br bond heterolysis, the above explanation of the rate difference must be modified. (As will be discussed shortly, the C-Br bond heterolysis is also the rate

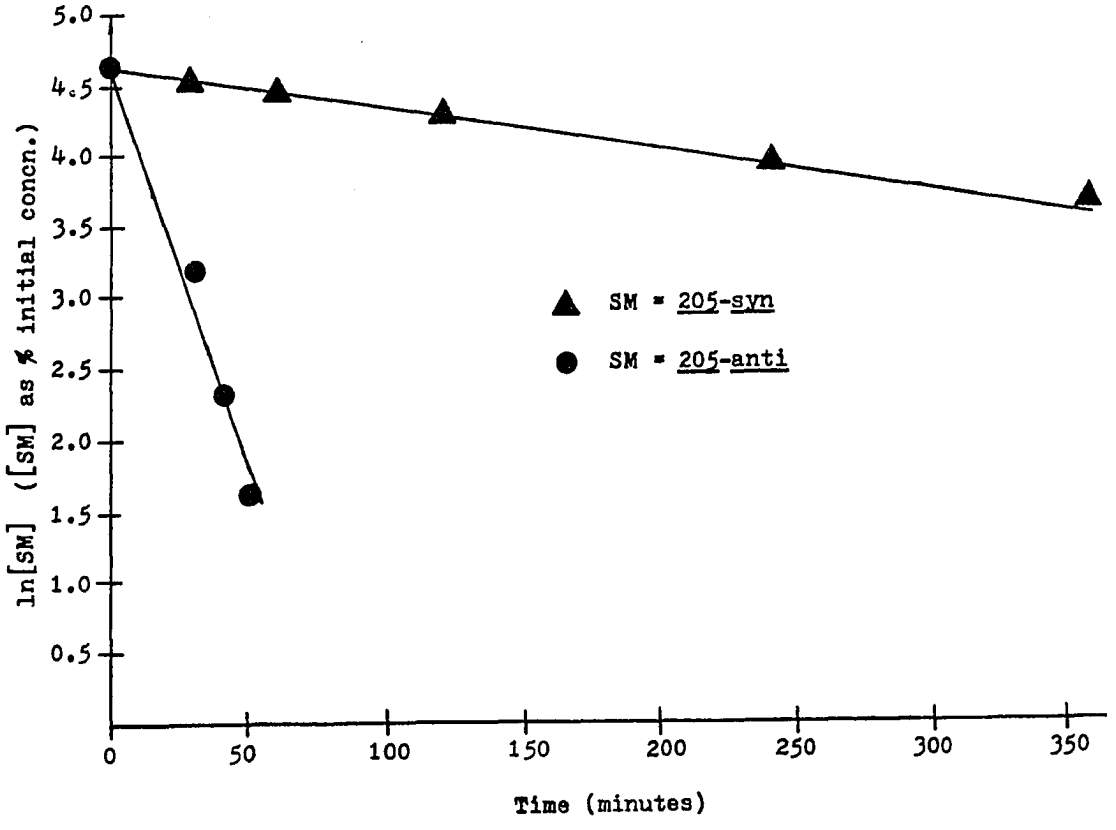


Figure 34. Rate plots of the pyrolysis reactions of 205-anti and 205-syn in cyclohexene solution at 160° to 164°

determining step.) When 205-anti undergoes C-Br bond heterolysis, the steric interaction between the trimethyltin group and the cyclohexyl ring is relieved, whereas if 205-syn undergoes the same heterolysis, such steric relief is not attained. Although the ionization of 205-syn is aided by cyclopropyl ring opening (attested to by the predomimance ring-opening products seen from 205-syn earlier in this chapter), it is not as facile as the ionization of 205-anti if they are conducted in non-polar solvents. As will be seen later, increased solvent polarity apparently enhances the ionic ring opening of 205-syn (to a cis-cycloheptenyl cation) much more than it enhances the C-Br heterolysis of 205-anti (to a cyclopropyl cation). This might be because, in non-polar solvents, much more solvent re-organization is required in order to stabilize the dispersed positive charge in the cycloheptenyl cation obtained from 205-syn, than to stabilize the localized positive charge of the cyclopropyl cation obtained from 205-anti.

The first order rate constants obtained for 205-anti and 205-syn in several batches of cyclohexene solvent are presented in Table XXXV. The uncertainties (calculated from least squares analyses, as described in entry 1 of the Experimental) ranged from $\pm$ 1% to $\pm$ 13%. An estimate of the reproducibility from one experiment to another can be obtained by considering the results of duplicate experiments.

Table XXXV. Rate constants for the pyrolyses of 205-anti and 205-syn in different batches of cyclohexene solvent[a] at 160° to 164°

Expt.	Cyclohexene batch	SM	Mmol of SM
1(X-9)[c]	1[d]	205-anti[e,f]	0.0332
1(X-9)[c]	1[d]	205-syn[e,f]	0.0207
2(X-10-1)[c]	1[d]	205-anti[e,f]	0.0228
2(X-10-1)[c]	1[d]	205-syn[e,f]	0.0142
3(X-15)[c]	2[g]	205-anti[e,h]	0.0173
3(X-15)[c]	2[g]	205-syn[e,h]	0.0108
4(X-18-1)[c]	2[g]	205-anti[e,h]	0.0131
4(X-18-1)[c]	2[g]	205-syn[e,h]	0.0082
5(X-66)[c]	3[g]	205-anti	0.0160
6(X-69)[c]	3[g]	205-syn	0.0124

[a]Base-washed glassware. Each sample was dissolved in cyclohexene; N_2-flushed; sealed under N_2.

[b]Least-squares anal. of a plot of ln [SM] vs. time.

[c]Notebook number, followed by page number.

[d]Distd. under Ar; refrigerated over K_2CO_3.

[e]205-anti and 205-syn mixed in the same sample.

[f,h]Same batch of starting material for these expts.

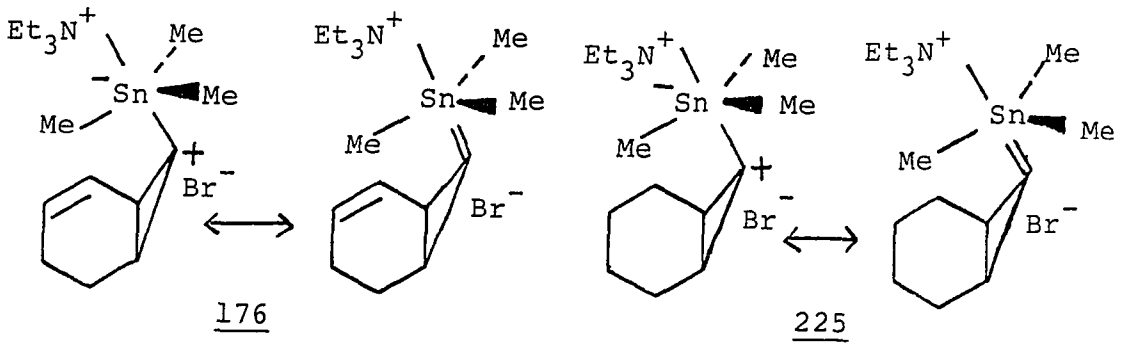
[g]Dist. from Na benzophenone ketyl; refrig. over Na, under Ar.

Soln. vol. (ml)	k^b (sec^{-1}) X 10^5	No. of data points	Uncer-tainty[b] X 10^5	Uncer-tainty[b] (%)	r^b (correlation factor)
ca. 0.3	108	3	± 1	± 1%	0.9999
ca. 0.3	7.8	5	± 0.1	± 1%	0.9995
ca. 0.3	90.3	3	± 0.7	± 1%	0.9999
ca. 0.3	8.0	5	± 0.2	± 3%	0.9985
ca. 0.3	31	3	± 4	± 13%	0.9640
ca. 0.3	5.3	3	± 0.3	± 6%	0.9958
ca. 0.3	27	3	± 3	± 11%	0.9743
ca. 0.3	4.85	6	± 0.04	± 1%	0.9997
ca. 0.3	96	4	± 4	± 4%	0.9908
ca. 0.3	4.73	6	± 0.08	± 2%	0.9994

Experiments 1 and 2 of Table XXXV (duplicates) gave an average rate constant for 205-anti of 99 x 10^{-5} sec^{-1} ± 9%, and experiments 3 and 4 (duplicates) gave 29 x 10^{-5} sec^{-1} ± 7%. Experiments 1 and 2 gave an average rate constant for 205-syn of 7.9 x 10^{-5} sec^{-1} ± 1%, and experiments 3 and 4 gave 5.1 x 10^{-5} sec^{-1} ± 4%. Thus, a reasonable estimate of the reproducibility is ± 9% for 205-anti, and ± 4% for 205-syn.

In Table XXXV, the reaction rate of 205-anti was almost the same in cyclohexene solvent batches 1 and 3 (average k = 98 ± 9 x 10^{-5} sec^{-1}), but was greatly reduced in batch 2 (average k = 29 ± 2 x 10^{-5} sec^{-1}). The maximum rate variation of 205-anti was 300% with a maximum uncertainty in each rate constant of ± 13%). The reaction rate of 205-syn, on the other hand, was much less sensitive, and had a maximum rate variation of only 65% (with a maximum uncertainty in each rate constant of ± 6%). These results parallel the reactivity patterns observed in Chapter III for the unsaturated analogs of 205-anti and 205-syn (35-anti and 35-syn, respectively). Recall that the reaction rate of 35-anti was much more sensitive to different batches of solvent than that of 35-syn. The acceleration of the 35-anti reaction rate by variable amounts of Lewis acids, such as tin tetrachloride and aluminum trichloride, through their coordination with the bromine, probably accounts for these rate fluctuations. Recall also that the 35-anti reaction was strongly in-

hibited by triethylamine, via deactivation of Lewis acid impurities, plus the formation of a complex (176) between triethylamine and the initially formed cyclopropyl ion pair (166). Because interaction between the tin and the bromide



176 225

ion was no longer favorable, and interaction between the double bond and the cyclopropyl cationic center was also no longer favorable, complex 176 preferred to return to starting material, plus triethylamine, thus lowering the reaction rate. It would seem completely reasonable to suggest the possibility of a similar triethylamine complex (225) for the saturated analog (cyclopropyl ion pair 211). Since the reaction of 205-syn, on the other hand, appears not to involve a distinct cyclopropyl cation intermediate, one might expect its reaction rate to be much less sensitive to triethylamine (by analogy with its unsaturated analog, 35-syn). The results of the pyrolysis of 205-anti and 205-syn, with and without triethylamine, are listed in Table XXXVI. The

Table XXXVI. Rate constants and product distributions for the pyrolyses of 205-anti and 205-syn in cyclohexene solution,[a] with and without triethylamine, at 160° to 164°

Expt.	SM	Mmol of SM	Mmol of Et_3N	Soln. vol. (ml)
1(X-10-1)[d]	205-anti[e]	0.0228	0	ca. 0.3
1(X-10-1)[d]	205-syn[e]	0.0142	0	ca. 0.3
2(X-10-2)[d]	205-anti[e]	0.0171	0.0086	ca. 0.3
2(X-10-2)[d]	205-syn[e]	0.0107	0.0086	ca. 0.3
3(X-66)[d]	205-anti[g]	0.0160	0	0.26
4(X-69)[d]	205-syn[h]	0.0124	0	0.26
5(X-64-1)[d]	205-anti[g]	0.0184	0.0057	0.27
6(X-64-2)[d]	205-syn[h]	0.0166	0.0057	0.27

[a,b]See footnotes a and b, respectively, under Table XXIX. For the structures of the products, see Scheme XLIX.

[c]Least squares anal. of a plot of ln[SM] vs. time.

[d]Notebook number, followed by page number.

[e]These experiments used same batches of starting mater. and solv. The 205-anti and 205-syn were mixed together in each sample.

[f]Distinct curvature for these first order plots (accel. with time), presumably due to a reaction between triethylamine and cyclohexene (white ppt. formed). Least squares anal. on only the first 33% of the reaction.

[g]Same batches of 205-anti and solv. for these expts.

[h]Same batches of 205-syn and solv. for these expts.

%Yield[b] 208	%Yield[b] 98	%Yield[b] 207	k (sec_5^{-1})[c] X 10^5	No. of data points	Uncer-tainty[c] X 10^5
Not Meas.	Not Meas.	Not Meas.	90.3	3	± 0.7
Not Meas.	Not Meas.	Not Meas.	8.0	5	± 0.2
Not Meas.	Not Meas.	Not Meas.	10[f]	3	± 1[f]
Not Meas.	Not Meas.	Not Meas.	4.1	5	± 0.1
ca. 0	53	16	96	4	± 4
ca. 4.5	18	58	4.73	6	± 0.08
ca. 0	59	25	36[f]	3	± 2[f]
ca. 2	23	48	5.4	9	± 0.1

product distributions did not depend upon whether or not triethylamine was present, but the reaction rates clearly did. By comparing experiments which used the same batches of starting material (see the footnotes under Table XXXVI), one can see that the reaction rate of 205-anti was much more sensitive to triethylamine than that of 205-syn. Averaging the results gave a $k(Et_3N)/k(\text{no } Et_3N)$ ratio for 205-anti of 0.24, while the same ratio for 205-syn was 0.83. It is very reasonable to postulate the involvement of triethylamine deactivation of Lewis acid catalysts, and probably also the formation of triethylamine complex 225, in order to explain the inhibition of the 205-anti reaction by triethylamine. As a further emphasis for this point, one should note that the first order rate constant for 205-anti at 160° to 164° in benzene-d_6 solution is lowered from $28 \pm 1 \times 10^{-5}$ sec^{-1} in the absence of diethylamine (experiment X-72) to $< 0.5 \times 10^{-5}$ sec^{-1}, i.e., no detectable reaction after 90 minutes, by the presence of 3 equivalents of diethylamine (experiment X-75)! For 205-syn, on the other hand, the rate constant in benzene-d_6 at 160° to 164° is only lowered from $20.6 \pm 0.2 \times 10^{-5}$ sec^{-1} ($r = 0.9995$) in the absence of diethylamine (experiment X-73-1) to 17.4×10^{-5} sec^{-1} ($r = 0.9997$) by the presence of 3 equivalents of diethylamine (experiment XI-6). Since no stable trapping products were

formed from the reaction of 205-anti with diethylamine, it is clear that diethylamine can function in a very similar manner to that of triethylamine (i.e., deactivation of Lewis acid catalysts, and formation of a complex analogous to 225), without losing its N-H proton.

Since C-Br bond heterolysis has been proposed to be the rate-determining step for both 205-anti and 205-syn, one would expect solvent polarity studies to be very informative. The results of a series of such studies are presented in Table XXXVII. It seems strange that the reaction rate of 205-anti in 27% methanol/73% benzene solution (experiment 2 of Table XXXVII; $k = 28 \times 10^{-5}$ sec^{-1}) was coincidentally the same as that in benzene solution (experiment 1; $k = 28 \times 10^{-5}$ sec^{-1}). This strange result most likely stems from the extreme sensitivity of the reaction rate of 205-anti to solvent impurities (presumably Lewis acids and bases). This complication was circumvented in experiments 3 through 6 of Table XXXVII by the presence of one equivalent of triethylamine, which deactivated any trace Lewis acid impurities, and leveled the effects of any trace Lewis base impurities. Within that set of experiments, the reaction rate of 205-anti steadily increased with increasing methanol concentration (see Figure 35), a result which is consistent with the proposed ionization mechanism. (Note

Table XXXVII. Solvent polarity studies of the pyrolyses of 205-anti and 205-syn[a] at 160° to 164°

Expt.	SM	Mmol of SM	Vol. ratio ($MeOH:C_6D_6$)	Mmol of Et_3N
1(X-72)[c]	205-anti	0.0142	0:100	0
2(X-71)[c]	205-anti	0.0133	27:73	0
3(XI-2)[c]	205-anti	0.0157	31:69	0.0172
4(XI-16)[c]	205-anti	0.0151	60:40	0.0151
5(XI-14)[c]	205-anti	0.0136	70:30	0.0151
6(XI-15)[c]	205-anti	0.0107	100:0	0.0115
7(X-73-1)[c]	205-syn	0.0127	0:100	0
8(XI-33)[c]	205-syn	0.0136	14:86	0.0151
9(X-74)[c]	205-syn	0.0121	29:71	0
10(XI-1)[c]	205-syn	0.0121	32:68	0.0143

[a]Base-washed glassware. Each sample of starting material was dissolved in the desired solv., flushed with N_2, and sealed under N_2, in an NMR tube.

[b]Least-squares anal. of a plot of ln[SM] vs. time.

[c]Notebook number, followed by page number.

Soln. vol. (ml)	k^b (sec_5^{-1}) X 10^5	No. of data points	Uncer-$_b$tainty^b X 10^5	r^b (correlation factor)
0.29	28	4	± 1	0.9904
0.36	28	4	± 2	0.9856
0.29	1.4	5	± 0.1	0.9967
0.33	4.6	5	± 0.3	0.9903
0.33	8.9	4	± 0.5	0.9911
0.33	22.5	3	± 0.3	0.9998
0.28	20.6	4	± 0.2	0.9995
0.36	64	2	--	--
0.32	220	2	--	--
0.29	240	2	--	--

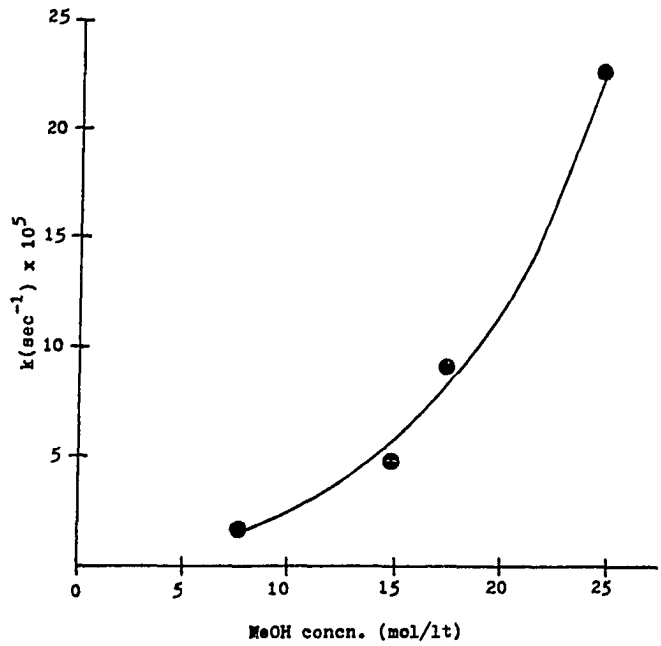


Figure 35. Effect of methanol concentration on the reaction rate of 205-anti (in the presence of triethylamine)

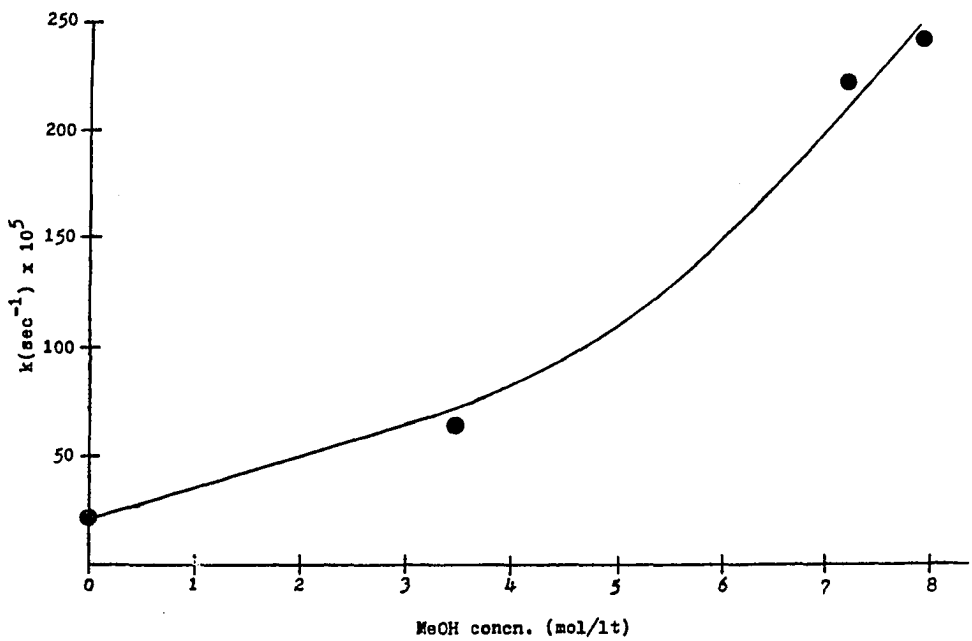
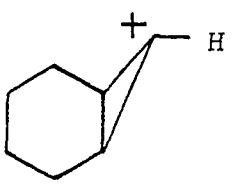


Figure 36. Effect of methanol concentration on the reaction rate of 205-syn

that the presence of triethylamine again very strongly inhibited the reaction of 205-anti, e.g., experiment 3 of Table XXXVII compared to experiment 2.) Experiments 7 through 10 of Table XXXVII showed that the reaction rate of 205-syn also steadily increased with increasing methanol concentration (see Figure 36). (Importantly, the effect of triethylamine was negligible in this case, e.g., experiment 10 compared to experiment 9.)

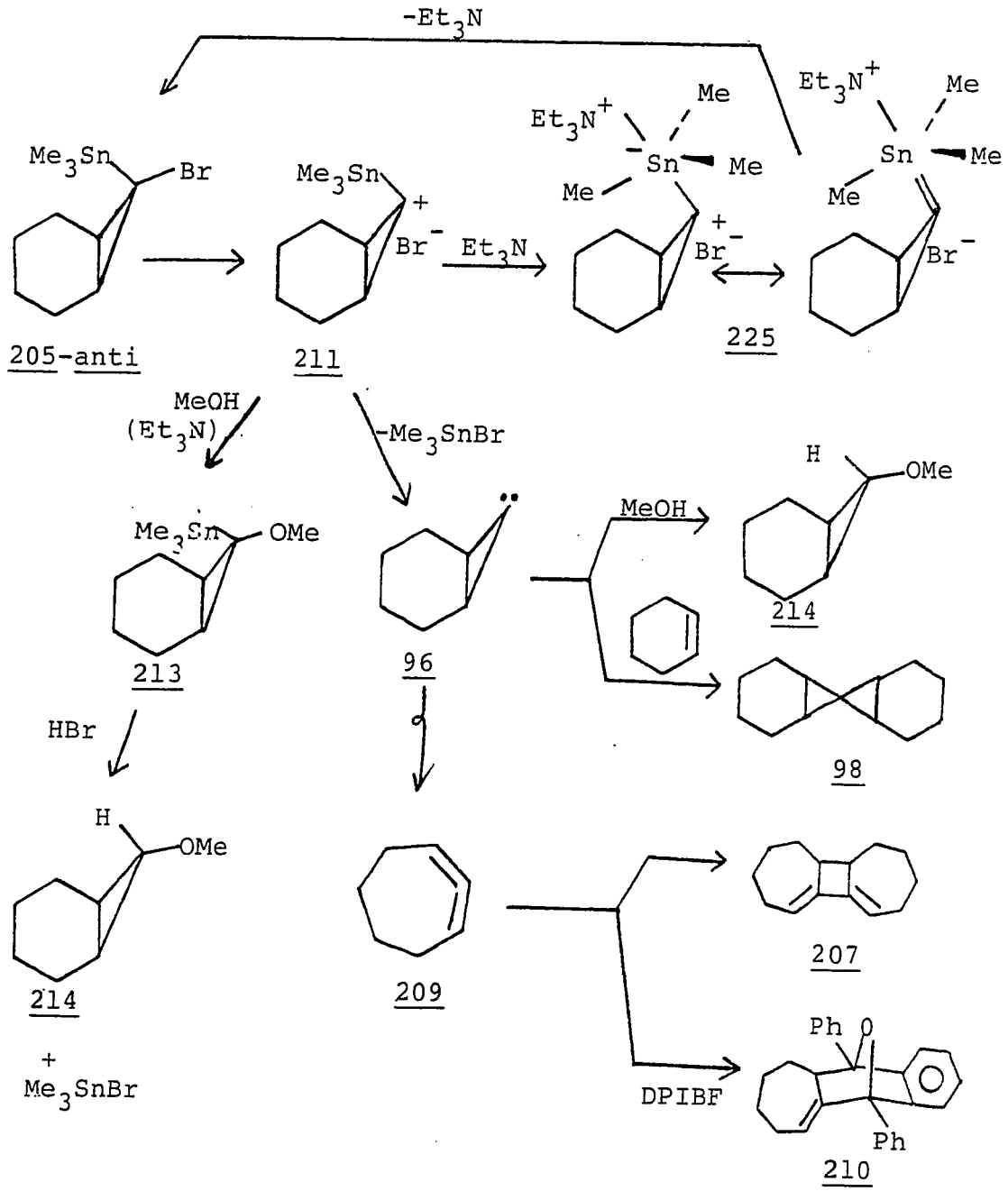
C. Conclusion

A summary of the mechanistic conclusions of this chapter is offered in Scheme XLIX. Notice that in the pyrolysis of 205-anti, allene 209 is written as arising entirely from carbene 96. This assumption is certainly correct, since, even in a polar medium such as 31% methanol/69% benzene solution (Scheme XLIV), there was no evidence for ring-opened cations 212 and 224. The 1 to 3% yield of ring-opened methoxy compound 217 formed under those conditions probably arose from the protonation of carbene 96, anti to the cyclohexyl ring, followed by rapid ring opening of the resulting anti-cyclopropyl cation (215a).

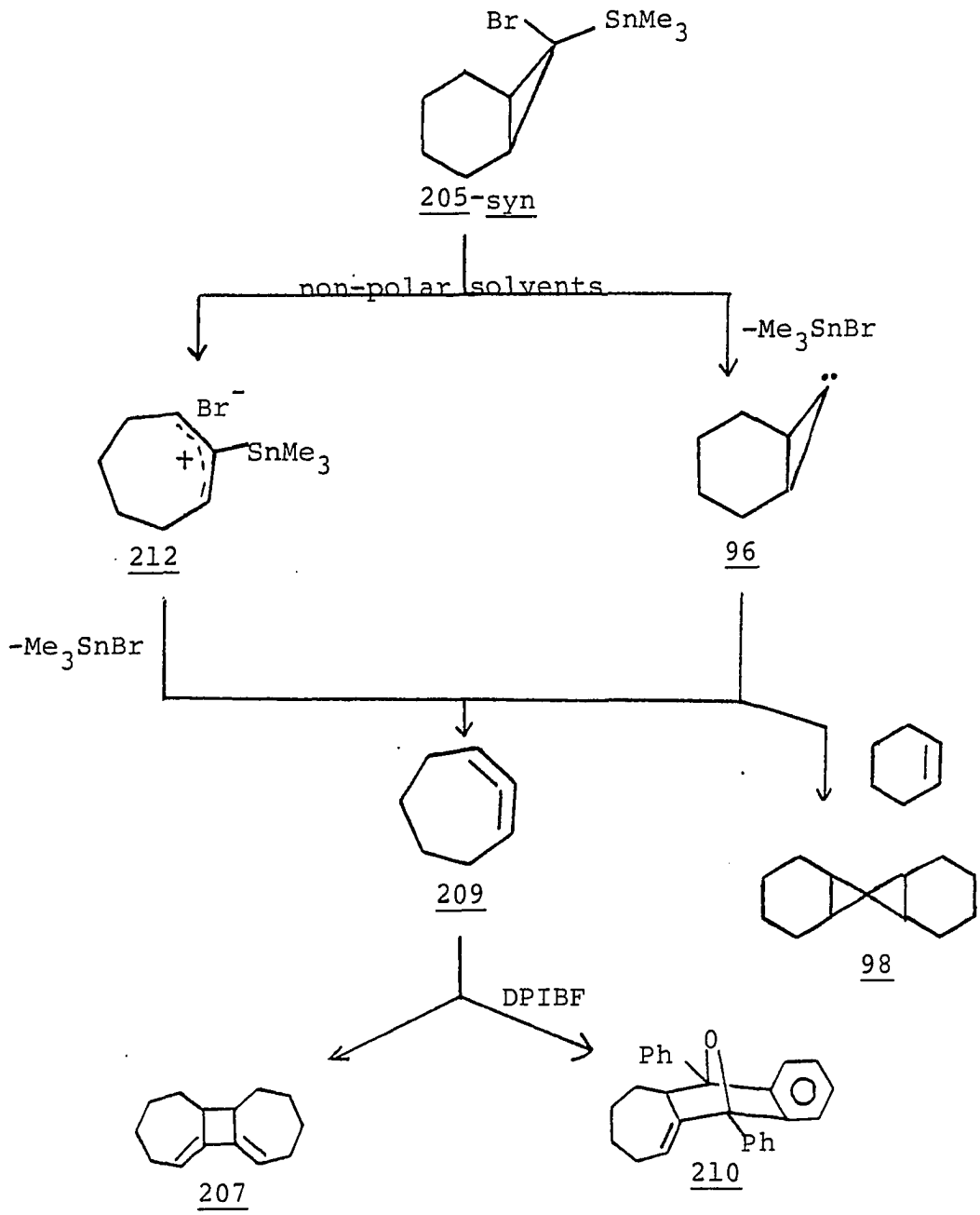


215a

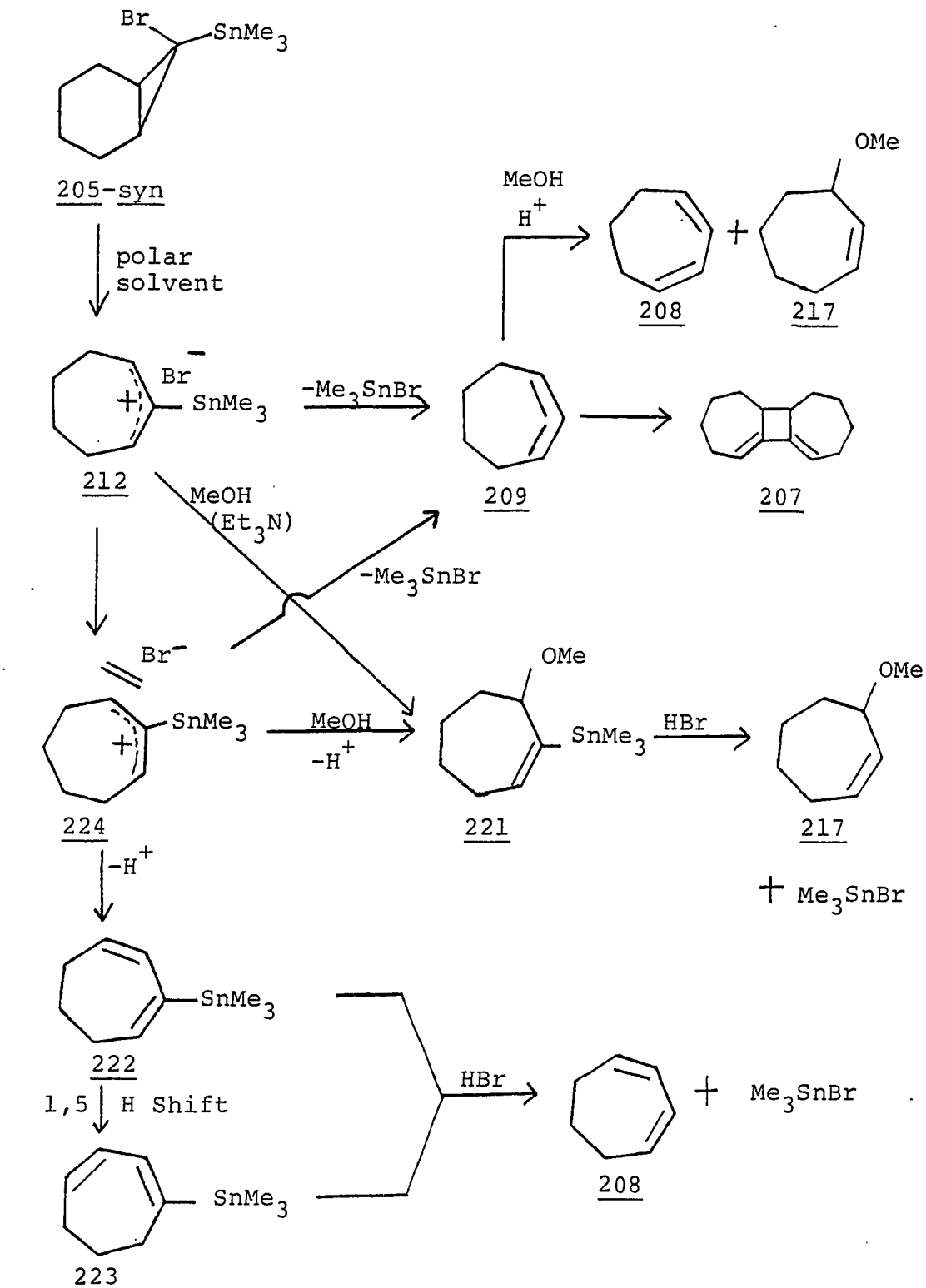
Scheme XLIX:


-Et3N
Me3Sn
Br
205-anti
Me3Sn
+
Br-
211
Et3N
Et3N+
Me
Sn
Me
Me
+-
Br
225
Et3N+
Me
Sn
Me
Me
Br-
MeOH
(Et3N)
-Me3SnBr
Me3Sn
OMe
213
96
MeOH
H
OMe
214
98
HBr
H
OMe
214
+
Me3SnBr
209
207
Ph
O
Ph
DPIBF
210

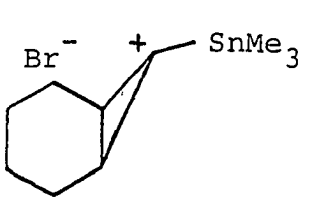
Scheme XLIX (Continued):



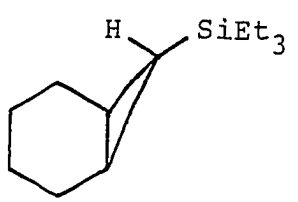
Scheme XLIX (Continued):



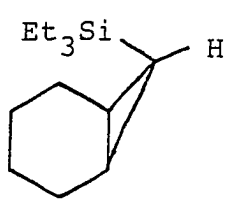
In polar solvents, the reaction of 205-syn clearly involves no cyclopropylidene intermediate. (Ionic ring opening is evidently too facile under those conditions to allow for the formation of the cyclopropylidene.) In the non-polar solvent cyclohexene, however, a substantial amount of cyclopropanation product 98 was formed. This product could in principle arise either from trapping of cyclopropylidene 96, or from an ionic mechanism involving nucleophilic attack of cyclohexene on cyclopropyl cation 226 (if it has a finite lifetime), followed by loss of trimethyltin bromide, or from a kinetically equivalent carbenoid mechanism. It might be very informative to run the reaction



226



127-anti



127-syn

of 205-syn in the presence of triethylsilane. If small amounts of both 127-anti and 127-syn are obtained, then the chemistry of 205-syn in non-polar solvents probably does involve cyclopropylidene 96. (One has to be very mindful, however, of the possibility for tin-silicon redistributions, and/or reduction of alkyl bromides by triethylsilane, such

as were described in Chapter III.) This triethylsilane experiment is being planned for the near future.

D. Experimental

1. General considerations

For the general considerations, see the experimental section of Chapter I.

The first order rate constants, and their uncertainty levels and correlation factors (r) were calculated as described in entry 1 of the experimental section of Chapter III.

2. Preparation of anti-7-bromo-syn-7-trimethylstannylbicyclo[4.1.0]heptane (205-anti) and syn-7-bromo-anti-7-trimethylstannylbicyclo[4.1.0]heptane (205-syn)

Compounds 205-anti and 205-syn were prepared by a slight modification, differing mainly in the method of temperature control, of the procedure used by Seyferth et al.,[26] as described below.

A 100 ml 3-neck round-bottom flask, equipped with a magnetic stirring bar, an addition funnel, and a nitrogen inlet, was nitrogen-flushed and dried, and then charged with a solution of 0.5028 g (1.980 mmol) of 7,7-dibromobicyclo[4.1.0]heptane (90) in 35 ml of dry (freshly dis-

tilled from LAH) THF. A solution of 0.4281 g (2.149 mmol) of trimethyltin chloride in 16 ml of dry THF was placed in the addition funnel, and the flask was next cooled to -100° to -105° with a "Skelly B" hexane slush bath. The 1.03 ml (2.20 mmol) of a 2.15 M n-butyllithium/hexane solution was syringed in, down the side of the flask, over a 2 minute period. After the resulting solution had been stirred at -100° to -105° for 20 minutes, the trimethyltin chloride solution in the addition funnel was added dropwise over a 3 minute period. The resulting solution was stirred at -100° to -105° for 10 more minutes, and then stirred under nitrogen while it was being allowed to slowly warm over a 3 hour period. The cooling bath was removed, and the stirring was continued for another 20 minutes, after which time a 10 ml saturated ammonium chloride solution was added as a quench. The mixture was concentrated in vacuo, and partitioned between 50 ml of ether and 10 ml of water. The ether layer was washed with 5 ml of water and with 5 ml of saturated sodium chloride solution, and was then dried (anhydrous magnesium sulfate), filtered, and concentrated on a rotary evaporator to give 0.23 g of a colorless liquid. Purification via preparative TLC on silica gel (hexane) afforded a 25% yield of 205-syn (rf = 0.73) and a 34% yield of 205-anti (rf = 0.63). Their

NMR spectra matched those reported in the literature.[26] 60 MHz ^{1}H NMR (CCl_4) of 205-anti: δ 2.35-0.90 (complex m, 10H), 0.13 (s, with $Sn^{117,119}$ satellites, 9H, J_{HCSn} = 52, 55 Hz). 60 MHz ^{1}H NMR (CCl_4) of 205-syn: δ 2.19-0.95 (complex m, 10H), 0.32 (s, with $Sn^{117,119}$ satellites, 9H, J_{HCSn} = 53, 55 Hz).

3. Pyrolysis of 205-anti and 205-syn in benzene-d_6 solution

a. 205-anti A 4.8 mg sample of 205-anti was dissolved in 0.29 ml of benzene-d_6, and placed in an NMR tube. After the tube had been flushed with argon for 2 minutes, it was sealed under nitrogen, in an NMR tube, and was then fully immersed in a preheated oil bath (160° to 164°), and heated. After 90 minutes, the NMR yield of trimethyltin bromide was 81%, and that of recovered starting material was 19%. Also obtained was a 78% yield (corrected GC yield), based on unrecovered starting material, of tricyclo[7.5.0.$0^{2,8}$]tetradeca-1(14),2-diene (207) whose isolation and spectral data will be described shortly. A trace (<<1% yield) of anti-7-bromobicyclo[4.1.0]heptane (128-anti) was also identified, by comparison of its GC retention time and GC-MS with those of an authentic sample.

b. 205-syn A 4.3 mg sample of 205-syn was similarly reacted. After 120 minutes, the NMR yield of trimethyltin

bromide was 77%, and that of recovered starting material was 23%. Product 207 was again obtained (this time the corrected GC yield was 77%, based on unrecovered starting material). Also obtained were a 1% yield (corrected GC yield) of syn-7-bromobicyclo[4.1.0]heptane (128-syn), and a 9% yield (corrected GC yield) of cyclohepta-1,3-diene (208), based on unrecovered starting material. (Compounds 128-syn and 208 were both identified by comparison of their GC retention times and GC-MS data with those of authentic samples.) In the case of product 208, comparison of the vinyl region of its crude NMR spectrum with that of an authentic sample also gave a positive identification.

Note that when a pyrolysis was conducted with a much higher concentration of starting material (a mixture of 32 mg of 205-anti and 28 mg of 205-syn in 0.3 ml of benzene-d_6), a substantial amount (ca. 50% of the amount of 207) of a mixture of 6 C_7H_{10} trimers was detected by GC-MS analysis (Finnegan GC-MS, Column C).

c. Isolation of the allene dimer, tricyclo[7.5.0.$0^{2,8}$] tetradeca-1(14),2-diene (207) A 117.3 mg crude sample of 205-anti plus 205-syn (isomeric ratio ca. 1:1) was dissolved in 2 ml of benzene, and placed in a 16 mm x 15 cm test tube (with a constriction for sealing). The tube was sealed under nitrogen, and heated at 160° to 164° for 240 minutes. Prod-

uct 207 (rf = 0.71) was isolated by preparative TLC on silica gel (hexane) in 35% yield. Its NMR spectrum matched the literature spectrum.[65] 60 MHz ^{1}H NMR of 207 (CCl_4): δ 5.63 (br t, 2H, J = 5.5 Hz), 2.75-0.7 (complex m, 18H). 70 eV MS (Finnegan GC-MS, Column D), m/e (%RIC): 188 (P, 4.64), 173 (1.76), 160 (1.35), 159 (2.85), 146 (2.11), 145 (6.85), 134 (1.60), 132 (1.74), 131 (6.14), 119 (2.44), 118 (1.50), 117 (5.18), 115 (1.91), 106 (1.52), 105 (4.27), 104 (1.20), 103 (1.08), 93 (2.05), 92 (2.30), 91 (9.36), 81 (1.15), 79 (4.77), 78 (1.35), 77 (3.80), 67 (3.35), 65 (2.67), 55 (2.10), 53 (2.33), 51 (1.53).

4. Pyrolysis of 205-anti and 205-syn in the presence of DPIBF

a. 205-anti A 31.5 mg (0.0933 mmol) sample of 205-anti and 25.8 mg (0.0956 mmol) of 1,3-diphenylisobenzofuran (DPIBF) were dissolved in 0.3 ml of benzene-d_6. The sample was degassed (3 freeze-high vacuum-thaw cycles), and sealed under nitrogen, in an NMR tube, and then fully immersed in a preheated oil bath, and heated at 159° to 163° for 264 minutes. NMR analysis showed that the starting material had been ca. 95% converted to trimethyltin bromide, plus product 210 (the Diels-Alder adduct between DPIBF and cyclohepta-1,2-

diene, 209). GC-MS (Column D) analysis verified that 210 was present. There were two GC peaks, in a ratio of 6 to 1, which, according to GC-MS analysis, were DPIBF adducts of a C_7H_{10} species. The major GC peak showed the m/e 364 parent ion (although it was weak), expected for compound 210. The minor GC peak and a mass spectrum virtually identical to that of the major GC peak, except that it did not show the parent ion. (The highest mass fragment observed, i.e., m/e 344, corresponded to the loss of water.) This lack of a parent ion for the minor GC peak may have been due to the fact that it was such a small GC peak. These two GC peaks were probably the two diastereomers of 210. The dimer (207) and the 6 C_7H_{10} trimers which were obtained in the pyrolysis of 205-anti without DPIBF, vide supra, were not present in this pyrolysis with DPIBF.

After the crude product mixture had been air-oxidized for 24 hours (in order to transform the unreacted DPIBF to the very polar, and easily separable 1,2-dibenzoylbenzene), product 210 (rf = 0.61) was isolated by preparative TLC on silica gel (10% ether/90% hexane) in 30% yield, as a white solid. (The low yield was probably due to decomposition during the air oxidation.) GC analysis showed that, of the two DPIBF adducts which had been detected in the crude product mixture, only the major one was present in this

purified sample. 60 MHz ^{1}H NMR of 210 (CCl_4): δ 8.0-7.05 (complex m, 14H), 5.70 (m, 1H), 3.21 (d, each peak was broadened, 1H, J = 11.5 Hz), 2.35-0.75 (complex m, 9H instead of 8H--possibly included impurities). Irradiation at a number of points within the δ 2.35-0.75 aliphatic absorption caused partial collapse of the δ 5.70 olefinic multiplet, but the doublet at δ 3.21 showed no tendency to collapse to a singlet. For that reason, a higher field NMR spectrum needed to be run in order to determine whether the doublet at δ 3.21 really was a doublet, and not two singlets. 90 MHz ^{1}H NMR, Jeol FX-90Q (CCl_4): in addition to aromatic, olefinic, and aliphatic absorptions, δ 3.22 (d with broadened peaks, 1H, J = 11.5 Hz). Because the spacing was the same as in the 60 MHz NMR spectrum, it was clear that the doublet at δ 3.22 really was a doublet, and not two singlets. Therefore, the isolated sample of 210 probably consisted of only one diastereomer. IR (CCl_4): 3100 (sh), 3075 (m), 3040 (m), 2940 (s), 2885 (w), 2862 (m), 2850 (sh), 1955 (w), 1607 (m), 1503 (m), 1490 (sh), 1460 (m), 1450 (s), 1362 (m), 1355 (sh), 1346 (w), 1330 (w), 1313 (br m), 1295 (sh), 1235 (m), 1180 (w), 1060 (w), 1025 (m), 1000 (sh), 995 (sh), 985 (s), 960 (w) cm^{-1}; (KBr): 3090 (w), 3062 (w), 3033 (w), 2928 (s), 2902 (sh), 2870 (w), 2848 (w), 2840 (sh), 1958 (w), 1813 (br w), 1600 (br w), 1499 (m), 1480 (sh), 1456 (w), 1446 (s),

1438 (sh), 1398 (br m), 1360 (m), 1353 (sh), 1338 (w), 1328 (w), 1309 (br m), 1294 (m), 1228 (m), 1208 (br w), 1180 (br w), 1153 (br w), 1128 (br w), 1095 (br w), 1073 (w), 1034 (sh), 1023 (m), 1013 (sh), 1000 (m), 993 (m), 980 (s), 960 (sh), 917 (m), 900 (m), 876 (w), 853 (m), 815 (m), 788 (w), 772 (w), 759 (sh), 755 (s), 742 (s), 723 (w), 702 (s), 694 (s), 671 (m), 622 (m) cm^{-1}. The literature IR spectrum[121] was as follows: 763, 759, 747, 705, 699 cm^{-1} (for the endo isomer), and 742, 703 cm^{-1} (for the exo isomer). The isolated sample of 210 seems to be the endo isomer. ^{13}C NMR, Jeol FX-90Q (CCl_4): δ 148.865 (rel. intens. 1063), 146.644 (924), 146.048 (780), 137.706 (584), 136.351 (712), 127.954 (4702), 127.792 (5118), 127.575 (4599), 127.141 (2540), 126.708 (4553), 126.546 (2684), 125.679 (2054), 121.074 (2113), 120.370 (1965), 118.690 (1953), 89.274 (997), 50.648 (1763), 30.444 (3930), 28.602 (2104), 26.922 (1865); (C_6D_6): δ 149.198 (rel. intens. 496), 147.140 (261), 146.490 (265), 138.147 (328), 136.955 (303), 128.395 (2553), 128.287 (3632), 128.070 (3040), 127.149 (2297), 126.228 (632), 126.120 (1088), 125.633 (204), 121.569 (959), 121.028 (977), 119.132 (953), 89.988 (295), 89.879 (309), 50.930 (884), 30.828 (851), 30.395 (985), 28.715 (924), 27.036 (1051). Gated Decoupled ^{13}C NMR (C_6D_6): The two peaks at δ 89.988 and δ 89.879 became one broadened singlet at δ 89.9, and the peak at δ 50.930 became

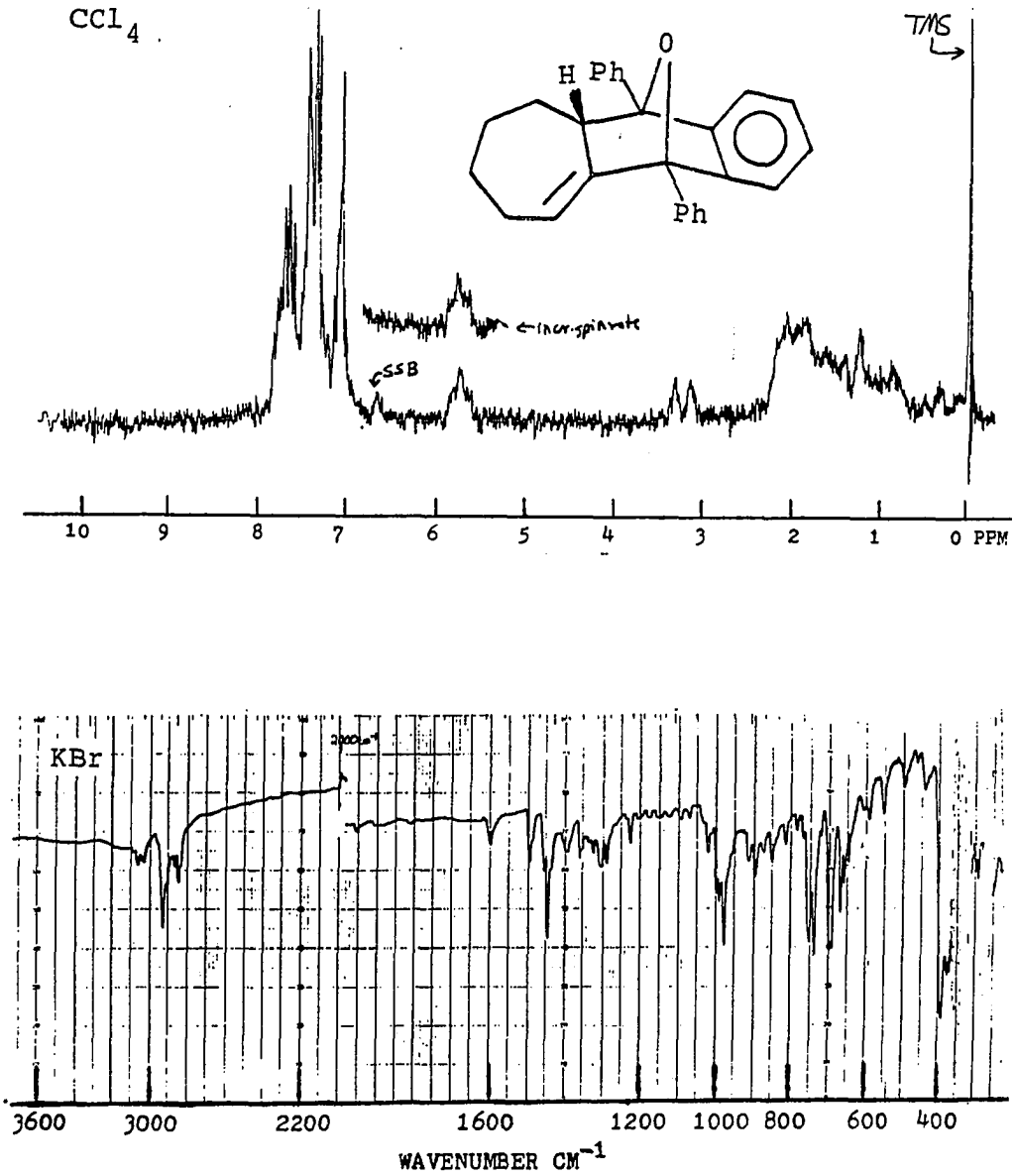


Figure 37. 60 MHz ^{1}H NMR and IR spectra of 210 (Diels-Alder adduct of 1,2-cycloheptadiene with DPIBF; endo isomer)

a doublet (spacing = 132 Hz). 70 eV MS (Finnegan GC-MS, Column C), m/e (%RIC): 364 (P, 0.23), 347 (P-17, 1.08), 346 (P-18, 3.72), 270 (P-94, 1.48), 259 (3.19), 241 (1.14), 239 (0.89), 217 (1.52), 215 (1.74), 203 (0.93), 202 (1.66), 181 (0.86), 167 (0.79), 165 (2.53), 152 (0.82), 141 (0.99), 129 (0.97), 122 (1.13), 117 (0.77), 115 (1.26), 105 (7.73), 91 (4.75), 79 (1.70), 78 (1.47), 77 (10.04), 55 (1.06), 53 (0.72), 51 (2.27). Analysis: Calcd. for $C_{27}H_{24}O$: m/e 364.18272. Found: 364.18361.

b. 205-syn Compound 205-syn (26.9 mg) was similarly pyrolyzed in the presence of DPIBF (25.8 mg). The product mixture was identical by NMR and GC with that obtained above from 205-anti, in part a above. The isolated yield of 210 was again 30%.

5. Pyrolysis of 205-anti and 205-syn in cyclohexene solution

a. 205-anti Cyclohexene was purified by distillation from sodium benzophenone ketyl, and was then stored over sodium, under argon, in a refrigerator.

A 5.4 mg sample of 205-anti was dissolved in 0.26 ml of the purified cyclohexene. The sample was briefly flushed with nitrogen, and then sealed under nitrogen, in an NMR tube. Next, the tube was fully immersed in a preheated 160° to 164°

oil bath, and heated. After 360 minutes of heating, the NMR yield of trimethyltin bromide was 98%, and that of recovered starting material was ca. 0%. Also obtained were the cyclopropanation product 98, and allene dimer 207 (eluted in that order from Column B, C, or D), which were identified by comparison of their GC retention times and GC-MS data with those of authentic samples. Their corrected GC yields were 53% and 16%, respectively.

b. 205-syn A 4.2 mg sample of 205-syn was similarly pyrolyzed in 0.26 ml of cyclohexene. After 357 minutes of heating at 160° to 164°, the NMR yield of trimethyltin bromide was 61%, and that of recovered starting material was 36%. Also identified were cyclohepta-1,3-diene (208), 98, and 207, all identified by comparison of their GC retention times and GC-MS data with those of authentic samples. Their corrected GC yields were 4.5%, 18%, and 58%, respectively, based on unrecovered starting material.

c. Isolation of the cyclopropanation product (98) from cyclohexene and bicyclo[4.1.0]heptan-7-ylidene A 66 mg sample of a 1.8 to 1 mixture of 205-anti and 205-syn was similarly pyrolyzed in 0.3 ml of cyclohexene, to ca. 100% conversion of the starting material. Preparative TLC on silica gel (hexane) afforded a 25% isolated yield of 98 (rf = 0.88). Product 98 was previously identified by

Seyferth and Lambert[65] as the major product of this reaction. 60 MHz ^{1}H NMR of 98 (CCl_4): δ 2.5-0.65 (complex m). 70 eV MS (Finnegan GC-MS, Column D), m/e (%RIC): 176 (P, 0.76), 161 (0.72), 148 (1.74), 147 (3.30), 134 (2.24), 133 (3.87), 120 (1.14), 119 (2.54), 108 (2.44), 107 (2.02), 106 (1.12), 105 (3.45), 95 (3.07), 94 (3.98), 93 (6.31), 92 (2.31), 91 (8.45), 81 (3.52), 80 (4.15), 79 (11.53), 78 (1.48), 77 (3.94), 67 (5.77), 66 (1.38), 65 (1.96), 55 (2.77), 54 (0.95), 53 (2.35), 52 (0.79), 51 (1.07).

6. Pyrolysis of 205-anti and 205-syn in methanolic benzene-d_6 solution

a. 205-anti A 4.5 mg sample of 205-anti was dissolved in 0.36 ml of 27% methanol/73% benzene-d_6 (measured by volume), in an NMR tube. The sample was briefly flushed with nitrogen, and then sealed under nitrogen. Next, the tube was fully immersed in a preheated oil bath, and heated at 160° to 164°. After a total of 90 minutes of heating, the NMR yield of trimethyltin bromide was 75%, and that of recovered starting material was 25%. Also identified (by comparison of their GC retention times and GC-MS data with those of authentic samples) were (listed in their order of elution from Columns B, C, and D): 208 (cyclohepta-1,3-diene), 217 (3-methoxycycloheptene), 214 (anti-7-methoxy-

bicyclo[4.1.0]heptane), 128-anti (anti-7-bromobicyclo[4.1.0]-heptane), 213 (anti-7-methoxy-syn-7-trimethylstannylbicyclo-[4.1.0]heptane), and 207 (allene dimer, tricyclo[7.5.0.$0^{2,8}$] tetradeca-1(14), 2-diene). They were formed in the following yields (corrected GC yields): 2%, 3%, 80%, 2%, <<1%, and <1%, respectively.

The identity of 214 was verified by similarly pyrolyzing two 14 mg samples of 205-anti, which were run to 100% and 91% conversion of starting material, respectively. After combination of the two samples, and evaporation of the solvent, 214 was essentially the exclusive product detectable in the crude NMR spectrum. Its identity was verified by comparison of its NMR spectrum and GC retention time with those of an authentic sample (see entry 9 below). 60 MHz ^{1}H NMR of 214 (CCl_4): δ 3.20 (2, 3H), 2.72 (t, 1H, J = 3 Hz), 2.15-0.7 (complex m, 16H, instead of 10H--possibly included some impurities). 70 eV MS (Finnegan GC-MS, Column D), m/e (%RIC): 126 (P, 5.52), 125 (P-1, 0.88), 111 (P-15, 2.90), 98 (1.43), 97 (8.58), 95 (P-31, 1.48), 94 (P-32, 5.96), 93 (1.62), 84 (2.23), 81 (4.38), 80 (2.22), 79 (13.06), 77 (2.35), 71 (6.43), 69 (3.63), 67 (6.83), 58 (4.50), 55 (8.21), 53 (4.31).

b. 205-syn A 4.1 mg sample of 205-syn was dissolved in 0.32 ml of 29% methanol/71% benzene-d_6 (measured by vol-

ume), and pyrolyzed as in part a above. After 30 minutes of heating at 160° to 164°, the NMR yield of trimethyltin bromide was 94%, and that of recovered starting material was 6%. After another 60 minutes of heating, the starting material was completely consumed. Also identified (listed in their order of elution from either Column D or G) were 208, 217, and 207, all identified by comparison of their GC retention times and GC-MS data with those of authentic samples. Their corrected GC yields were 27%, 25%, and 25%, respectively.

The identity of 217 was verified by heating a 64 mg sample of 205-syn in 2 ml of 30% methanol/70% benzene (measured by volume) in a sealed tube at 160° to 164° for 70 minutes, and then isolating 217 in 7% yield (the low yield was due to the volatility of the product) by preparative TLC on silica gel (10% ether/90% hexane, rf = 0.6). Compound 217 was identified by comparison of its GC retention time and NMR spectrum with those of an authentic sample (synthesized as in entry 10 below). 60 MHz ^{1}H NMR of 217 (CCl_4): δ 5.64 (m, 2H), 3.7 (m, 1H), 3.21 (s, 3H), 2.5-0.6 (complex m, >8H, partially due to impurities). 70 eV MS (Finnegan GC-MS, Column D), m/e (%RIC): 126 (P, 5.39), 125 (P-1, 1.19), 111 (P-15, 5.92), 98 (2.99), 97 (13.54), 95 (P-31, 2.33), 94 (P-32, 5.88), 84 (2.24), 81 (1.76), 79 (8.89), 77 (2.10), 72 (2.82), 71 (4.34), 69 (2.42), 67 (7.84), 65 (1.67), 58 (4.46), 55 (6.78), 53 (3.52).

7. Pyrolysis of 205-anti and 205-syn in methanolic benzene-d_6 in the presence of triethylamine

a. 205-anti A 5.3 mg (0.0157 mmol) sample of 205-anti was dissolved in 0.29 ml of 31% methanol/69% benzene-d_6 (measured by volume), along with 0.0172 mmol of triethylamine (previously purified by distillation from potassium hydroxide). The sample was then pyrolyzed in a sealed NMR tube at 160° to 164°. After 1140 minutes, the NMR yield of recovered starting material was 40%, and that of trimethyltin bromide was 51%. Also detected (listed in their order of elution from Column D and G) were 208 (cyclohepta-1,3-diene), 128-anti (anti-7-bromobicyclo[4.1.0]heptane), 217 (3-methoxycycloheptene), 214 (anti-7-methoxybicyclo[4.1.0]-heptane), 213 (anti-7-methoxy-syn-7-trimethylstannylbicyclo-[4.1.0]heptane), and 207 (the allene dimer, tricyclo[7.5.0.$0^{2,8}$] tetradeca-1(14),2-diene), which were all identified by comparison of their GC retention times and GC-MS data with those of authentic samples). Their corrected GC yields were 1%, 8%, 1%, 58%, 15%, and <1%, respectively, based on unrecovered starting material. (Note that compounds 217 and 214 were separable only on a capillary GC column.)

For the isolation of product 213, three large scale pyrolyses were run with 13.9, 28.5, and 29.9 mg of 205-anti. Each sample was dissolved, along with 1.1 equivalents of tri-

ethylamine, in 0.4 ml of 63% to 73% methanolic benzene-d_6, and then pyrolyzed in a sealed NMR tube at 160° to 164°. After the starting material was approximately 65% consumed, each tube was opened. The pyrolysates were combined, and subjected to purification via preparative TLC on silica gel (10% ether/90% hexane). Compound 213 (rf = 0.64) was isolated in 14% yield, based on unrecovered starting material. The low isolated yield was due to the volatility of 213. 60 MHz ^{1}H NMR of 213 (C_6D_6): δ 3.02 (s, 3H), 2.1-0.8 (complex m, 11H, instead of 10H--possibly includes impurities), 0.32 (s, with $Sn^{117,119}$ satellites, 9H, J_{HCSn} = 50, 52 Hz). 300 MHz ^{1}H NMR, Nicolet NT-300 (C_6D_6): δ 3.02 (s, 3H), 1.80 (m, 2H), 1.55 (m, 2H), 1.28 (m, 2H), 1.1 (m, 2H), 0.99 (m, 2H), 0.32 (s, with $Sn^{117,119}$ satellites, 9H). A 2D NOE NMR experiment demonstrated that there was a substantial NOE between the trimethylstannyl protons and the exo cyclohexyl ring protons, but none between the methoxy protons and the exo cyclohexyl ring protons. ^{13}C NMR (C_6D_6): δ 72.263 (rel. intens. 70), 55.618 (184), 22.387 (433), 22.127 (460), 21.867 (517), -6.938 (242). IR (CCl_4): 3070 (sh), 2985 (m), 2940 (s), 2915 (sh), 2877 (sh), 2863 (m), 2823 (w), 1464 (w), 1448 (m), 1197 (sh), 1188 (m), 1092 (s), 1037 (br w), 980 (br w), 918 (w), 860 (br w) cm^{-1}. 70 eV MS (Finnegan GC-MS, Column D), m/e (%RIC): FPTC (first peak of a $Sn^{120,118,116}$ cluster)

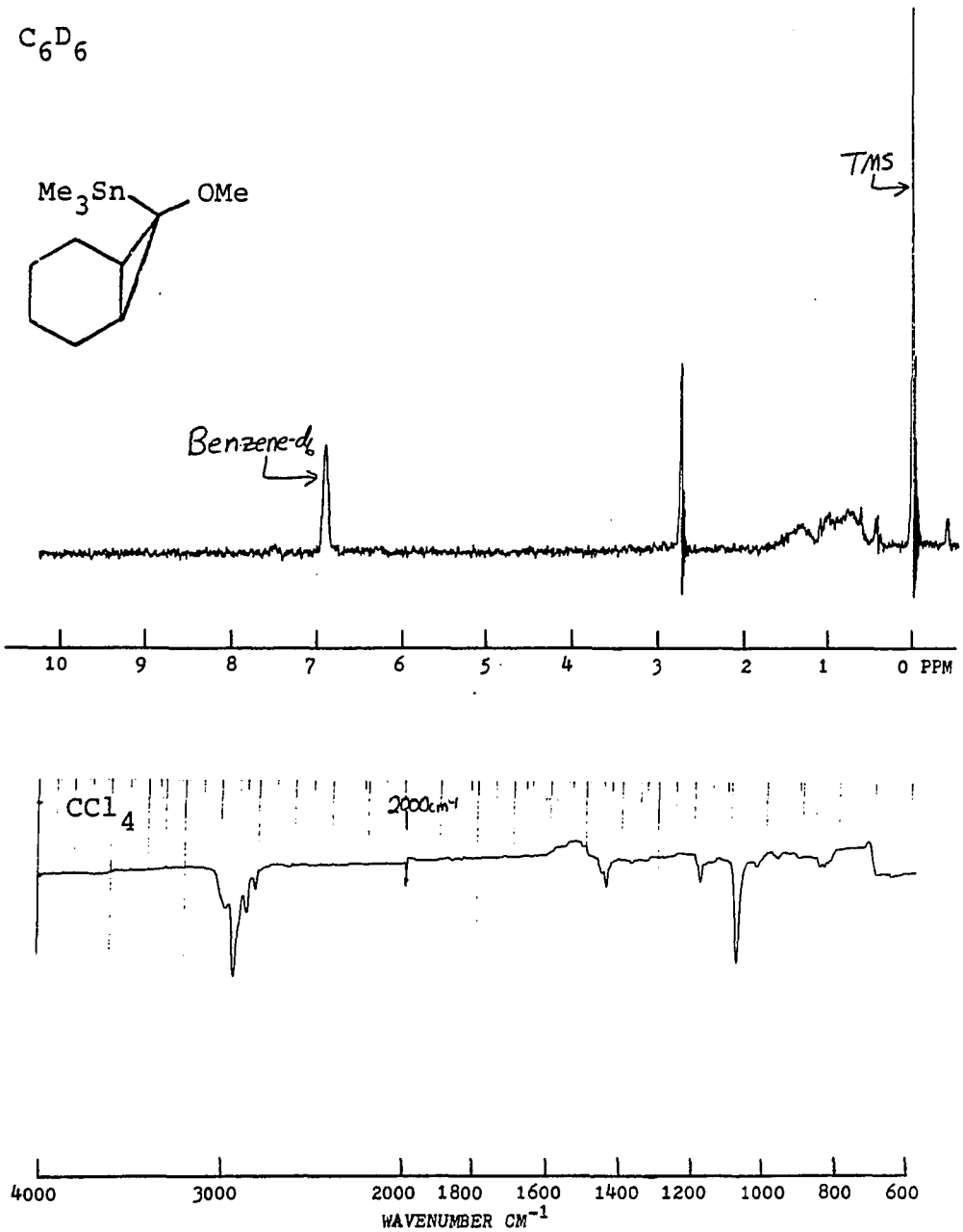


Figure 38. 60 MHz ^1H NMR and IR spectra of 213 (anti-7-methoxy-syn-7-trimethylstannylbicyclo[4.1.0]-heptane)

at 290 ($P^{Sn,120}$, present but < 0.01), FPTC at 275 ($P^{Sn,120}$-15, 0.13), FPTC at 245 ($P^{Sn,120}$-45, 0.37), FPTC at 165 ($P^{Sn,120}$-125, 4.65), FPTC at 151 (1.53), FPTC at 135 (1.98), 126 (2.70), 125 ($P^{Sn,120}$-165, 32.58), 124 (1.64), FPTC at 120 (Sn^{120}, 0.48), 109 (0.78), 95 (2.62), 93 (8.71), 91 (2.48), 77 (2.57), 71 (1.23), 67 (2.79), 55 (1.42), 53 (1.44). Analysis: Calcd. for $C_{11}H_{22}SnO$: m/e 290.06927. Found: m/e 290.07070. Calcd. for $C_{10}H_{19}SnO$ (P-15): m/e 275.04579. Found: m/e 275.04646.

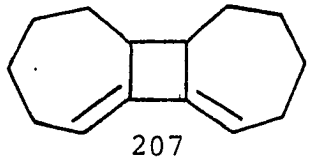
b. 205-syn A 4.1 mg (0.0121 mmol) sample of 205-syn and 0.0143 mmol of triethylamine were dissolved in 0.29 ml of 32% methanol/68% benzene-d_6 (measured by volume), and pyrolyzed in a sealed NMR tube. After the sample had been heated for 12 minutes, the NMR yield of recovered starting material was 17%, and that of trimethyltin bromide was 70%. Also identified (listed in their order of elution from Column D and G) were 208 (cyclohepta-1,3-diene), 222 and 223 (tentatively identified as 2-trimethylstannyl- and 1-trimethylstannylcyclohepta-1,3-diene, in either a 1.3 to 1 or a 1 to 1.3 isomeric ratio), 221 (3-methoxy-2-trimethylstannylcycloheptene), and 207 (allene dimer, tricyclo[7.5.0.$0^{2,8}$]tetradeca-1(14),2-diene). Their corrected GC yields were 2.4%, 4% (222 and 223 combined), 3%, and 65%, respectively, based on unrecovered starting material. (The GC correction factors

for 222, 223, and 221 were assumed to be the same as that measured for 35-anti and 213.)

Compounds 222, 223, and 221 were tentatively identified by GC-MS and on the basis of mechanistic considerations. There were two GC peaks (peak A and peak B) identified as 222 and 223. 70 eV MS (Finnegan GC-MS, Column D) for peak A, m/e (%RIC): FPTC (first peak of a $Sn^{120,118,116}$ cluster) at 258 ($P^{Sn,120}$, 0.60), FPTC at 243 ($P^{Sn,120}$-15, 3.31), FPTC at 211 (0.40), FPTC at 165 ($P^{Sn,120}$-93, 1.33), FPTC at 151 (1.60), FPTC at 135 (2.79), FPTC at 120 (Sn^{120}, 1.30), 94 (2.23), 93 ($P^{Sn,120}$-165, 32.02), 91 (10.84), 77 (5.59), 65 (1.67). 70 eV MS (Finnegan GC-MS, Column D) for peak B, m/e (%RIC): FPTC (first peak of a $Sn^{120,118,116}$ cluster) at 258 ($P^{Sn,120}$, 0.33), FPTC at 243 ($P^{Sn,120}$-15, 2.38), FPTC at 211 (0.24), FPTC at 165 ($P^{Sn,120}$-93, 4.49), FPTC at 151 (1.37), FPTC at 135 (2.56), FPTC at 120 (Sn^{120}, 1.23), 94 (2.02), 93 (29.57), 91 (11.05), 77 (5.63), 65 (1.93). The GC retention time and mass spectral fragmentation pattern were very different from those of anti-7-methoxy-syn-7-trimethylstannylbicyclo[4.1.0]hept-2-ene (213). 70 eV MS (Finnegan GC-MS, Column D) for compound 221, m/e (%RIC): FPTC (first peak of a $Sn^{120,118,116}$ cluster) at 275 ($P^{Sn,120}$-15, 2.19), FPTC at 245 ($P^{Sn,120}$-45, 3.99), FPTC at 215 (0.18), FPTC at 181 (0.65), FPTC at 165 ($P^{Sn,120}$-125, 1.41), FPTC at

151 (7.10), FPTC at 135 (2.72), 125 ($P^{Sn,120}$-165, 1.60), FPTC at 120 (Sn^{120}, 0.64), 109 (0.75), 95 (3.60), 94 (0.87), 93 (9.90), 91 (3.07), 79 (1.48), 77 (2.50), 67 (1.24), 65 (1.00), 55 (0.79), 53 (1.11).

8. Pyrolysis of the allene dimer, 207, in methanolic benzene-d_6 in the presence of 0.1 equivalent of hydrogen bromide



207

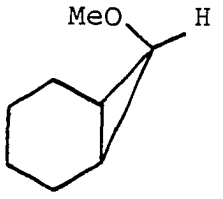
A sample of 207 (the allene dimer, tricyclo[7.5.0.$0^{2,8}$]-tetradeca-1(14),2-diene) was prepared by pyrolyzing 4.5 mg (0.0133 mmol) of 205-anti in 0.30 ml of benzene-d_6, as described in entry 7a above. After 180 minutes of heating at 160° to 164°, the NMR yield of trimethyltin bromide was 100%. The corrected GC yield of 207 was 75%.

To 3/4 of this crude benzene-d_6 solution of 207 was added a solution of 0.0013 mmol of hydrogen bromide (48% aqueous hydrobromic acid) in 0.10 ml of absolute methanol. The resulting solution (30% methanol/70% benzene-d_6 by volume) was sealed in an NMR tube, under nitrogen, and heated, fully immersed in an oil bath, at 160° to 164° for 30 minutes. At this time, the pH of the solution was still ca. 2, as it had

been before the pyrolysis. The corrected GC yield of 207, based on 205-anti, was now 49%. The loss of ca. 35% of the 207 during the heating with hydrogen bromide was probably due to acid catalyzed polymerization. Importantly, there was no detectable amount of either 208 (cyclohepta-1,3-diene) of 217 (3-methoxycycloheptadiene) in the product mixture. The GC peak due to 207 became broader as a result of this pyrolysis, probably because of some isomerization. Also, there appeared a trace (ca. 2% yield) of a new product, whose GC retention time was only slightly longer than that of 207. It was probably an isomer of 207.

9. Preparation of anti-7-methoxybicyclo[4.1.0]heptane (214)

Initial attempts to prepare compound 214 involved bubbling oxygen through a solution of 7-lithiobicyclo-[4.1.0]heptane (129), prepared by treating 7-bromobicyclo-[4.1.0]heptane (128-anti and 128-syn) with n-butyllithium,[122] followed by etherification with methyl iodide. A complex mixture was obtained, the major component of which was tentatively identified by GC-MS as 7-n-butylbicyclo[4.1.0]heptane (102), presumably generated during the initial lithium-bromine exchange reaction. Only trace amounts of 214 and its syn isomer, 227, were present.



227

The above oxidation procedure probably would have worked much better if the 129 had been generated from 128-anti and 128-syn with lithium metal. However, a much simpler procedure was found to work quite well, as described below.

Compound 214 was prepared according to the procedure of Schöllkopf and Paust,[123] with some slight modifications. The first step required preparation of a methyllithium-lithium iodide complex. A 25 ml 3-neck round-bottom flask, equipped with a magnetic stirring bar and a nitrogen inlet, was nitrogen-flushed and dried, and then charged with 0.811 g (6.05 mmol) of anhydrous lithium iodide powder. The addition of 2 ml of dry (freshly distilled from LAH) ether initiated an exothermic process, and the lithium iodide formed a large clump. After a few minutes of standing at room temperature under nitrogen, with the magnetic stirring motor turned on, the clump of lithium iodide loosened enough so that the mixture could be stirred. Next, 8.5 ml (10.9 mmol) of a 1.28 M methyllithium/ether solution was syringed

dropwise into the stirred lithium iodide suspension, over a 10 minute period. The resulting cloudy solution was stirred for 1 hour at room temperature under nitrogen, and then kept under nitrogen, ready for use.

A 50 ml 3-neck round-bottom flask, equipped with a magnetic stirring bar and a nitrogen inlet, was purged with nitrogen and dried prior to being charged with 10.0 ml (98.7 mmol) of cyclohexene and 0.450 ml (4.96 mmol) of α,α-dichloromethyl methyl ether. The the methyllithium-lithium iodide ether solution (prepared above) was syringed in dropwise over a 15 minute period. A white precipitate quickly formed. After another 95 minutes of stirring at room temperature under nitrogen, the mixture was cooled with a room temperature bath, while being quenched by the slow addition of 1 ml of water. (Caution: vigourous bubbling!) The mixture was then diluted with 6 ml of water and 5 ml of ether, and transferred to a separatory funnel, and agitated. The aqueous layer was reextracted with 2 x 10 ml of ether. (Because of emulsions, it was necessary to add some saturated sodium chloride solution during the first re-extraction.) The ether layers were combined, and washed sequentially with 2 x 5 ml of water, 2 x 5 ml of 10% sodium bisulfite solution (to remove any molecular iodine), 5 ml of water, and 5 ml of saturated

sodium chloride solution, and then dried (anhydrous sodium sulfate), and filtered. NMR analysis showed that a 5.6 to 1 mixture of 214 and its syn isomer, 227, had been formed. Purification via preparative TLC on silica gel (10% ether/ 90% hexane) afforded a 7% isolated yield of 214 and a ca. 1% isolated yield of 227. (Note that the volatility of these products most likely accounts for the low isolated yields.) Their NMR spectra matched those reported in the literature.[123] Compound 214 (rf = 0.45) had the following 60 MHz ^{1}H NMR (CCl_4): δ 3.22 (s, 3H), 2.72 (t, 1H, J = 3 Hz), 2.15-0.7 (complex m, 13H, instead of 10H--possibly includes some impurities). Compound 227 (rf = 0.61) had the following 60 MHz ^{1}H NMR (CCl_4): δ 3.33 (s, ca. 3H), 2.87 (t, ca. 1H, J = 7 Hz), 2.2-0.7 (complex m). (Because of the small sample of 227, the NMR spectrum could not be integrated accurately.)

Compounds 214 and 227 were indistinguishable by GC on Column G.

10. Preparation of 3-methoxycycloheptene (217)

a. Cyclohept-2-enol The following one-step reduction of commercial (Aldrich) cyclohept-2-enone was used instead of the three-step literature procedure.[124a,b]

A 100 ml 3-neck round-bottom flask, equipped with a magnetic stirring bar, a nitrogen inlet, and an addition funnel,

was dried and nitrogen-flushed. The addition funnel was charged with a solution of 0.25 g (2.25 mmol) of cyclohept-2-enone in 10 ml of dry (freshly distilled from LAH) ether, and the flask was charged with 15 ml of dry ether and 91.9 mg (2.42 mmol) of LAH. The flask was cooled to 0°, prior to the dropwise addition of the cyclohept-2-enone solution (over a 20 minute period) to the stirred LAH suspension (under nitrogen). The resulting mixture was stirred at room temperature under nitrogen for 24 hours (which was perhaps longer than necessary), then cooled to 0°, and quenched by the cautious addition of 10 ml of 20% Rochelle salt, followed by 10 ml of saturated ammonium chloride solution. The mixture was diluted with 10 ml of ether, and transferred to a separatory funnel. The ether layer was removed and the aqueous layer was re-extracted with 10 ml of ether. The ether layers were combined, washed sequentially with 5 ml of saturated ammonium chloride solution and 3 ml of saturated sodium chloride solution, dried over anhydrous magensium sulfate, and cautiously concentrated *in vacuo*. NMR analysis showed that cyclohept-2-enol was the major product. *60 MHz ^{1}H NMR* of cyclohept-2-enol (CCl_4): δ 5.56 (m, 2H), 4.18 (m, 1H), 2.3-1.0 (complex m, 12H, instead of 8H--possibly included impurities). There was an impurity present (two closely spaced singlets at δ 3.78), tenta-

tively identified as a condensation product from the starting material.

b. 3-Methoxycycloheptene (217) A 100 ml 3-neck round-bottom flask, equipped with a magnetic stirring bar, an addition funnel, and a nitrogen inlet, was nitrogen-flushed and dried. First 2.56 g (53 mmol) of a 50% sodium hydride-mineral oil dispersion were placed in the flask, and washed with three 5 ml portions of hexane. Then, 10 ml of dry (freshly distilled from LAH) ether were added to the flask, and the addition funnel was charged with a solution of 0.24 g (ca. 2.1 mmol) of crude cyclohept-2-enol (prepared as in part a above) in 15 ml of dry ether. While the flask was being cooled with a room temperature bath, the solution in the addition funnel was added dropwise, over an 11 minute period, to the stirred sodium hydride suspension, under nitrogen. After the resulting mixture had been stirred under nitrogen at room temperature for 2 hours, 1.5 ml (24 mmol) of methyl iodide were syringed in over a 2 minute period. The mixture was then stirred at room temperature, under nitrogen, for 72 hours, cooled to 0°, and quenched by the cautious addition of 5 ml of water, followed by 8 ml of saturated ammonium chloride solution, and 20 ml of ether. (There was a large amount of brown polymer present.) After the ether layer was removed, the aqueous layer was re-extracted with 10 ml of ether. The ether layers were

combined and washed sequentially with 3 x 5 ml of saturated ammonium chloride solution, 5 ml of water, and 2 x 3 ml of saturated sodium chloride solution. The organic solution was then dried over anhydrous magnesium sulfate, filtered, and carefully (avoiding volatilization of the product) concentrated *in vacuo*. NMR analysis showed the desired product (217) plus the cyclohept-2-ene condensation product mentioned under part a above. The NMR spectrum of 217 matched that reported in the literature.[124a] Crude 60 MHz ^{1}H NMR of 217 (CCl_4): δ 5.63 (m, 2H), 3.7 (m, 1H) 3.21 (s, 3H), 2.5-0.5 (complex m, <8H, partially due to impurities).

11. *Pyrolysis of anti-7-bromo-syn-7-trimethylstannyl-bicyclo[4.1.0]heptane (205-anti) in the presence of methanol-0-d*

a. In 29% methanol-0-d/71%benzene-d_6 An 8.5 mg sample of 205-anti was dissolved in 0.35 ml of 29% methanol-0-d (99.5$^+$ atom %D)/71% benzene-d_6 (measured by volume), placed in an NMR tube, briefly flushed with nitrogen, and then sealed under nitrogen. The tube was fully immersed in a preheated oil bath, and then heated at 160° to 164° until NMR analysis indicated that the starting material had undergone 85% conversion. NMR analysis also revealed that the proton in the 7-position of compound 214 (anti-7-methoxy-

bicyclo[4.1.0]heptane) was fully deuterated. (The experiment in entry 7a above established that, under these conditions, ca. 20% of the product was due to acid cleavage of anti-7-methoxy-syn-trimethylstannylbicyclo[4.1.0]hept-2-ene, 213.) See entry 6 above for the product yields. Comparison of the GC-MS analyses (Table XXXVIII) of this deuterated sample of 214, and of an authentic sample of 214 (from entry 9 above) suggested that the 214 prepared in this experiment was 100% deuterated, within the detection limits of the mass spectrometer. The $(P+1)^D/P^D$ ratio was 0.08918, which is very close to the natural abundance isotopic ratio of 0.0891.

b. In 29% (0.98:1, methanol-0-d:methanol)/71% benzene-d_6

A sample of 4.0 mg (0.0118 mmol) of 205-anti was dissolved in 0.35 ml of 29% methanol/71% benzene-d_6 (measured by volume, via syringe), which was made up using a 0.98:1 (mole ratio measured by syringe, and double-checked by NMR integration) methanol-0-d/methanol mixture. Next 1.8 µl (0.0129 mmol) of triethylamine (previously distilled from sodium hydroxide) were added, and the solution (in an NMR tube) was briefly flushed with nitrogen, and sealed under nitrogen. The tube was fully immersed in a preheated oil bath, and heated at 160° to 164° until NMR analysis indicated that the starting material had undergone 85% conversion. (See entry 7 above for the product yields.) The GC-MS

data for product 214 are given in Table XXXVIII. The following equation was used to calculate the % deuterium incorporation:

$$\%D = \frac{(P+1)^D + P^D + (P-1)^D + (P-2)^D}{(\text{Numerator}) + (P+1)^H + P^H + (P-1)^H + (P-2)^H},$$

where $(P+1)^D$ = (P+1) intensity for the deuterated 214 (mass 128), etc.

$(P+1)^H$ = (P+1) intensity for non-deuterated 214 (mass 127), etc.

The key to calculating the values of $(P+1)^D$, P^D, etc. was the following relationship:

$$\frac{(P+1)^H}{P^H} = \frac{(P+1)^D}{P^D}$$

$$P^D = (P+1)^D \times \frac{P^H}{(P+1)^H}$$

The remainder of the terms were then calculated by simple algebra. (Since the $(P+1)^D/P^D$ ratio for the fully deuterated 214, entry 10b of Table XXXVIII, 0.08918, was very close to the $(P+1)^H/P^H$ natural abundance ratio of 0.0891, 0.08918 was used as the $(P+1)^H/P^H$ ratio for the above calculation of P^D. The following values were calculated:

$(P+1)^D = 3.236$, $P^D = 36.286$, $(P-1)^D = 2.768$,

$(P-2)^D = 0.588$

$(P+1)^H$ = 1.586, P^H = 97.232, $(P-1)^H$ = 8.075,

$(P-2)^H$ = 0.095 (considered negligible)

Table XXXVIII. GC-MS data for deuterated and non-deuterated samples of 214, at 20 eV

Source	Intens. of m/e 125	Intens. of m/e 126	Intens. of m/e 127	Intens. of m/e 128
Entry 9 (non-deuterated)	7.646_H $(P-1)^H$	100.000 P^H	9.131_H $(P+1)^H$	0.549_H $(P+2)^H$
Entry 10b (fully deuterated)	1.621_D $(P-2)^D$	7.629_D $(P-1)^D$	100.000 P^D	8.918_D $(P+1)^D$
Entry 10a (partially deuterated)	8.663_H $(P-1)^H$ $+(P-2)^D$	100.000 P^H $+(P-1)^D$	37.872 $(P+1)^H$ $+P^D$	3.236_H $(P+2)^H$ $+(P+1)^D$

The %D incorporation for 214 in entry 10b above was calculated to be 29%. The deuterium isotope effect was then calculated to be 2.4, as follows:

$$\frac{k_H}{k_D} = \frac{\%214\text{-}H}{\%214\text{-}D} \times \frac{[MeOD]}{[MeOH]}$$

$$= \frac{71\%}{29\%} \times \frac{0.98}{1.00} = 2.4$$

CONCLUSION

The results discussed in Chapter I of this dissertation showed that anti-7-bromo-syn-7-lithiobicyclo[4.1.0]hept-2-ene (34-anti) underwent a 1,3-rearrangement reaction much faster than did its C^7-epimer (34-syn), even though the former is thermodynamically more stable. The major product of the reaction was a stereoisomeric mixture of the two carbenoid coupling compounds 42-syn and 42-anti (in a 7.5 to 1 ratio, respectively, from 34-anti, and in a 1.5 to 1 ratio, respectively, from 34-syn). The most economical explanation for these results is a carbenoid mechanism, which inolves double bond participation, which is possible for 34-anti, but not for 34-syn. The argument against free carbene involvement can be strengthened by combining a) the lack of any carbene trapping by a large excess of isobutylene, cyclohexene, or triethylsilane with b) the fact that the saturated analogs of 34-anti and 34-syn (89-anti and 89-syn, respectively) apparently do not generate the corresponding cyclopropylidene, i.e, bicyclo[4.1.0]heptan-7-ylidene (96) under reaction conditions, according to the studies discussed in Chapter II. Thus, it can now be stated with confidence that, in solution at least, carbenoids 34-anti and 34-syn participate in a Skattebol-type rearrangement without involving a free carbene intermediate.

Carbenoids 89-anti and 89-syn evidently did not, according to trapping studies with triethylsilane, generate the corresponding free cyclopropylidene (96) under any of the reaction conditions investigated (-78° to +53°, in ether or THF, with or without 12-crown-4-ether). Instead, the carbenoids underwent dimerization, protonation by solvent, or nucleophilic attack either by solvent or by any excess n-butyllithium, all apparently via carbenoid mechanisms.

A further conclusion of Chapter II is that triethylsilane shows promise as a less ambigous alternative to olefins as a carbene trap at low temperatures.

In Chapter III of this dissertation, the pyrolysis reactions of anti-7-bromo-syn-7-trimethylstannylbicyclo[4.1.0]-hept-2-ene (35-anti) and its C^7-epimer (35-syn) were studied, in hopes of observing the Skattebol rearrangement of bicyclo-[4.1.0]hept-2-en-7-ylidene (10) to bicyclo[2.2.1]hept-2-en-7-ylidene (11). The results of the gas-phase pyrolysis studies are not understood at present, but it is known that products resulting from a 1,3-rearrangement reaction accounted for only a very tiny fraction of the product mixture. The solution-phase pyrolysis reactions of 35-anti and 35-syn both involved C-Br bond heterolysis, with no carbene involvement (as evidenced by studies with the carbene traps methanol, cyclohexene, and triethylsilane). The reaction of 35-anti involved an ionic 1,3-rearrangement, to yield the ion pair

7-trimethylstannylbicyclo[2.2.1]hept-2-en-7-ylium bromide (157a), which was trappable by methanol. In the absence of methanol, it underwent a Wagner-Meerwein rearrangement to a [3.2.0] bicyclic allylic cationic species (157b), which then lost trimethyltin bromide, to yield bicyclo[3.2.0]hepta-1,3-diene, which then quickly rearranged to spiro[2,4]hepta-4,6-diene (29). The reaction of 35-syn involved an ionic ring-opening reaction, concomitant with C-Br bond heterolysis, to give a cis-cycloheptenyl cationic species (160), which was trappable by methanol. Ion pair 160, in the absence of methanol, lost trimethyltin bromide, to form the allene cyclohepta-1,2,4-triene (153), which either oligomerized, or was trapped by 1,3-diphenylisobenzofuran (DPIBF), or underwent a 1,5-hydrogen shift, to generate cyclohepta-1,3,5-triene (148).

Chapter IV describes studies of the solution-phase pyrolysis reactions of anti-7-bromo-syn-7-trimethylstannyl-bicyclo[4.1.0]heptane (205-anti), and its C^7-epimer (205-syn). The major reaction pathway of 205-syn was a cationic ring-opening reaction, concomitant with C-Br bond heterolysis (similar to that of 35-syn, described above) to yield a cis-cycloheptenyl cationic species (212), which was trappable by methanol. In the absence of methanol, ion pair 212 lost trimethyltin bromide, to form the allene cyclohepta-1,2-

diene (209), which then either oligomerized, or was trapped by DPIBF. In non-polar solvents, a minor amount of cyclopropylidene generation evidently was involved (according to trapping studies with cyclohexene), but in polar solvents, no cyclopropylidene was generated (according to trapping studies with methanol). The major reaction pathway of 205-anti was C-Br bond heterolysis, leading to the generation of a cyclopropyl cationic species (211), whose stereochemistry renders an ionic ring-opening reaction unfavorable. Ion pair 211 (which was trappable by methanol) chose to lose trimethyltin bromide, thereby generating the corresponding cyclopropylidene (96), which was trappable by either methanol or cyclohexene.

One can generalize by saying that, in solution, α-bromocyclopropyllithium derivatives do not seem to generate significant amounts of the corresponding free cyclopropylidenes under any reaction conditions so far investigated, and the α-bromocyclopropyltin derivatives (in solution-phase pyrolysis reactions) generate the corresponding cyclopropylidene derivatives only if both of the following conditions are met: a) there is no facile cationic ring-opening reaction available, and b) there is no nearby double bond (or perhaps other nucleophilic group) to interact with the cyclopropyl cationic center.

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