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I. The cycloheptatriene-norcaradiene equilibrium problem: Solvolysis of norcaradienylcarbinyl derivatives. II. Solvolytic formation of bridgehead olefins. III Studies of certain cyclopropyl anions and radicals

Shih-Lai Lu
Iowa State University

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I. THE CYCLOHEPTATRIENE-NORCARADIENE EQUILIBRIUM PROBLEM. SOLVOLYSIS OF NORCARADIENYLCARBINYL DERIVATIVES. II. SOLVOLYTIC FORMATION OF BRIDGEHEAD OLEFINS. III. STUDIES OF CERTAIN CYCLOPROPYL ANIONS AND RADICALS.

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by

Shih-Lai Lu

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ABSTRACT

The kinetics of solvolysis of the epimeric tricyclo-[4.3.1.$0^{1,6}$]deca-2,4-diene-10-carbinyl 3,5-dinitrobenzoates, as well as their monoolefin and saturated derivatives, were determined in aqueous acetone. It was found that the anti series solvolyzed faster than the syn analogs. The rate constants were employed to calculated the equilibrium constant for the monosubstituted cycloheptatriene-norcaradiene equilibrium; the estimated energy barrier was ca. 4.5 kcal/mole.

The second part concerns the study of the silver-assisted hydrolysis (in aqueous acetone) and buffered acetolysis of some monobromo- and dihalopropellanes. The major products formed upon solvolysis of the 10,10-dibromo[4.3.1]propellanes indicated that the reactions occurred via bridgehead olefins transoid in a 7-membered ring, followed by protonation and rearrangement. The solvolysis of 11,11-dihalo[4.4.1]propellanes were also shown, via the use of ^{13}C-labeling at the C_{11} position, to proceed via the intermediacy of a bridgehead olefin species, contrary to earlier conjecture. The relative difficulty of generating a bridgehead double bond transoid in a 6-membered ring was demonstrated by the minor amount of such products isolated from the hydrolysis of 9,9-dibromo-[3.3.1]propellane. Comparison of the percentage of products which arose from the bridgehead olefin intermediates with

that which arose from collaps at the bridge position allowed one to estimate an energy difference between the two type of bridgehead olefins (i.e., 7 and 6-membered rings) of ca. 6 kcal/mole. Combination of the rate and product data required that all the anti-10-bromo[4.3.1]propellanes solvolyze via a "partially-opened" cyclopropyl cation intermediate.

Part three describes an investigation of the Grignard reagents derived from the epimeric 10-bromo[4.3.1]propellanes; radical intermediates were indicated. The results revealed that the stereoselective formation of the product arose from reduction of the cyclopropyl radicals anti the the 6-membered ring, regardless of the stereochemistry of the starting bromid bromides or the presence of double bonds in the 6-membered ring. Inversion of syn cyclopropyl radicals to the more stable anti analogs was rationalized by arguing that nonbonding interaction between two hydrogens is worse than that between one hydrogen and one half-filled orbital.

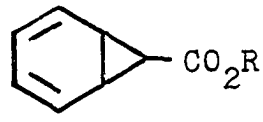
PART I:

THE CYCLOHEPTATRIENE-NORCARADIENE EQUILIBRIUM PROBLEM. SOLVOLYSIS OF NORCARADIENYLCARBINYL DERIVATIVES

INTRODUCTION

The Cycloheptatriene-Norcaradiene Equilibrium Problem

The first substituted norcaradiene, 1, formed from the thermal decomposition of diazoacetic ester in benzene, was reported in 1888 by Buchner.[1] It had been generally accepted that the Buchner esters were mixtures of the basic monocyclic and bicyclic structures until Doering and co-workers[2] reinvestigated the subject. These authors concluded that the Buchner esters are just the four positionally isomeric cycloheptatriene esters, with the ester group occupying 1, 2, 3, and 7 of the seven-membered ring 2. A third structure 3 was considered by Doering, i.e., an intermediate structure which would be regarded as a pseudoaromatic planar compound, a homobenzene; 3 was proposed on the basis of the heat of hydrogenation of cycloheptatriene.



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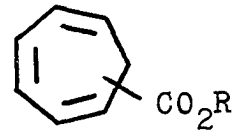

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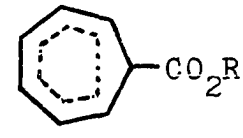

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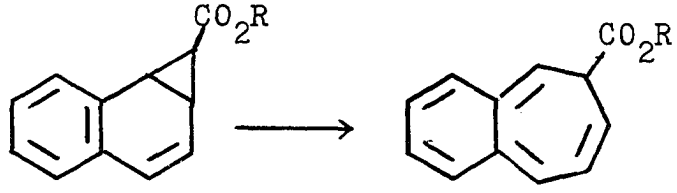
The problem associated with the valence-tautomeric equilibrium has received a great deal of attention since Doering's work. Until 1967, many experimental results

showed that cycloheptatriene and its simple substitution products exist entirely in the monocyclic form.[3] Nevertheless, it was found that the isomerization of 4 to 5 takes place only at high temperature, due to dearomatization of the benzene ring[4,5] during the process. Conversely, benzocycloheptatrienes 6 and 7 do not isomerize to the norcaradiene form 8 and 9, respectively.[6]

Vogel and coworkers[7,8] discovered a very elegant method of fixing the norcaradiene structure. In compound 10 the carbon atoms 1 and 6 of the norcaradiene are held in position by an additional five-membered ring (bracket effect). On the other hand, compounds[9, 10, 11, 12, 13] containing a tetramethylene bridge are more stable in the cycloheptatriene form, 11.



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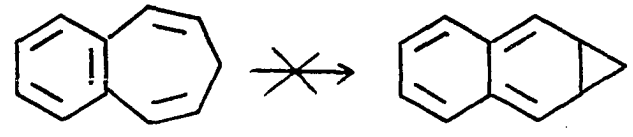

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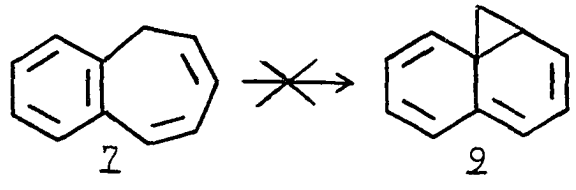

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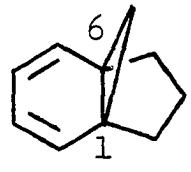

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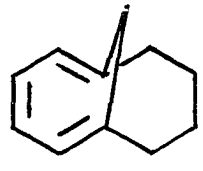

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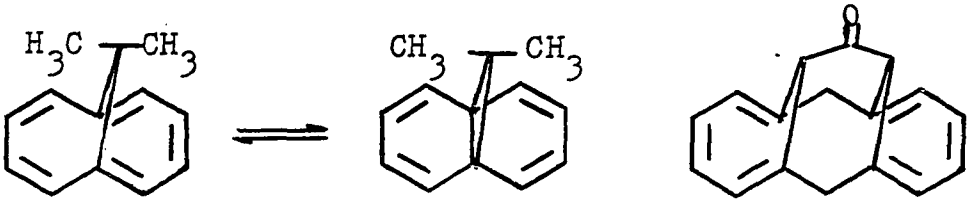
Günther, et al.[14] found that 12 was more stable than 13 by 0.2 kcal/mole and that the barrier for the process 12 ⇌ 13 was less than 6.6 kcal/mole on the basis of results obtained from variable temperature cmr experiments. It has been shown by Günther[13] that compound 14 also exists in valence-tautomeric equilibrium with the norcaradiene form.



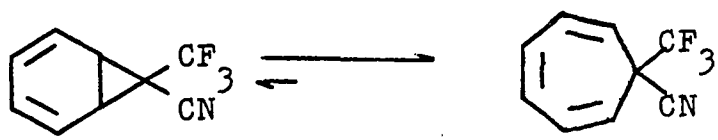
12 13 14

The magnitude of the H-H coupling constant between the methylene protons (3-5 Hz for norcaradienes and 7-12 Hz for cycloheptatriene derivatives[7, 8, 15-23] the ^{13}C-H coupling constants[17-23] and UV data[15-23] have been used to analyze for the presence of the norcaradiene form.

There is no doubt that both compounds with the bicyclic and monocyclic form can exist, but the energy barrier between the two systems may vary considerably. Evidence also exists[3] that the intimate structure of the cycloheptatriene and norcaradiene is sensitive to the demands of the substituent groups, particularly at C_7. For example, compound 15 exists exclusively in the bicyclic form[24] while compound 16 is an open triene.[25]

15 16

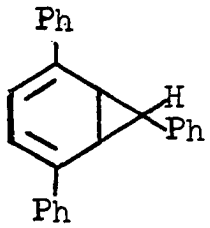
However, a rapidly equilibrating valence tautomeric mixture, 17 and 18, was detected by pmr spectroscopy,[26] in which the cycloheptatriene 18 was the major component. Ciganek[27] later showed the mixture contained 85% of 18 at room temperature, with $\Delta H^\circ = 0$, $\Delta S^\circ = 5$ eu and Ea for 18 $\rightleftharpoons$ 17 equal to about 7 kcal/mole.



17 18

In order to shed more light on the stabilization, by two cyano groups, of the norcaradiene relative to the valence isomeric cycloheptatriene, 15, Ciganek[27] studied a series of compounds where he varied the substituents at C_7 and attempted to estimate the ground-state enthalpy difference for each pair of valence isomers obtained. The thermodynamic parameters of the norcaradiene-cycloheptatriene systems are compiled in Table 1. There are also other compounds (21[28] 22[29] 23[30] and 24[31]) for which no thermodynamic parameters have been reported, but which exist in the norcaradiene form. Thus Ciganek[27] concluded that with the exception of 21, two substituents containing π-systems are necessary for the stabilization of the norcaradiene valence isomer. It is no surprise to see lower entropies for 19 relative to 20 due to the fact that the former is a

much more rigid molecule than the latter.



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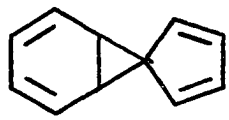

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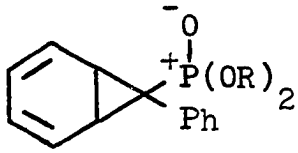

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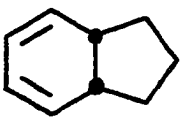
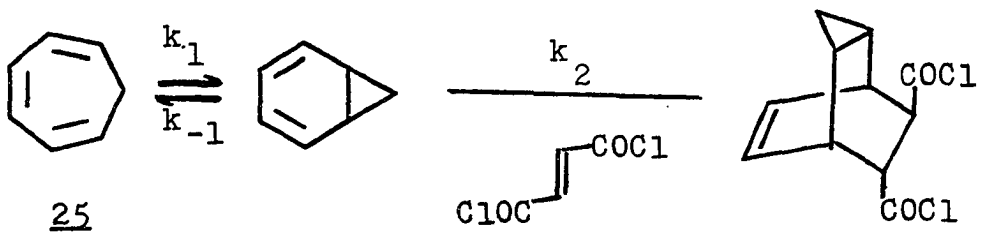
Table 1. Ground-State Enthalpy and Entropy Difference of Norcaradiene-Cycloheptatriene Systems.

19 20

R_1	R_2	$\Delta H°$, kcal/mole	$\Delta S°$, eu	reference
CN	CN	6	-	32
CN	CO_2Me	4	-	27
CN	Ph	3 ~ 5	-	27
CO_2Me	Ph	5.4	16.8	33
CO_2Me	p-$MeOC_6H_4$	2.3	7.4	33
CO_2Me	p-$O_2NC_6H_4$	3.5	11.0	33
CN	CF_3	0.4	5	27
CO_2Me	CO_2Me	0.2	3	34
OMe	OMe	0.25	-	34

Since rapid valence isomerization has been demonstrated for a number of norcaradiene-cycloheptatriene systems, it should be noted that such equilibria exist in all compounds of this type even though they may escape detection by the methods currently available. However using dilatometry, Tsuji, et al. [35] were able to measure the cycloheptatriene-norcaradiene equilibrium. They studied the Diels-Alder reaction of cycloheptatriene 25, dihydroindan and propelladiene 10 with an excess of fumaryl chloride.





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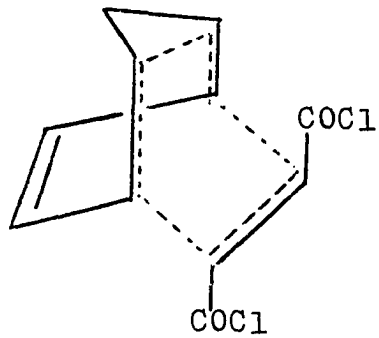
Their results were consistent with a pseudo first-order kinetic expression for the reaction. Equilibrium constants ($K_{eq} = k_1/k_{-1}$) were therefore calculated on the basis of observed rate constants. Two of the calculated equilibrium constants were chosen and led to a value for the free energy difference between cycloheptatriene and norcaradiene of 4.0 - 4.5 kcal/mole. When the authors compared these values with the 11 ± 4 kcal/mole proposed by

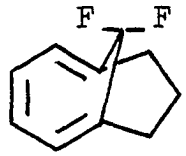
Doering and Willcott[36] on the basis of bond energies, they suggested that the most preferable mechanism for the Diels-Alder reaction of cycloheptatriene is not through the norcardiene form, but through a transition state visualized by the authors as 26.



26

There are several explanations for the effect that C_7 π-substituents exert on the norcaradiene-cycloheptatriene equilibrium. One possibility takes into account the differences in the σ bond energies between differently hybridized carbon atoms: bonds between sp, sp^2 and sp^3 hybridized substituents and C_7 of the norcaradiene (which, as a cyclopropane carbon, is approximately sp^2 hybridized) will be stronger than the bonds between the same substituents and the sp^3 hybridized C_7 of the cycloheptatriene.[37] Alternative rationales include dipole-dipole repulsion between substituents on C_7 and possible electronic interactions between the endo substituent and the planar diene system of the norcaradiene.[38] However, the most popular interpretation[39, 40] is that electronic interaction between the cyclopropane ring and the acceptor substituents results

in a strengthening of the bond between C_1 and C_6 of the norcaradiene by weakening the antibonding contribution to that bond (see Fig. 1a). On the other hand, an electron rich group attached to the cyclopropane ring leads to the weakening of the bond by strengthening the antibonding contribution to that bond.[40] (see Fig. 1b). One representative of the latter type is 27, which exists as a bicyclic triene,[40] in juxtaposition to the hydrogen analog 10, which is a tricyclic diene.



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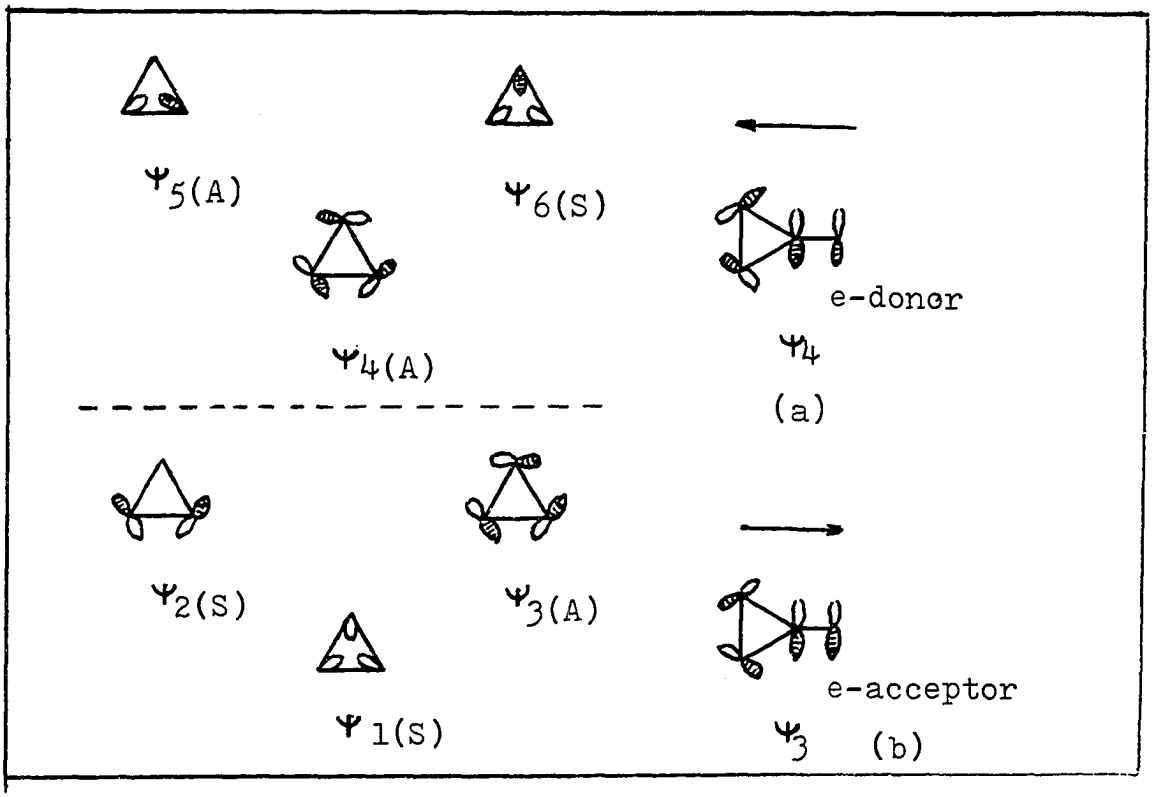
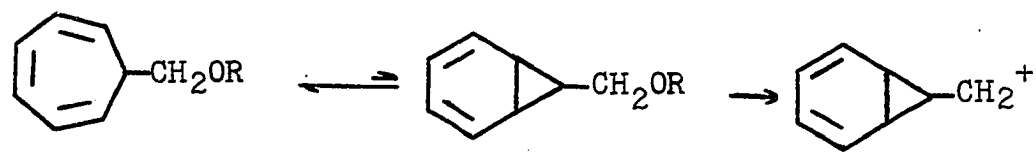


Fig. 1. Qualitative Walsh-Orbital of Cyclopropane and Its Interaction with a Substituent.

Norcaradienylcarbinyl Cations

The first case of cyclopropane participation initiated by valence tautomerism in cycloheptatrienyl carbinyl derivatives was reported by Sargent, et al.[41] The solvolysis of 7-cycloheptatrienylcarbinyl 3,5-dinitrobenzoate 28b in 60% aqueous acetone followed first order kinetics, with $k_1(100°) = 2.6 \times 10^{-6}$ sec^{-1} and $k_1(125°) = 3.0 \times 10^{-5}$ sec^{-1} ($\Delta H^{\ddagger} = 28.3$ kcal/mole, $\Delta S^{\ddagger} = -8.9$ eu).



28b

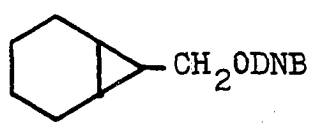
29b

a, R=H

b, R=3.5DNB

H_2O

28a



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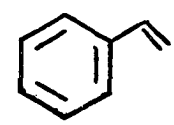
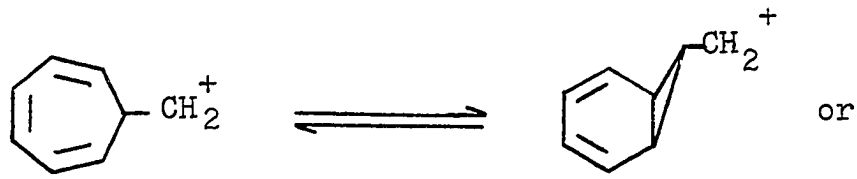


The products from solvolysis in the presence of excess urea were unrearranged 28a (73 ± 6%) and styrene. The latter was shown to be a primary product. The enhanced rate constants and the nature of the observed products led the authors to postulate that solvolysis of 28b involves prior isomerization to the valence tautomer 29b. Furthermore, since the pmr of the starting material 28b shows no

trace of 29b, Sargent estimated the minimum free energy difference between 28b and 29b as 6 kcal/mole. The actual rate constant for 29b at 100° was thus calculated as 2.6×10^{-2} sec^{-1}, approximately 300 times greater than that for the model compound 30 [$k_1(100°) = 9.65 \times 10^{-5}$ sec^{-1}][42]. If the rate enhancement of 28b is due to the electron donating capability associated with a preformed cyclopropane ring in the transition state, the factor of 300 is probably too big to be explained by the error arising from the assumption of the free energy difference (i.e., 6 kcal/mole), unless there is some extra participation by the diene in the norcaradiene form. However, the configuration of the carbinyl carbon in Sargent's system could not be determind, since, in the mobile equilibrium, the presence of the bicyclic tautomer, 29, could not be detected directly. Therefore, Hoffmann's[39] explanation of the electronic factors involved in determining the cycloheptatriene-norcaradiene equilibrium did not take the stereochemistry of the norcaradiene into consideration. Clearly, direct evidence on the nature of ions such as 31 and 32 can only be obtained from an investigation of compounds whose ground-state structure is of the norcaradiene type. Therefore, we chose to study the derivatives of the tricyclo [$4.3.1.0^{1,6}$] decadiene series which have been shown[7] to exist exclusively

in the norcaradiene form.



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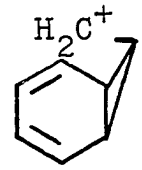

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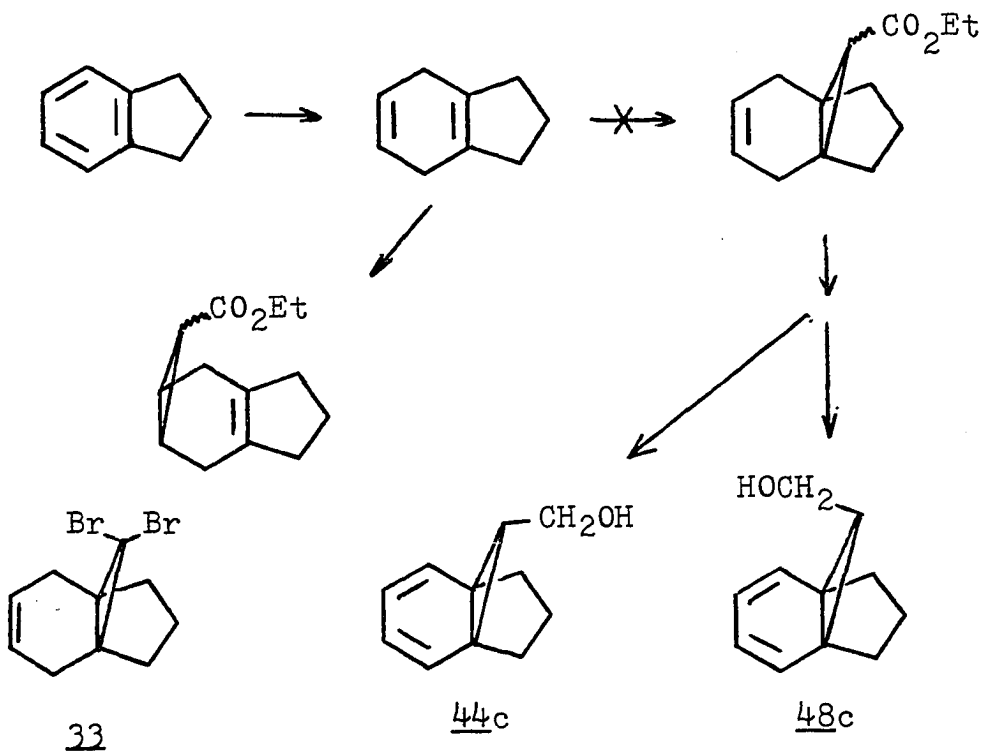
RESULTS AND DISCUSSION

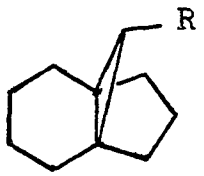
Synthesis

The most obvious route to the desired compounds 44c and 48c is the photo- or copper-catalyzed addition of ethyl diazoacetate to 4,7-dihydroindan. However, only end adducts were obtained in both reactions.[43] An alternative route (Schemes 2 and 3) was thus followed. The compounds used in this study are listed in Scheme 1. Vogel, et al.,[7] have demonstrated that dibromopropellane 33 can be synthesized from 4,7-dihydroindan and dibromocarbene in good yield.



33 44c 48c

Scheme 1



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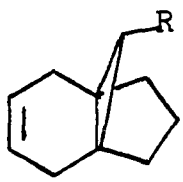

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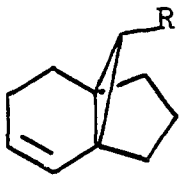

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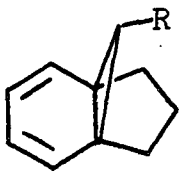

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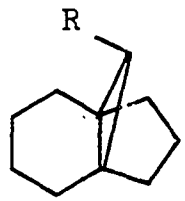

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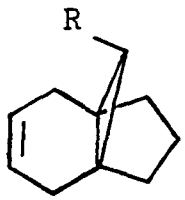

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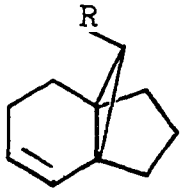

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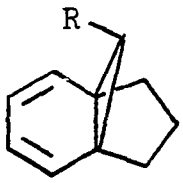


48

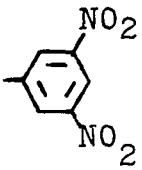
a, R=CO_2H

b, CO_2CH_3

c, CH_2OH

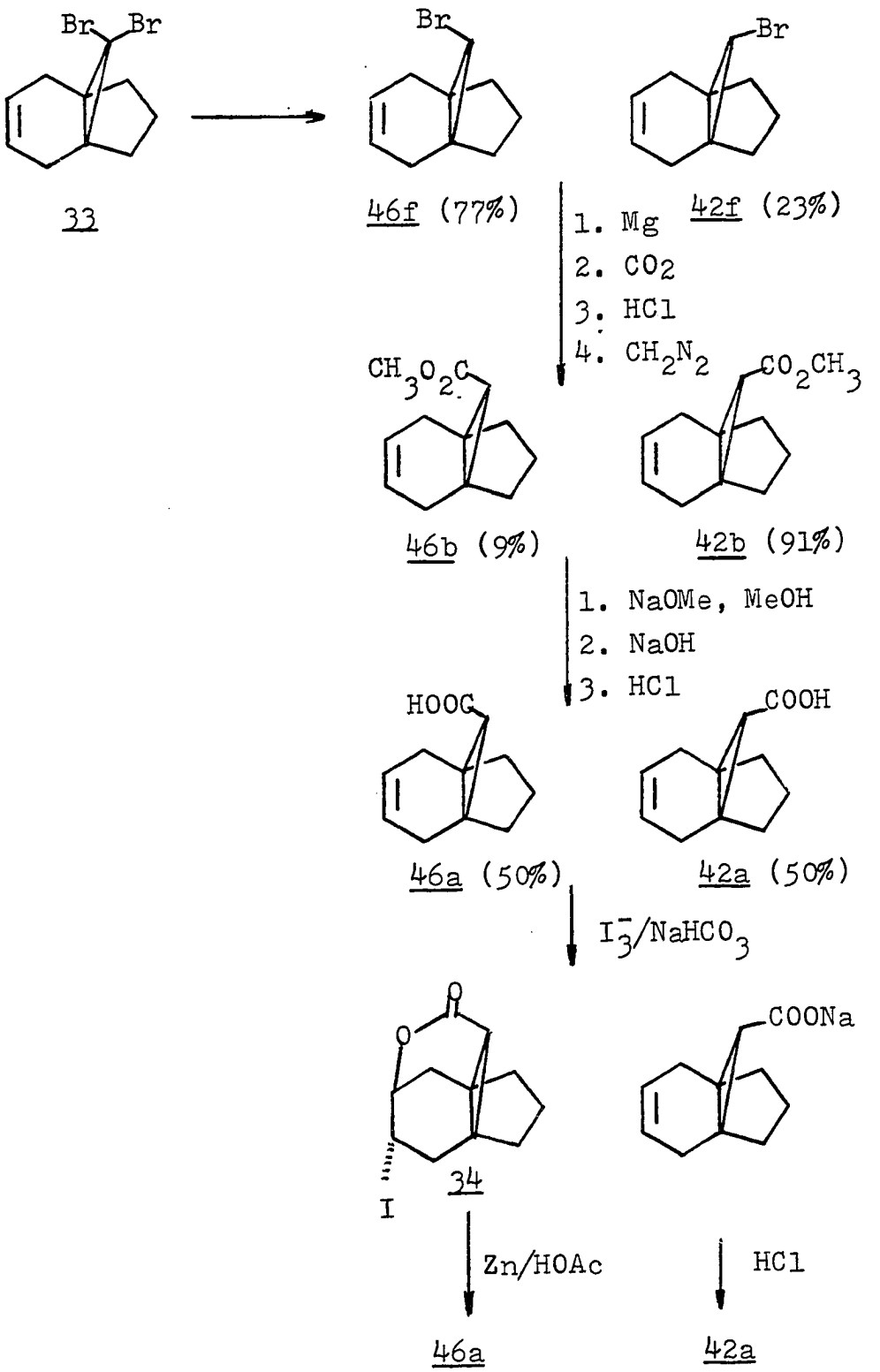
d, CH_2O-(THP)

e, R=CH_2O-C(=O)-(DNB)

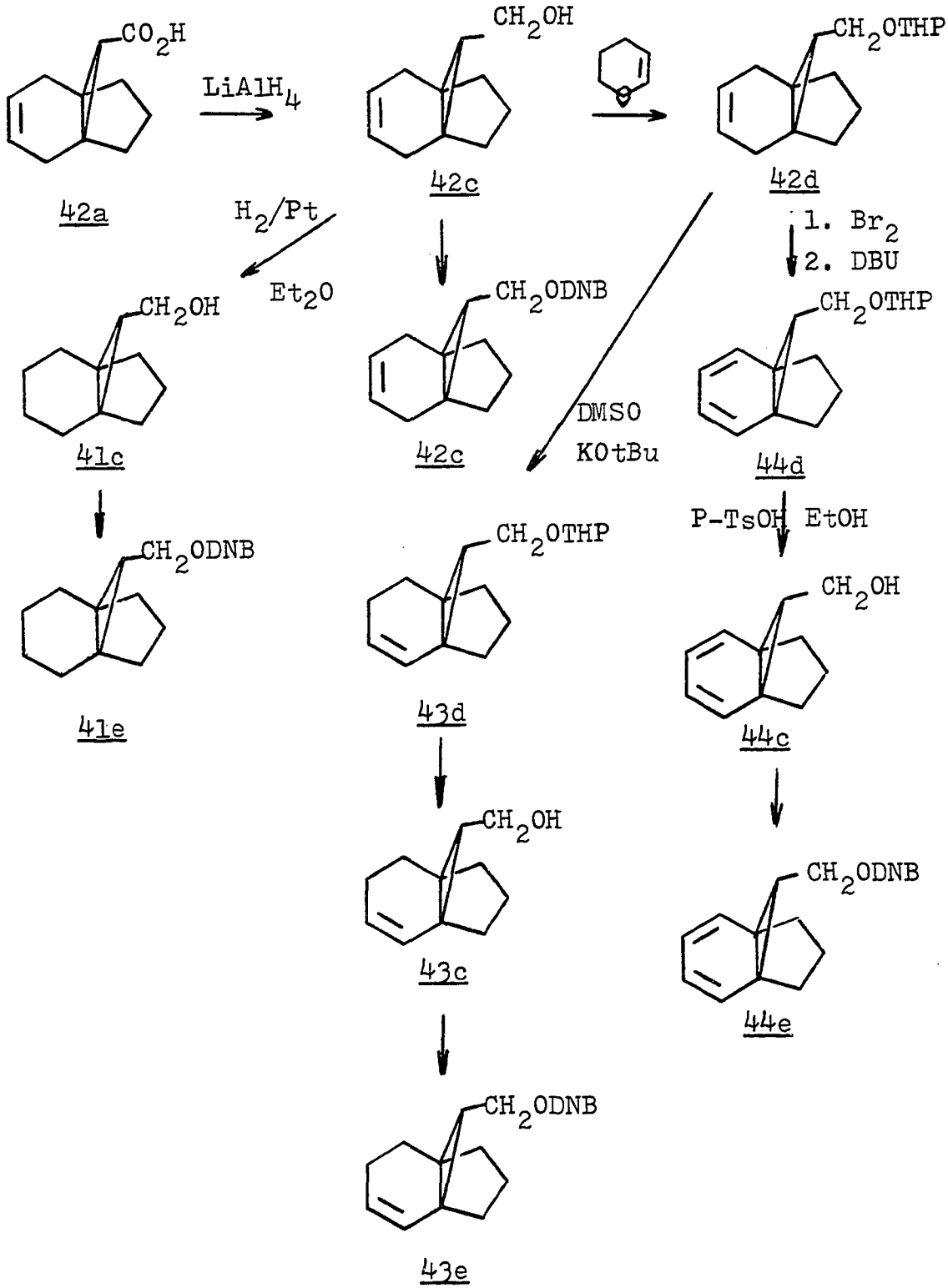


f, Br

Scheme 2


Br Br
33
Br
46f (77%)
Br
42f (23%)
1. Mg
2. CO2
3. HCl
4. CH2N2
CH3O2C
CO2CH3
46b (9%)
42b (91%)
1. NaOMe, MeOH
2. NaOH
3. HCl
HOOC
COOH
46a (50%)
42a (50%)
I3-/NaHCO3
O
O
I
34
COONa
Zn/HOAc
HCl
46a
42a

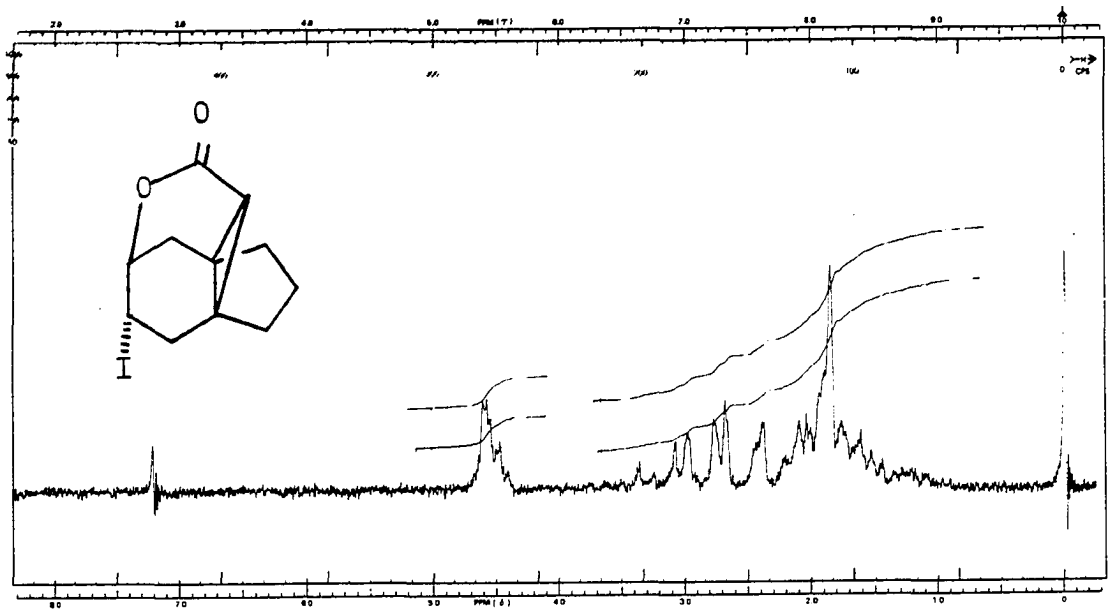
Scheme 3


CO2H
LiAlH4
CH2OH
CH2OTHP
42a
42c
42d
H2/Pt
Et2O
1. Br2
2. DBU
CH2OH
CH2ODNB
CH2OTHP
41c
42c
44d
DMSO
KOtBu
P-TsOH EtOH
CH2ODNB
CH2OTHP
CH2OH
41e
43d
44c
CH2OH
CH2ODNB
43c
44e
CH2ODNB
43e

Treatment of 33 with one equivalent of tri-n-butyltin hydride afforded a 77:23 mixture of monobromides 46f and 42f. Conventional carbonation of the Grignard reagent derived from a mixture of 46f and 42f, followed by reaction with diazomethane in ether, yielded a mixture of methyl esters 46b and 42b in a 9:91 ratio. Assignment of the stereochemistry of 46b and 42b followed from the synthesis of the individual epimers (vide infra). Separation of the isomeric carboxylic acids 46a and 42a was achieved via iodolactonization[44] of the syn-acid 46a whereby the anti-acid salt remaind in the sodium bicarbonate solution. Oily iodolactone 34 was isolated by simple extraction. This light sensitive compound was purified by recrystallization and gave correct analyses (see Fig. 2 for ir and pmr spectra). syn-Acid 46a was thereby established to be the minor component from the carbonation reaction. Base-catalyzed epimerization of esters 46b and 42b in refluxing methanol prior to the iodolactionization reaction was thus undertaken. The pure syn-epimer 46a was quantitatively recovered after reduction of iodolactone 34 with zinc dust in glacial acetic acid.[45] (see Fig. 3 and 4) The desired propelladiene derivative 44e was synthesized via the route depicted in Scheme III. Acidification of the basic solution obtained from the iodolactonization reaction produced pure anti-acid 42a (see Fig. 3 and 4) which could be converted to its

methyl ester 42b with diazomethane (see Fig. 5 and 6). Reduction of 42a with lithium aluminum hydride afforded the corresponding alcohol 42c (see Fig. 7 and 8). Subsequent protection with dihydropyran (see Fig. 9 and 10), treatment with bromine, and dehydrobromination with 1,5-diaza-bicyclo [5, 4, 0] undec-5-ene (DBU) gave 44d (see Fig. 11 and 12); hydrolysis in the presence of p-toluenesulfonic acid yielded the corresponding alcohol 44c (see Fig. 13 and 14) in 31% overall yield from 42a. Confirmation of the norcaradiene structure for 44c was gained from the following spectral data: $\lambda_{max}^{C_6H_{12}}$ 272(4170), 254(3960), 248(4000)nm; δ^{CDCl_3} 6.4-5.6 (m, 4H of AA'BB'), 4.60 (s, OH), 3.95 (d, 2H, J = 7Hz) 2.7-1.3 (m, 6H), 0.35 (t, cyclopropyl H, J = 7Hz) (see Fig. 13 and 14). The subsequent conversion to the 3,5-dinitrobenzoate 44e proceeded normally (see Fig. 15 and 16).

In a manner exactly analogous to that described for 44e in Scheme 3, syn-alcohol 48c was obtained in 34% yield starting from 46a. The spectral properties of 48c are quite different from those of 44c: $\lambda_{max}^{C_6H_{12}}$ 246(3230), 252(4040), 257(3230)nm; $\delta_{TMS}^{CCl_4}$ 6.4-5.6 (narrowly split mult., 4H), 4.50 (s, OH), 2.88(d, 2H, J = 7Hz), 2.7-1.2(m, 6H), 1.18(t, cyclopropyl H, J = 7Hz) (see Fig. 13 and 14). Alcohol 48c was conventionally converted to its 3,5-dinitrobenzoate (48e), obtained as a pale yellow crystalline material which gave satisfactory spectra and analysis (see Fig. 15 and 16).



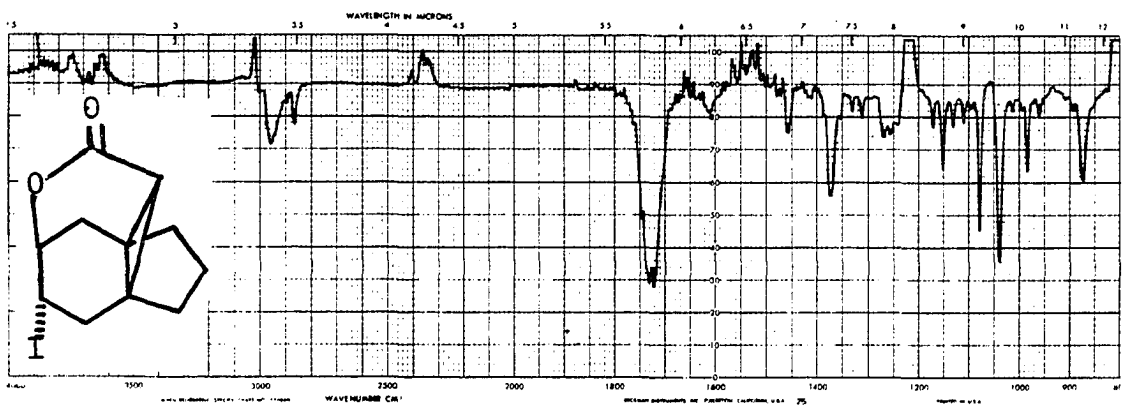
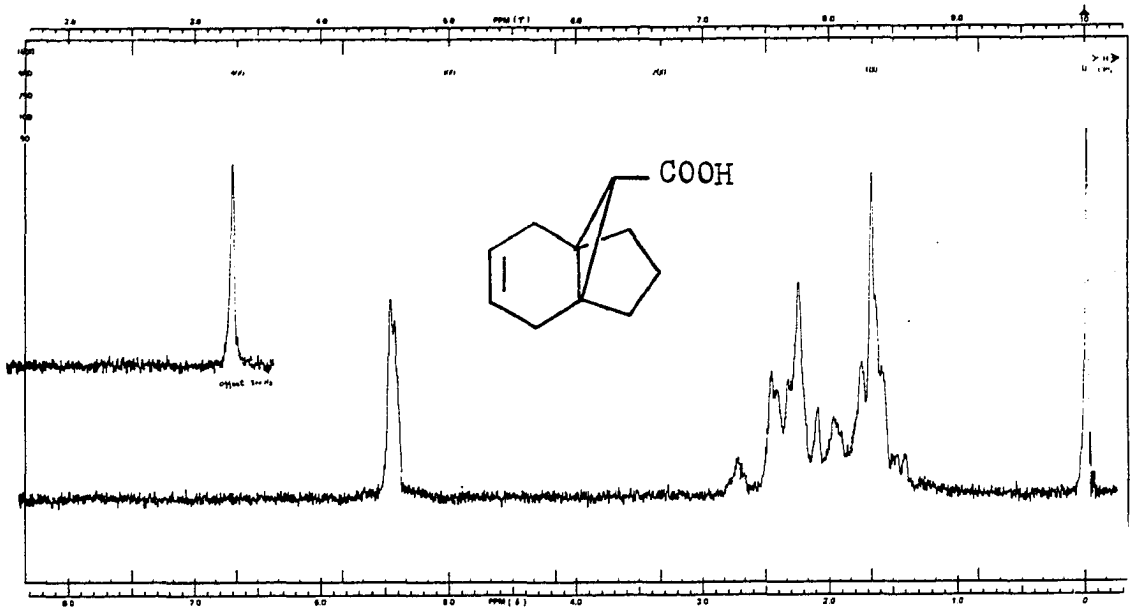


Figure 2. Pmr (Top) and Ir (Bottom) Spectra of exo-3-Hydroxy-endo-4-iodotricyclo[4.3.1.$0^{1,6}$]decane-10α-carboxylic Acid δ-Lactone, (34).



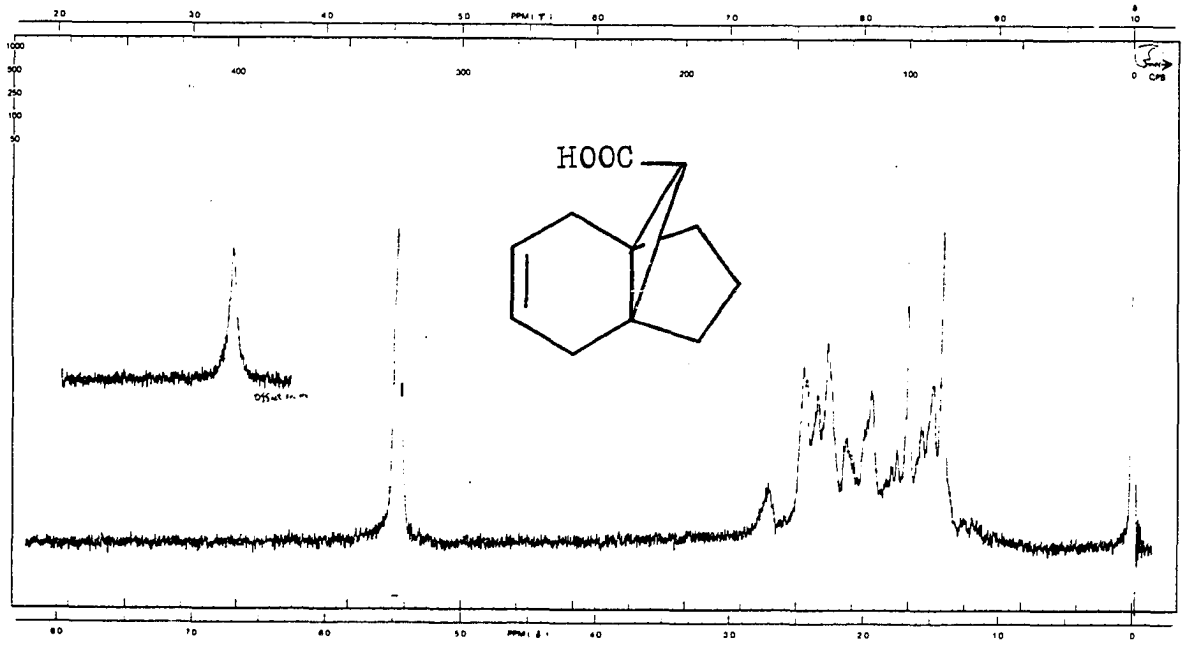
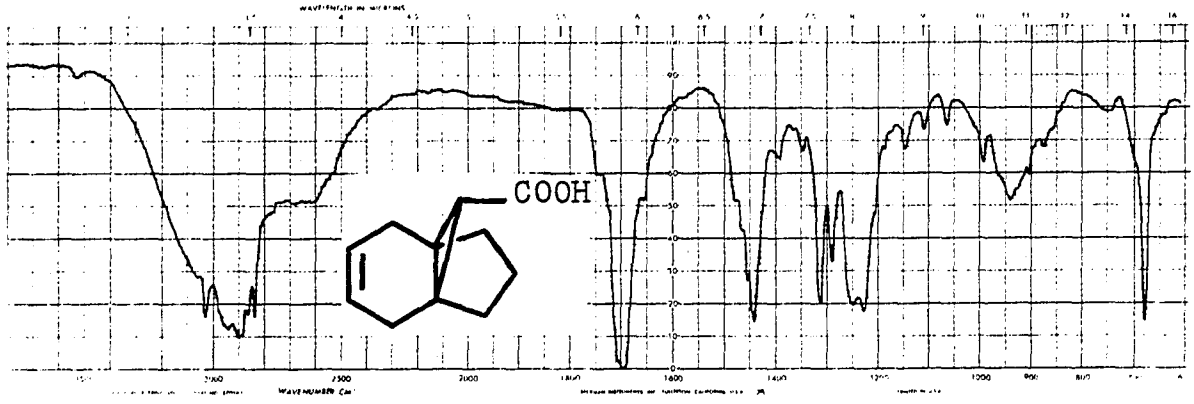


Figure 3. Pmr Spectra of Tricyclo[4.3.1.$0^{1,6}$]deca-3-ene-10-carboxylic Acids: 42a (Top) and 46a (Bottom).



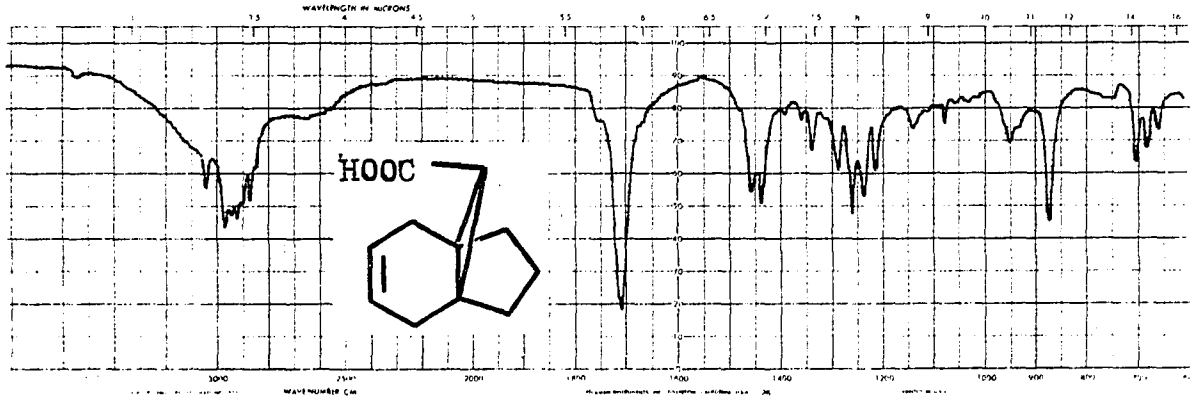


Figure 4. Ir Spectra of Tricyclo[4.3.1.$0^{1,6}$]deca-3-ene-10-carboxylic Acids: 42a (Top) and 46a (Bottom).

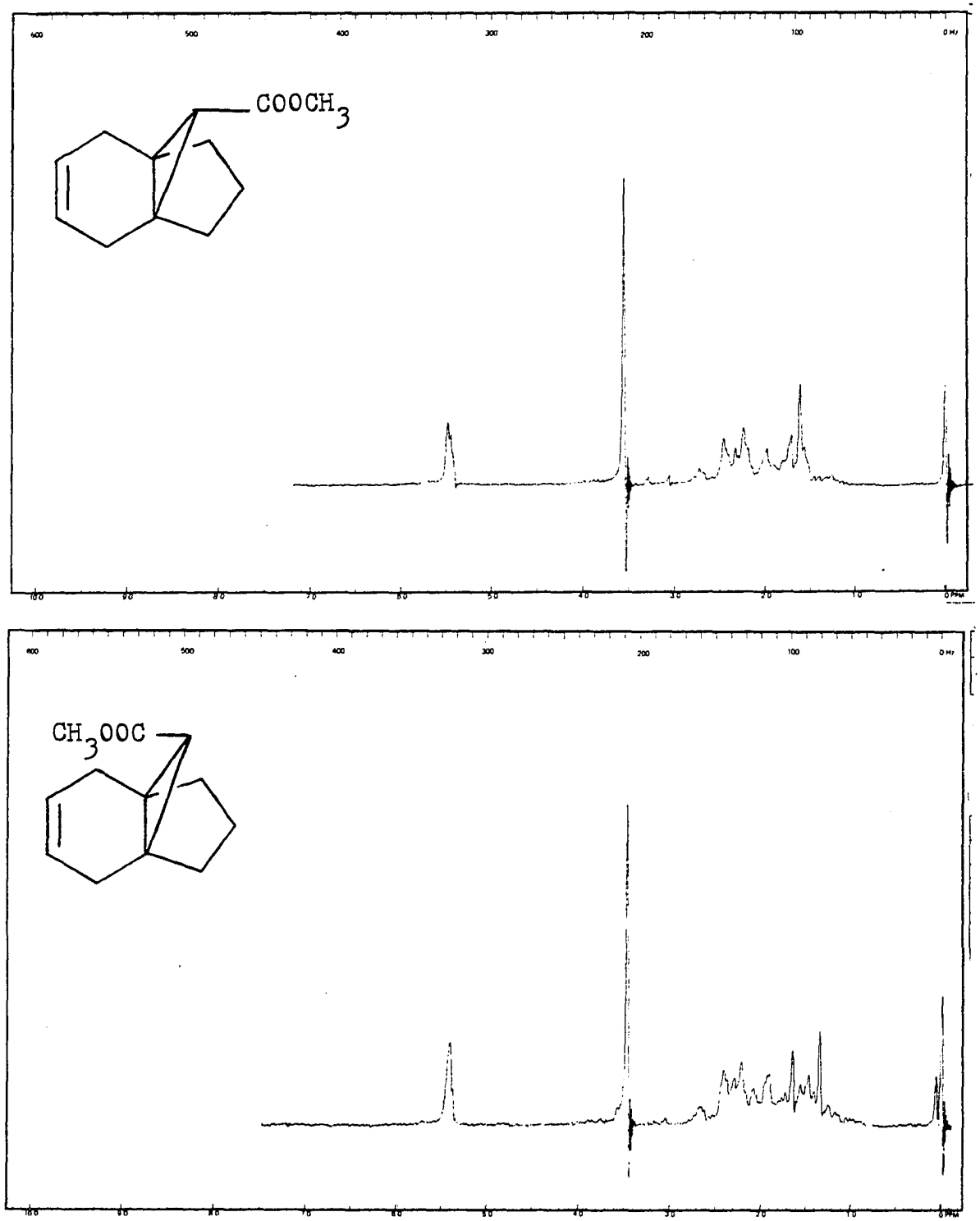


Figure 5. Pmr Spectra of 10-Methoxycarbonyltricyclo-[4.3.1.$0^{1,6}$]deca-3-enes: 42b (Top) and 46b (Bottom).

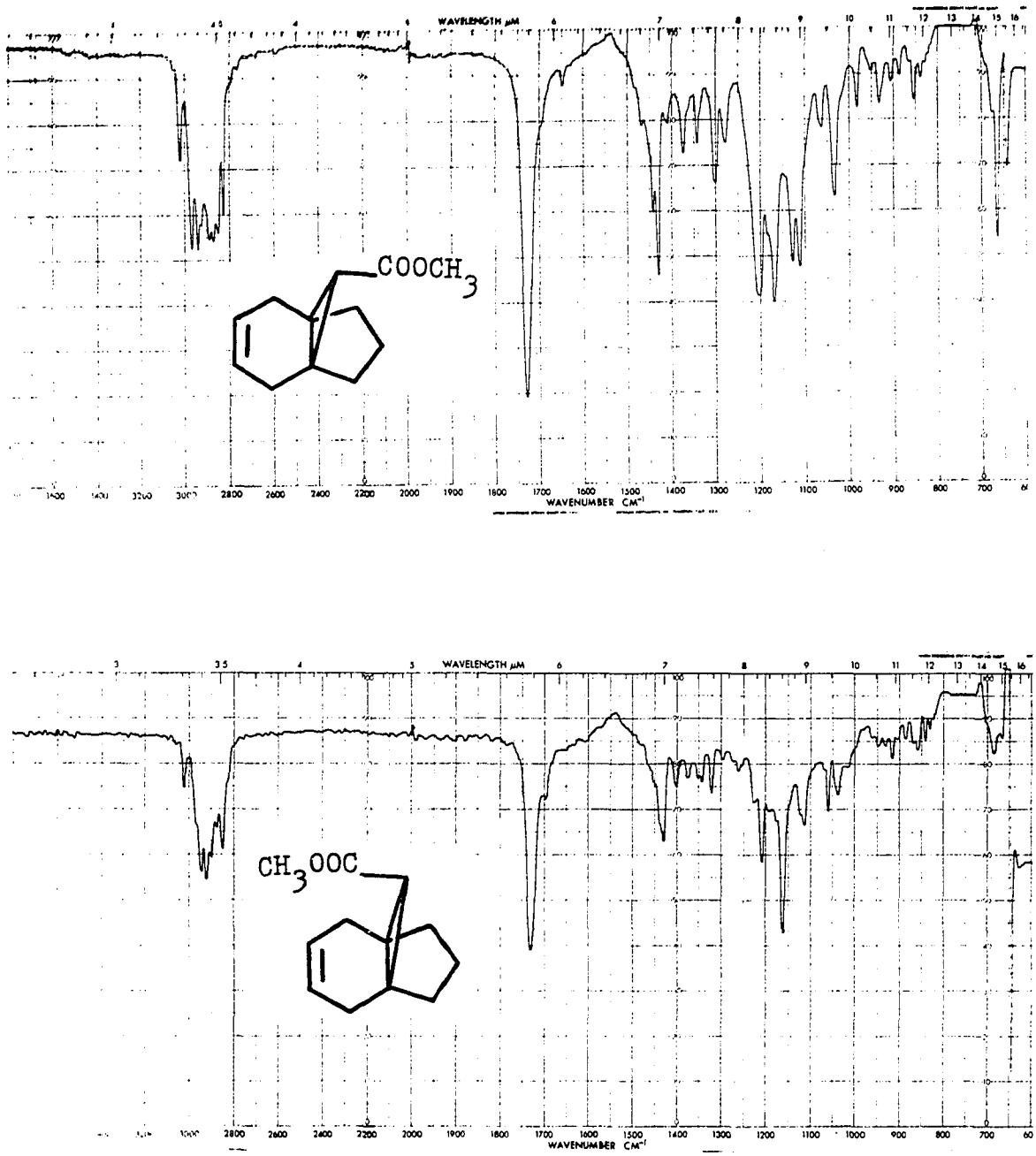


Figure 6. Ir Spectra of 10-Methoxycarbonyltricyclo-[4.3.1.$0^{1,6}$]deca-3-enes: 42b (Top) and 46b (Bottom).

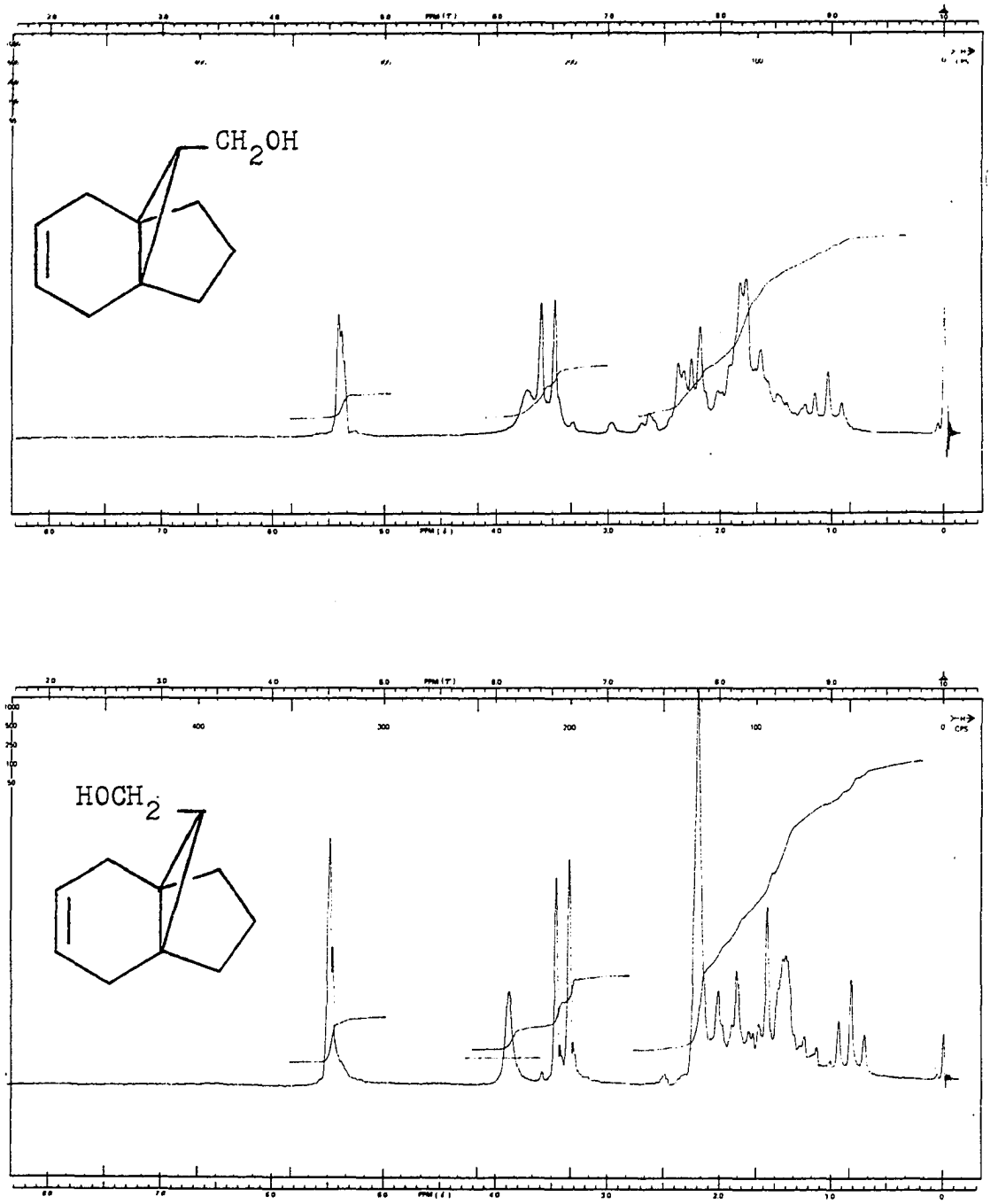
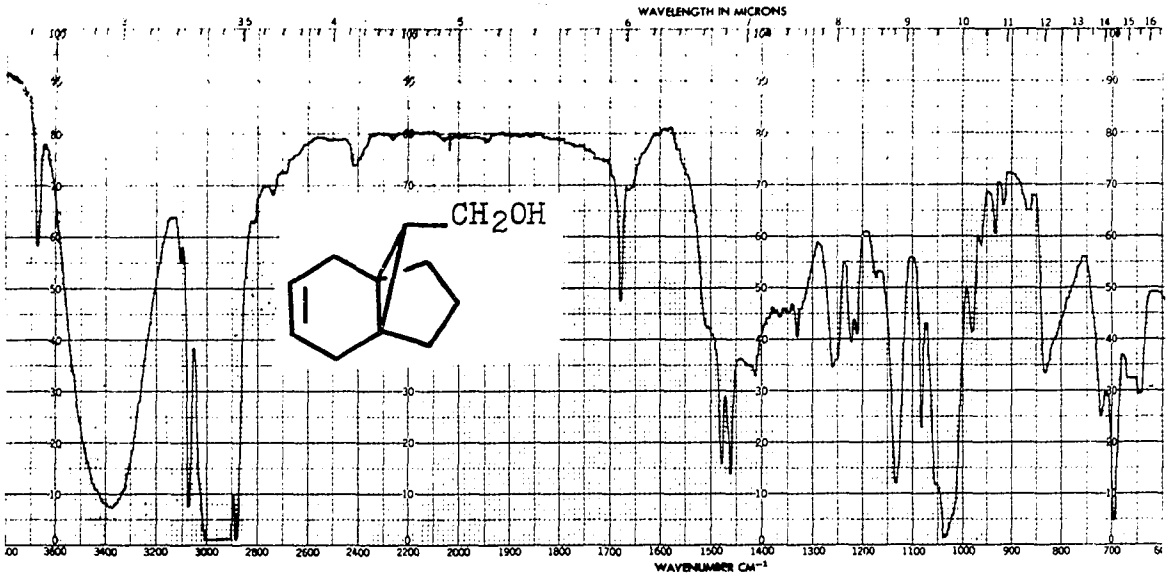


Figure 7. Pmr Spectra of 10-Hydroxymethyltricyclo-[4.3.1.$0^{1,6}$]deca-3-enes: 42c (Top) and 46c (Bottom).



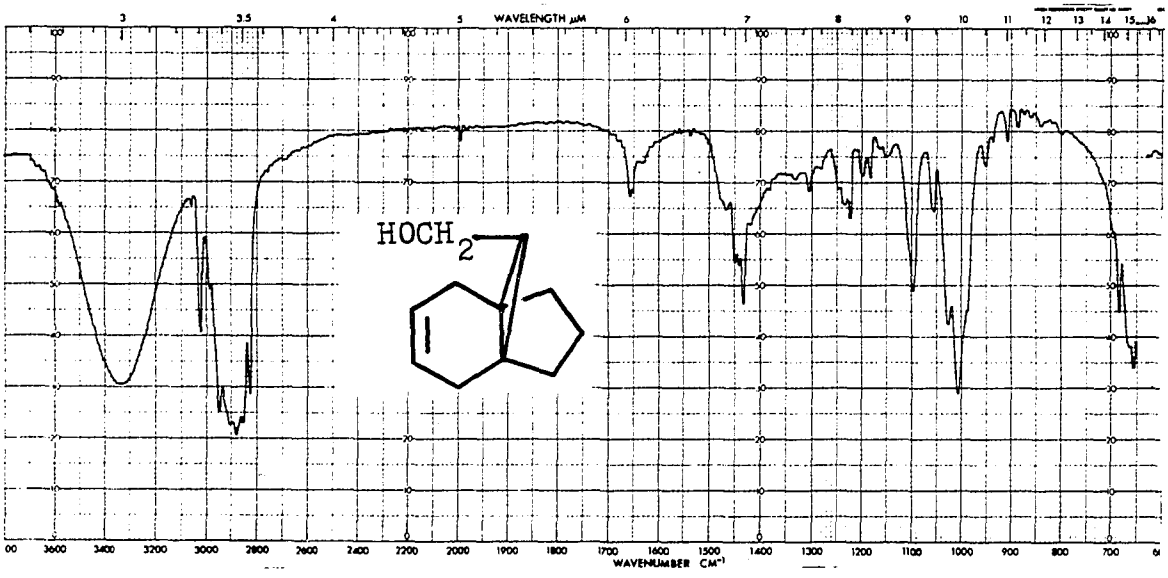
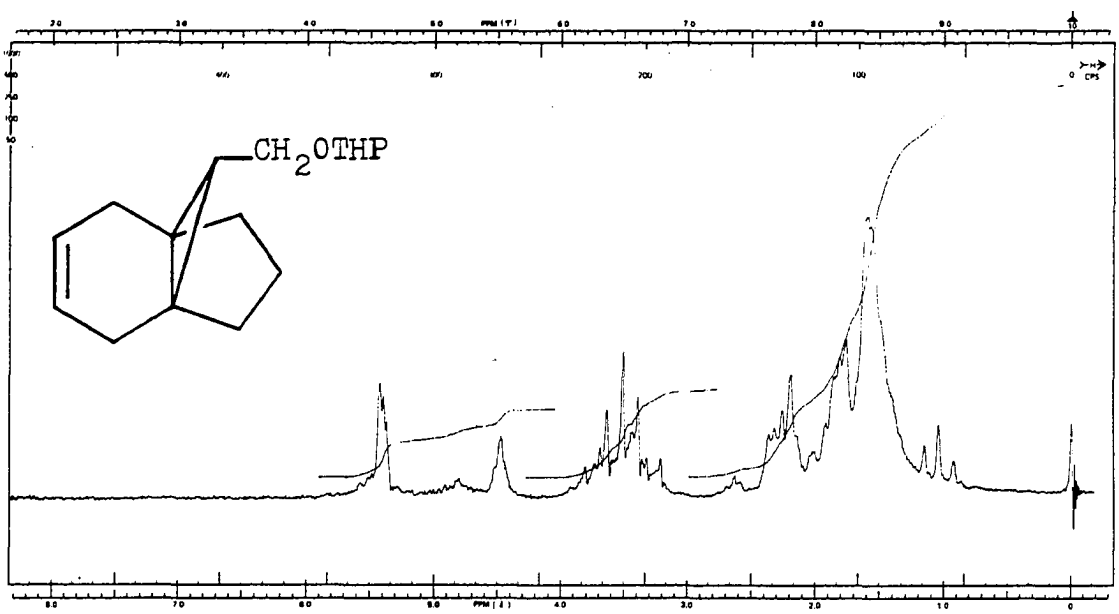


Figure 8. Ir Spectra of 10-Hydroxymethyltricyclo-[4.3.1.$0^{1,6}$]deca-3-enes: 42c (Top) and 46c (Bottom).



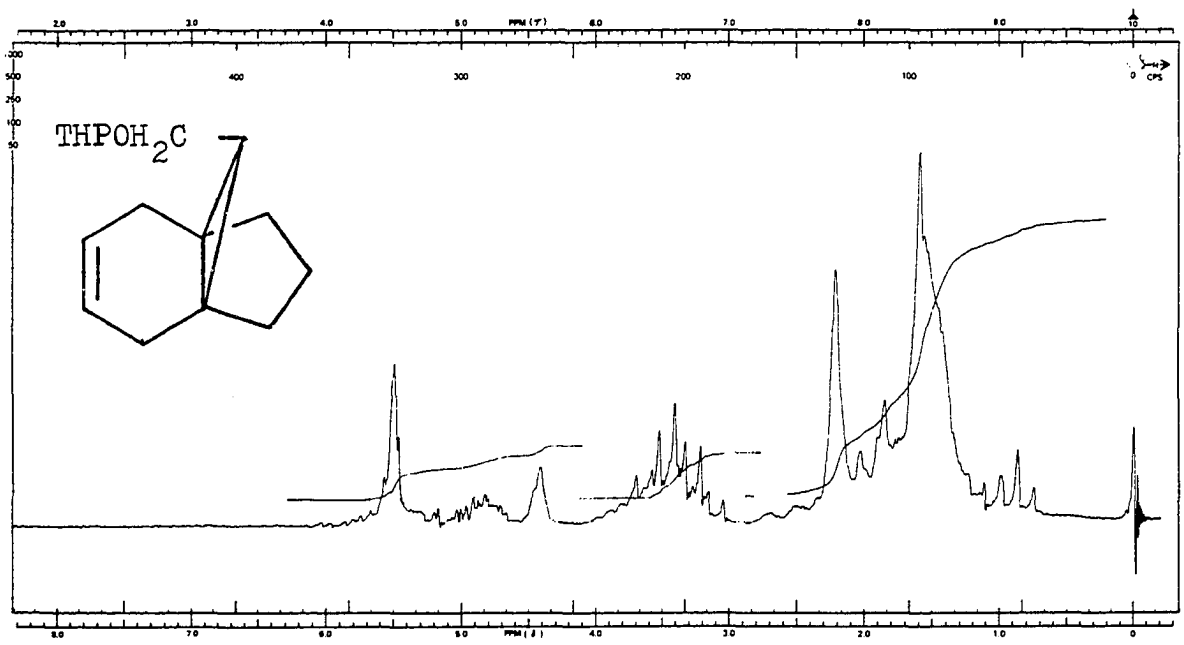
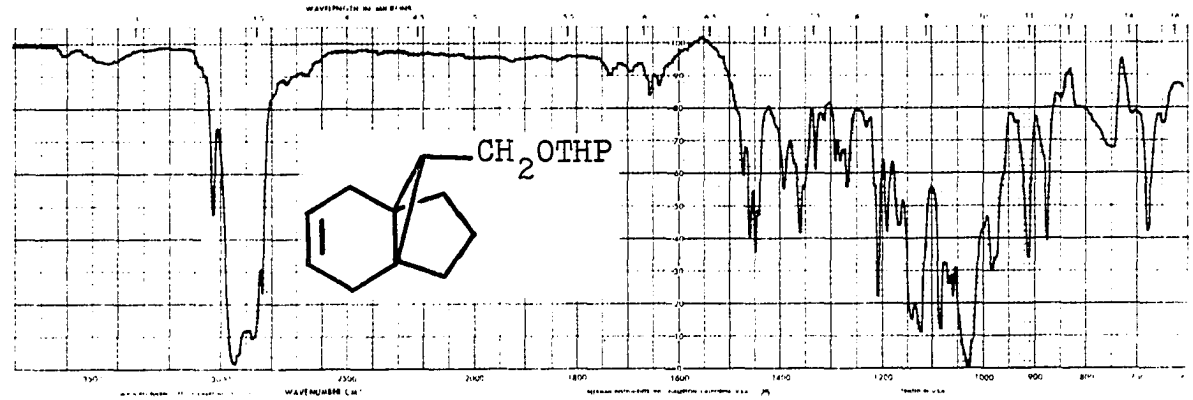


Figure 9. Pmr Spectra of 10-Tetrahydropyranyloxymethyl-tricyclo[4.3.1.$0^{1,6}$]deca-3-enes: 42d (Top) and 46d (Bottom).



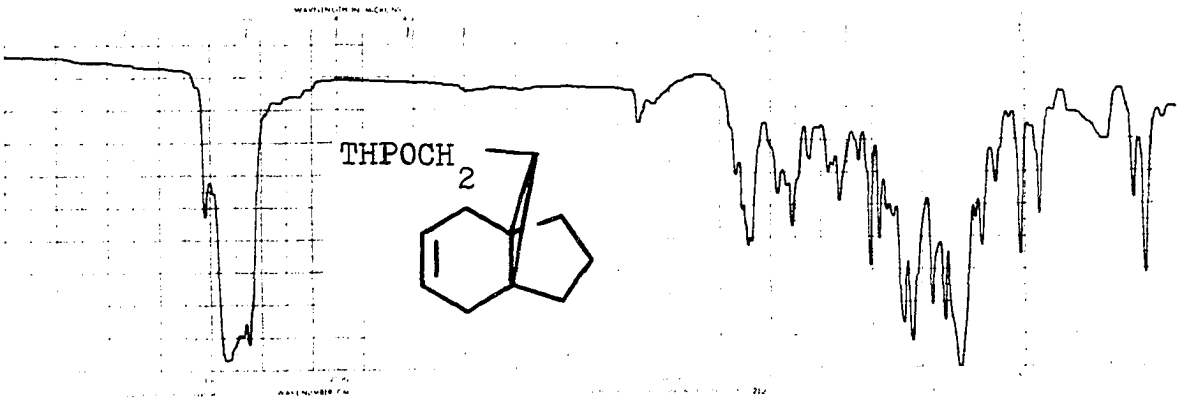


Figure 10. Ir Spectra of 10-Tetrahydropyranyloxymethyl-tricyclo[4.3.1.$0^{1,6}$]deca-3-enes: 42d (Top) and 46d (Bottom).

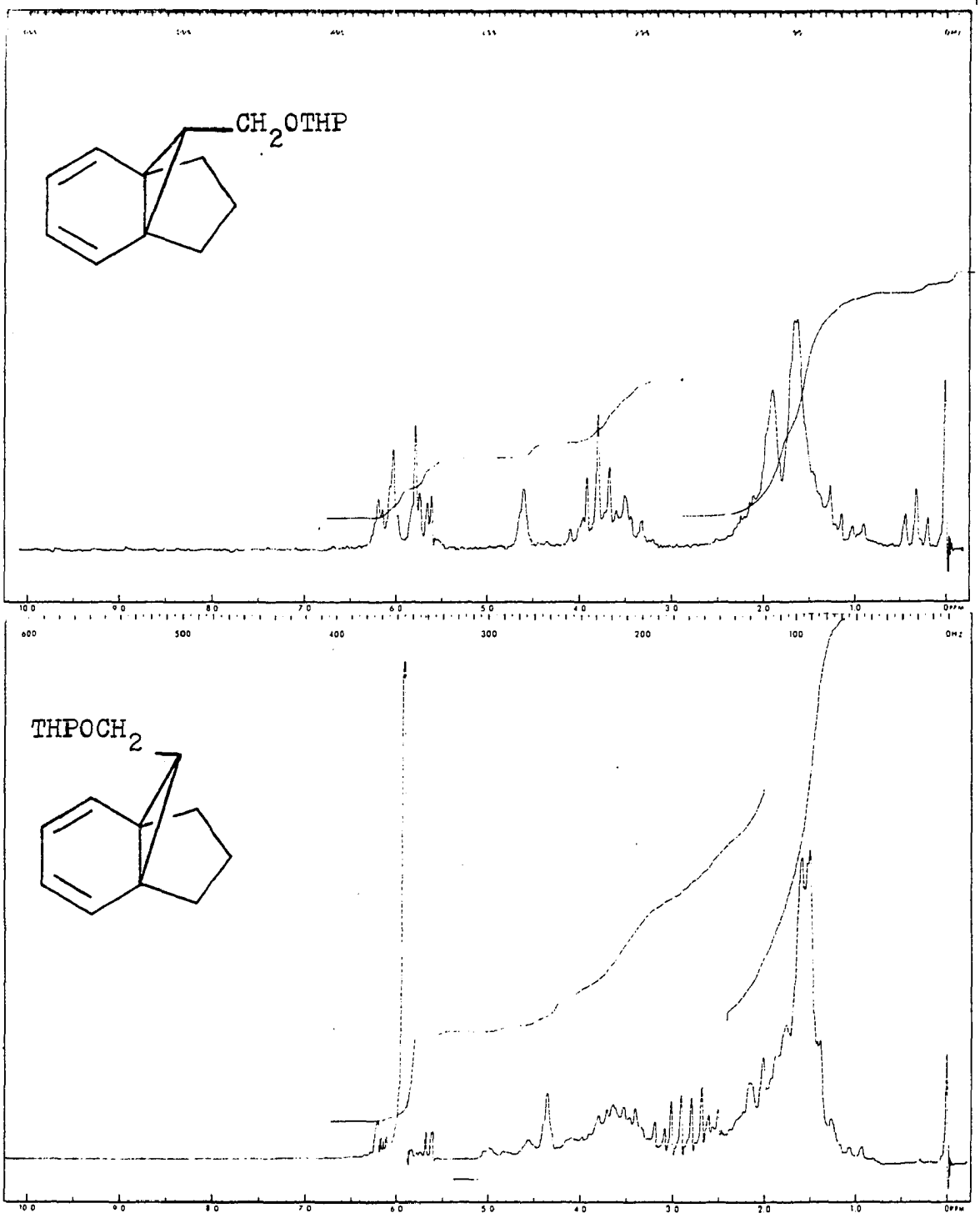
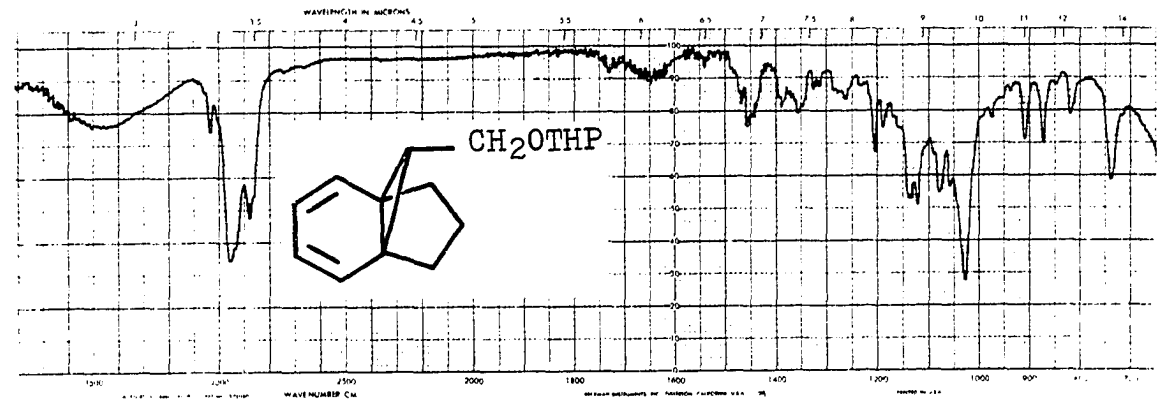


Figure 11. Pmr Spectra of 10-Tetrahydropyranyloxymethyl-tricyclo[4.3.1.$0^{1,6}$]deca-2,4-dienes: 44d (Top) and 48d (Bottom).



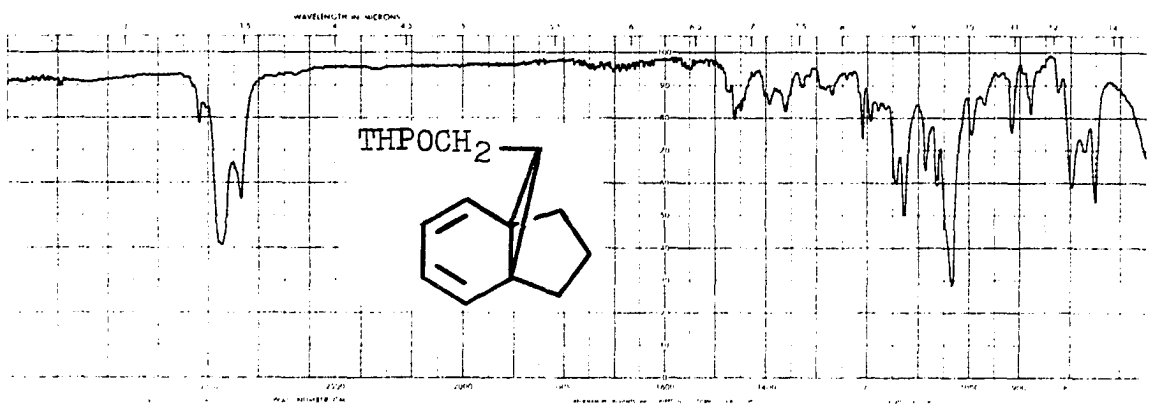


Figure 12. Ir Spectra of 10-Tetrahydropyranyloxymethyl-tricyclo[4.3.1.$0^{1,6}$]deca-2,4-dienes: 44d (Top) and 48d (Bottom).

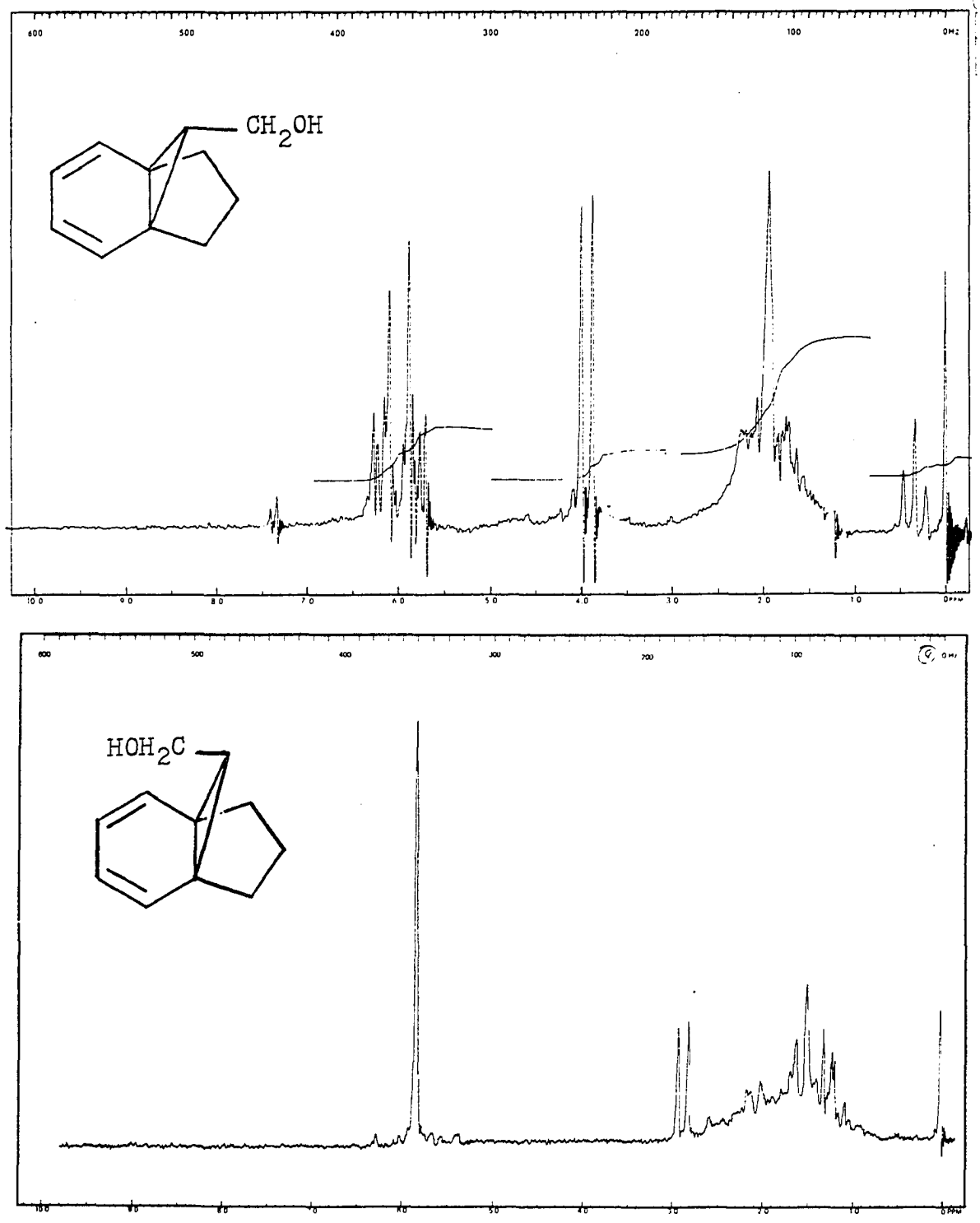
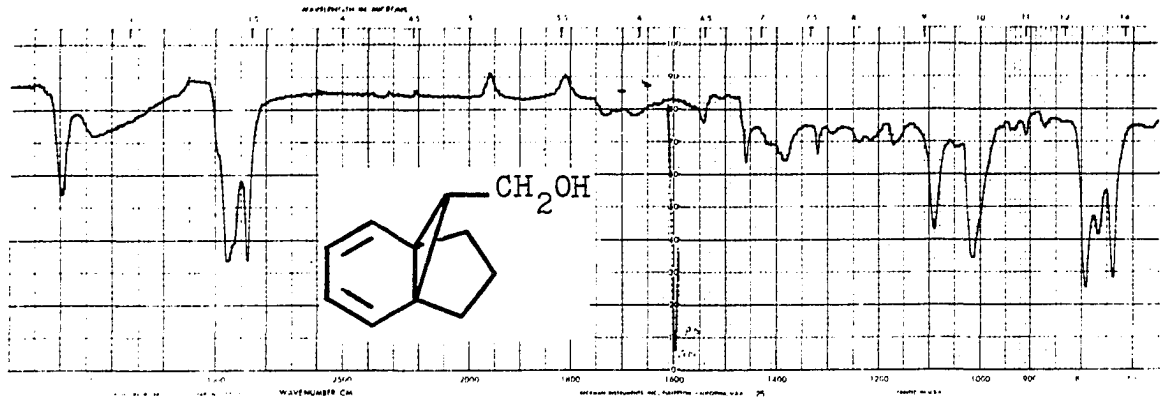


Figure 13. Pmr Spectra of 10-Hydroxymethyltricyclo-[4.3.1.$0^{1,6}$]deca-2,4-dienes: 44c (Top) and 48c (Bottom).



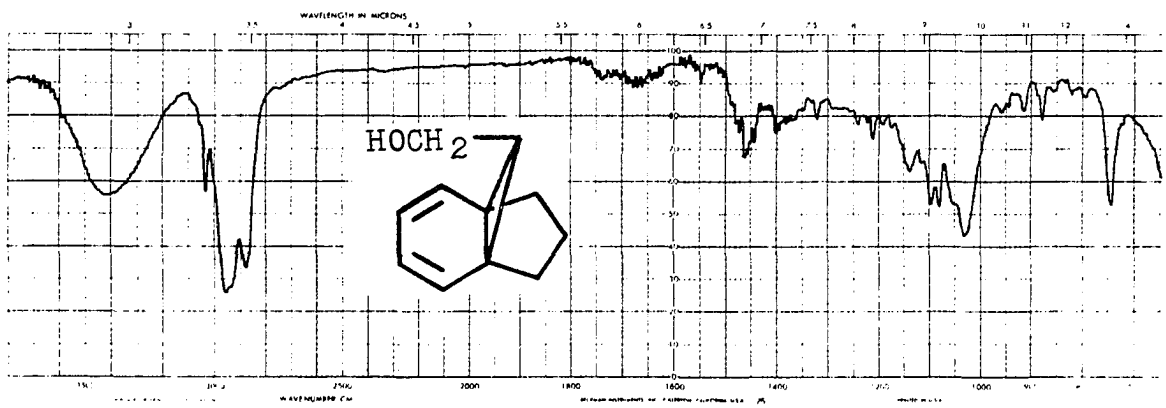


Figure 14. Ir Spectra of 10-Hydroxymethyltricyclo-[4.3.1.$0^{1,6}$]deca-2,4-dienes: 44c (Top) and 48c (Bottom).

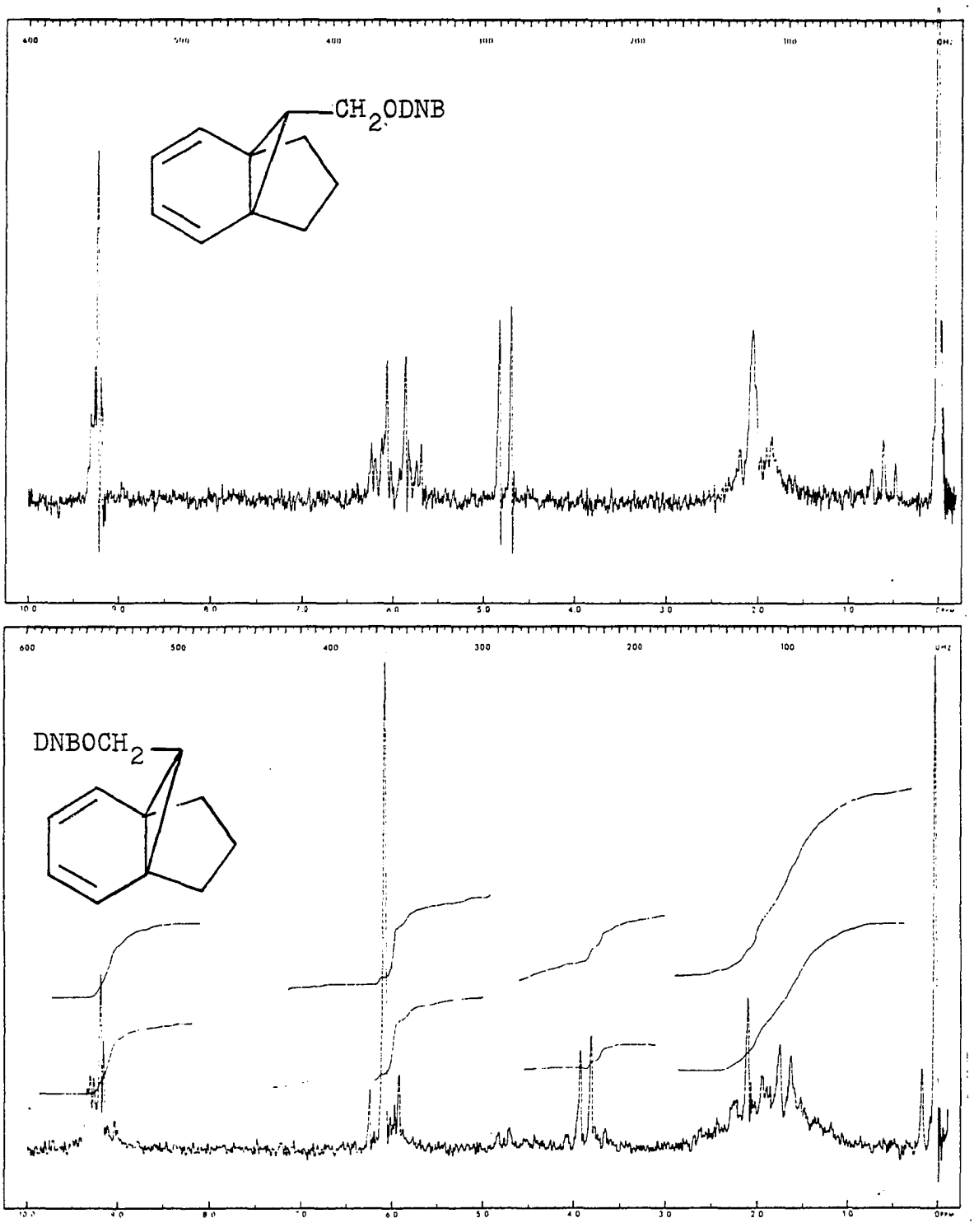


Figure 15. Pmr Spectra of 10-(2,4-Dinitrobenzoyloxymethyl)-tricyclo[4.3.1.$0^{1,6}$]deca-2,4-dienes: 44e (Top) and 48e (Bottom).

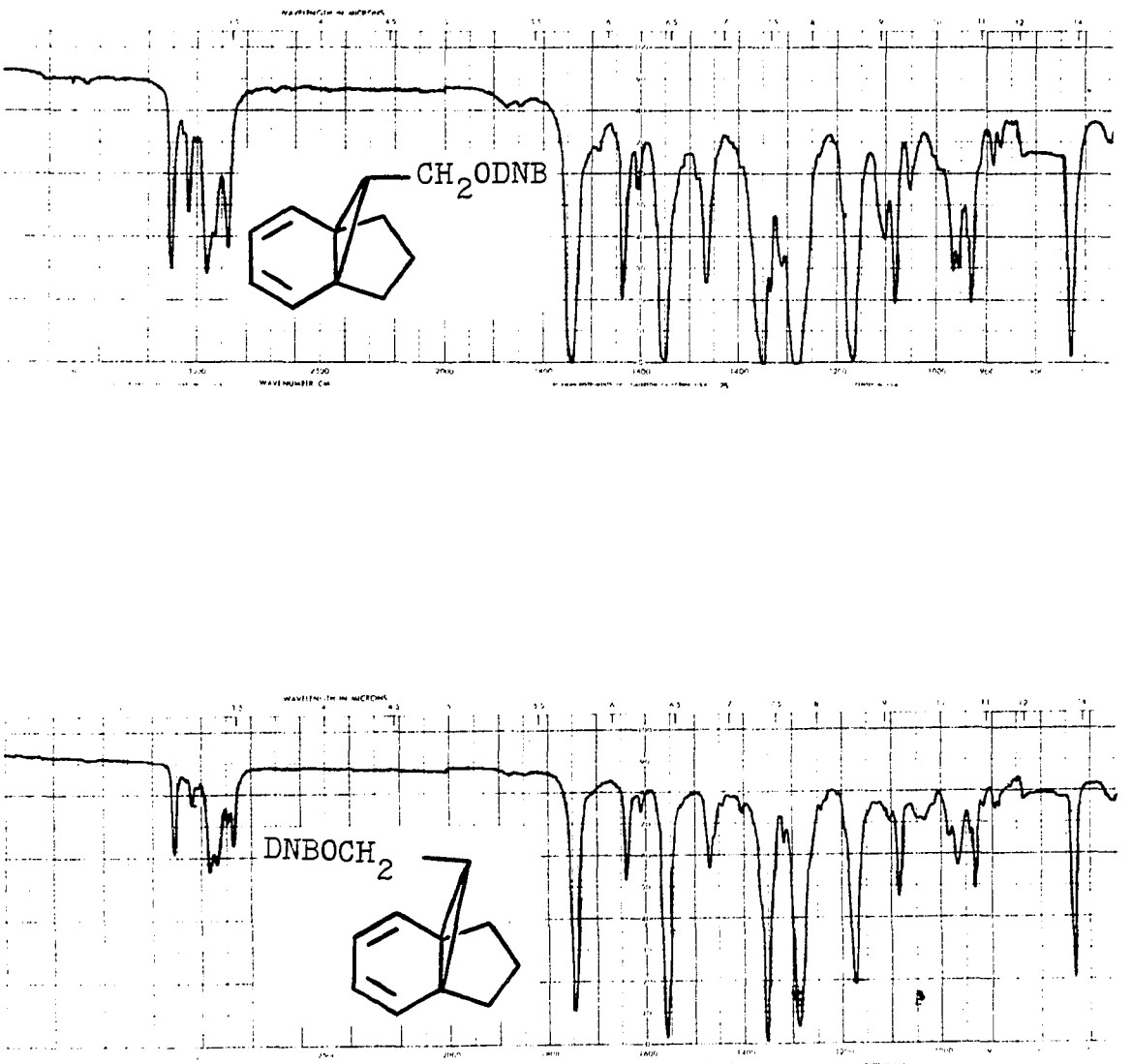


Figure 16. Ir Spectra of 10-(2,4-Dinitrobenzoyloxymethyl)-tricyclo[4.3.1.$0^{1,6}$]deca-2,4-dienes: 44e (Top) and 48e (Bottom).

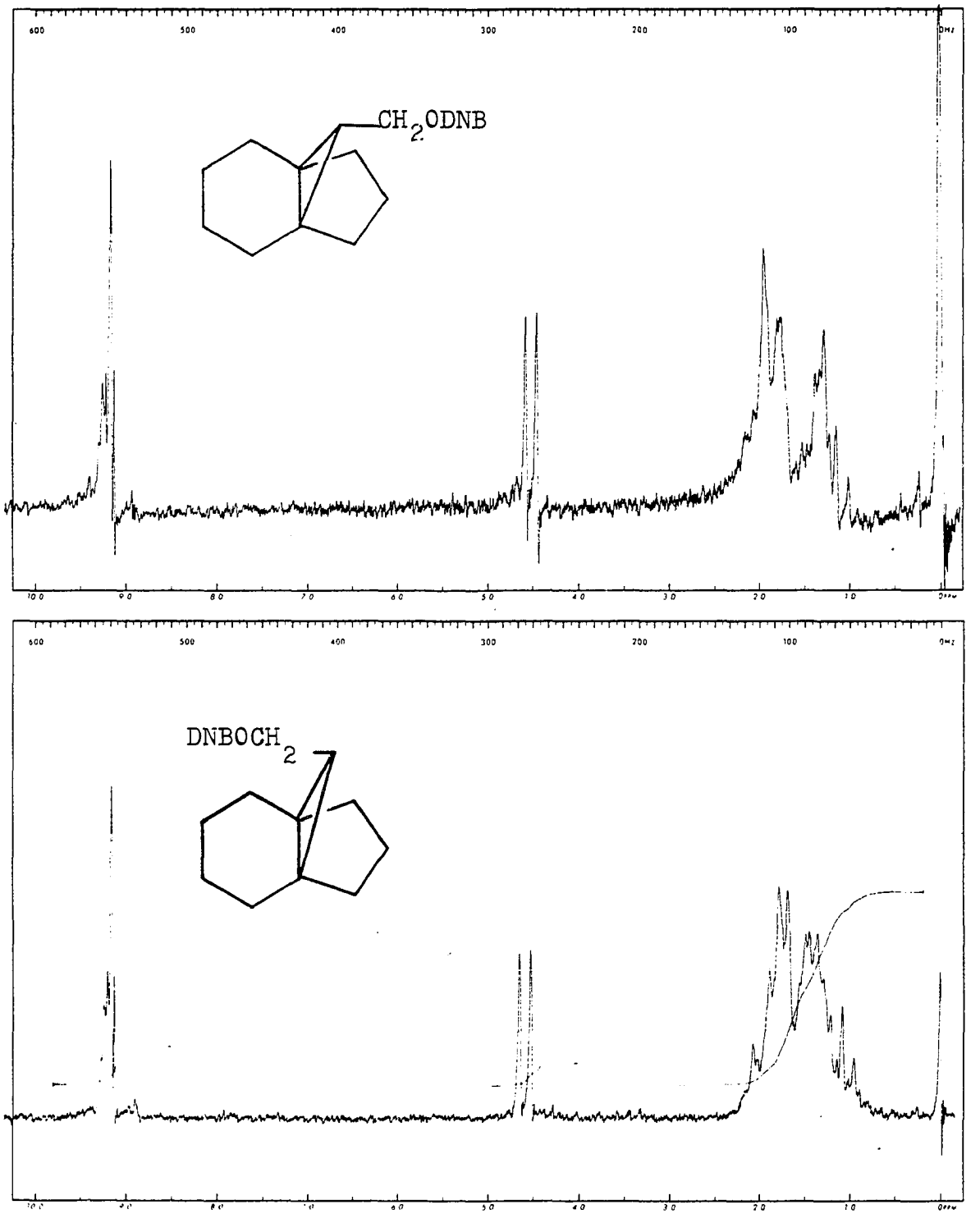


Figure 17. Pmr Spectra of 10-(2,4-Dinitrobenzoyloxymethyl)-tricyclo[4.3.1.$0^{1,6}$]decane: 41e (Top) and 45e (Bottom).

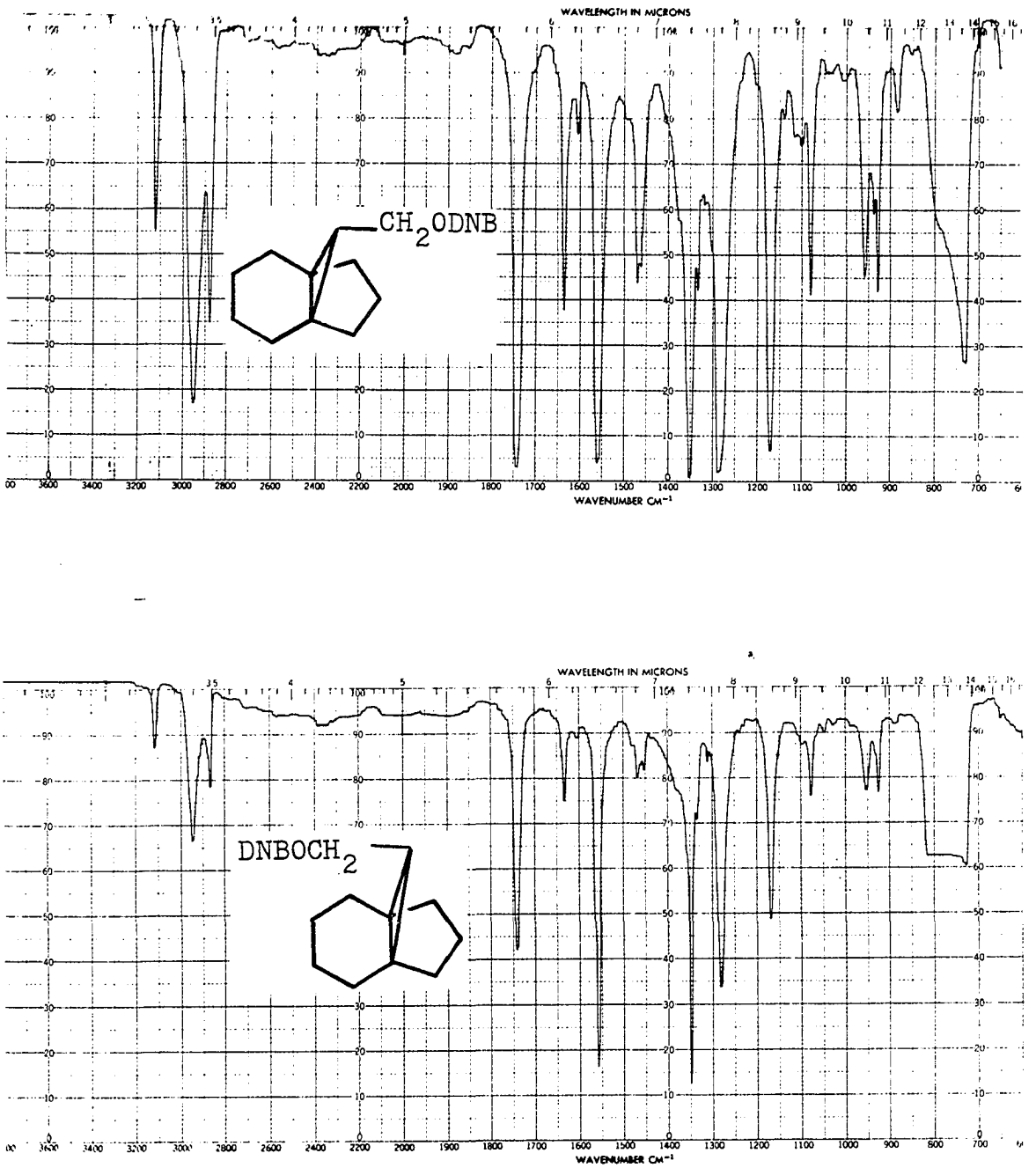


Figure 18. Ir Spectra of 10-(2,4-Dinitrobenzoyloxymethyl)-tricyclo[4.3.1.$0^{1,6}$]decane: 41e (Top) and 45e (Bottom).

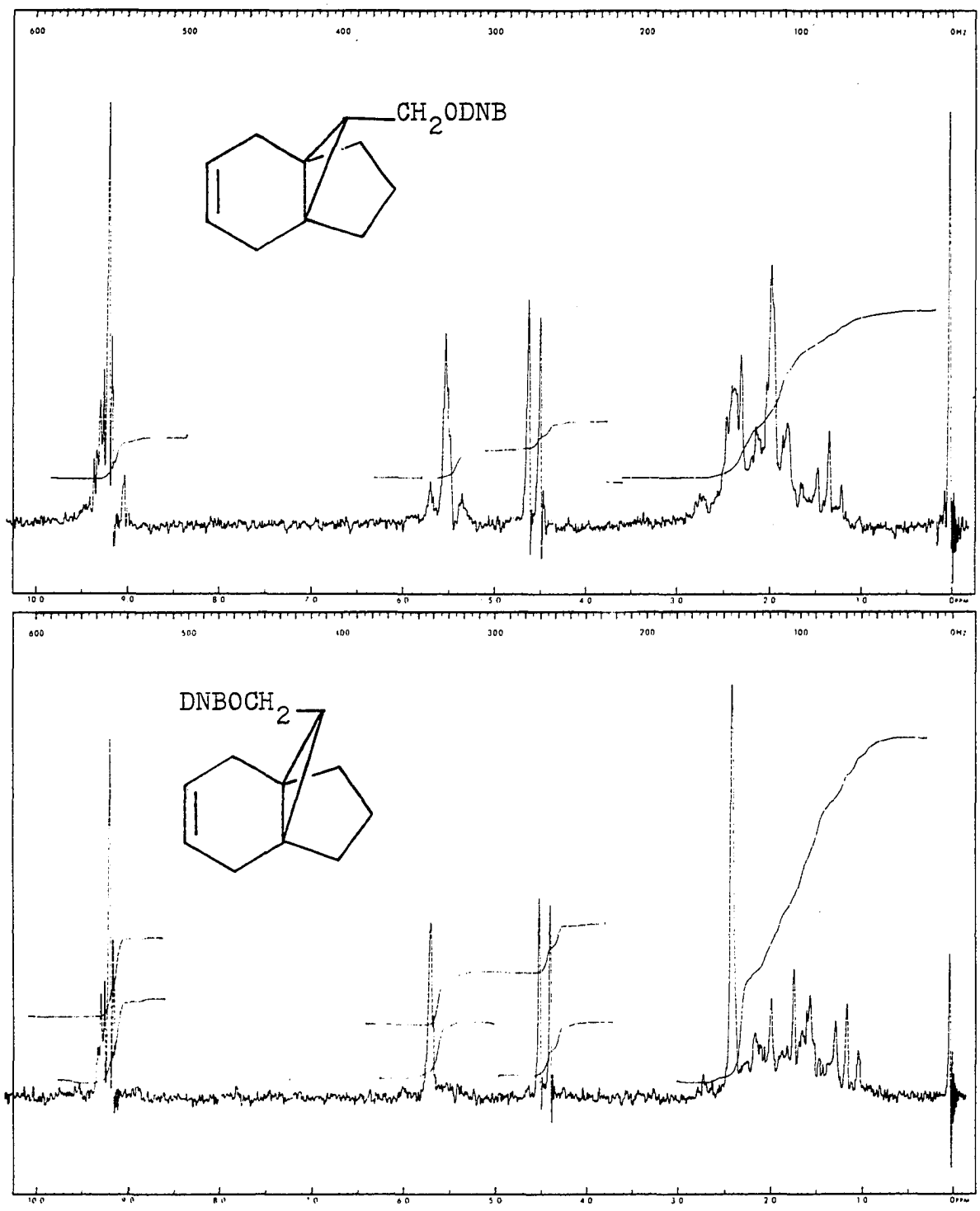


Figure 19. Pmr Spectra of 10-(2,4-Dinitrobenzoyloxymethyl) tricyclo[4.3.1.$0^{1,6}$]dec-3-ene: 42e (Top) and 46e (Bottom).

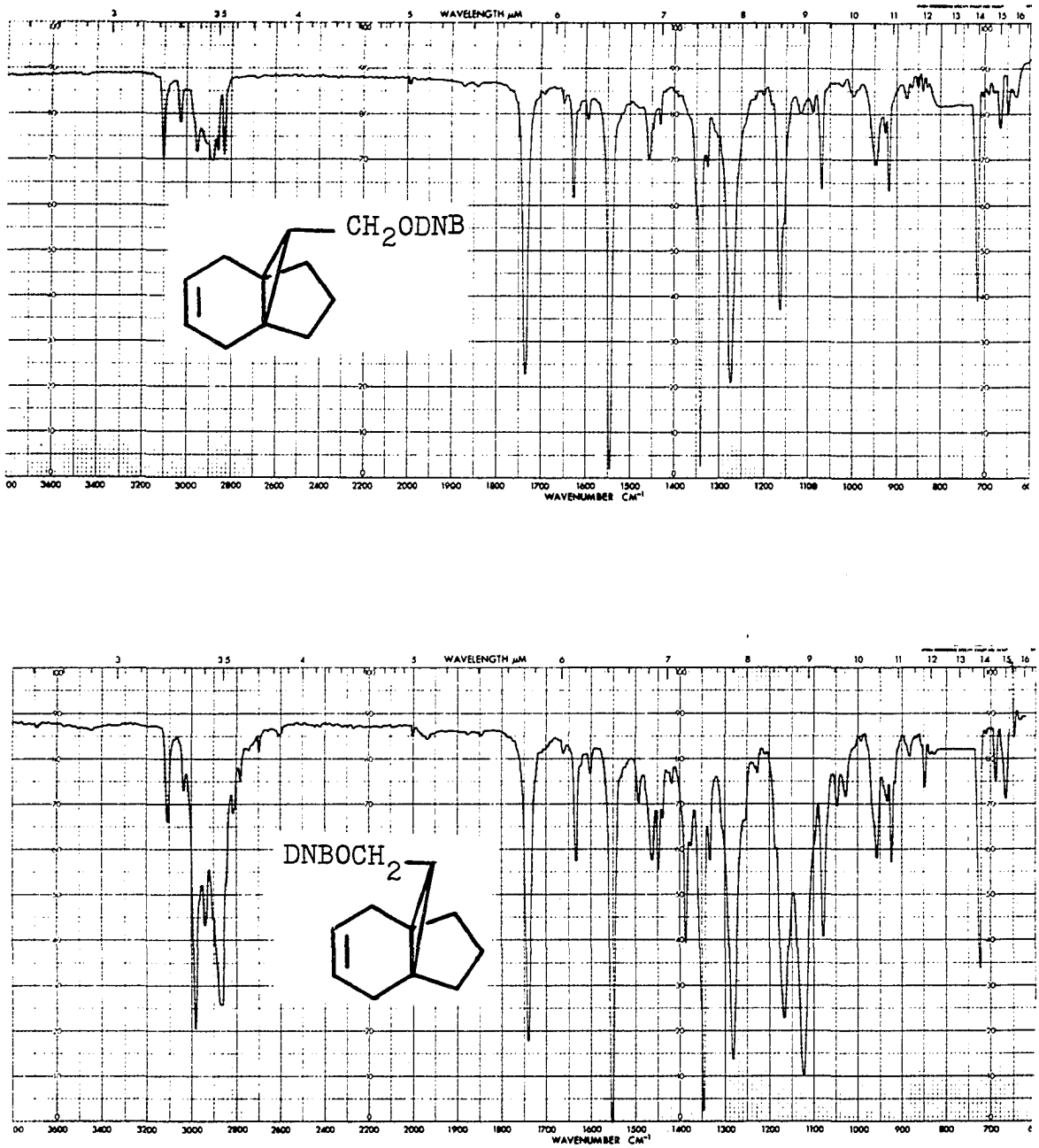


Figure 20. Ir Spectra of 10-(2,4-Dinitrobenzoyloxymethyl)-tricyclo[4.3.1.$0^{1,6}$]dec-3-ene: 42e (Top) and 46e(Bottom).

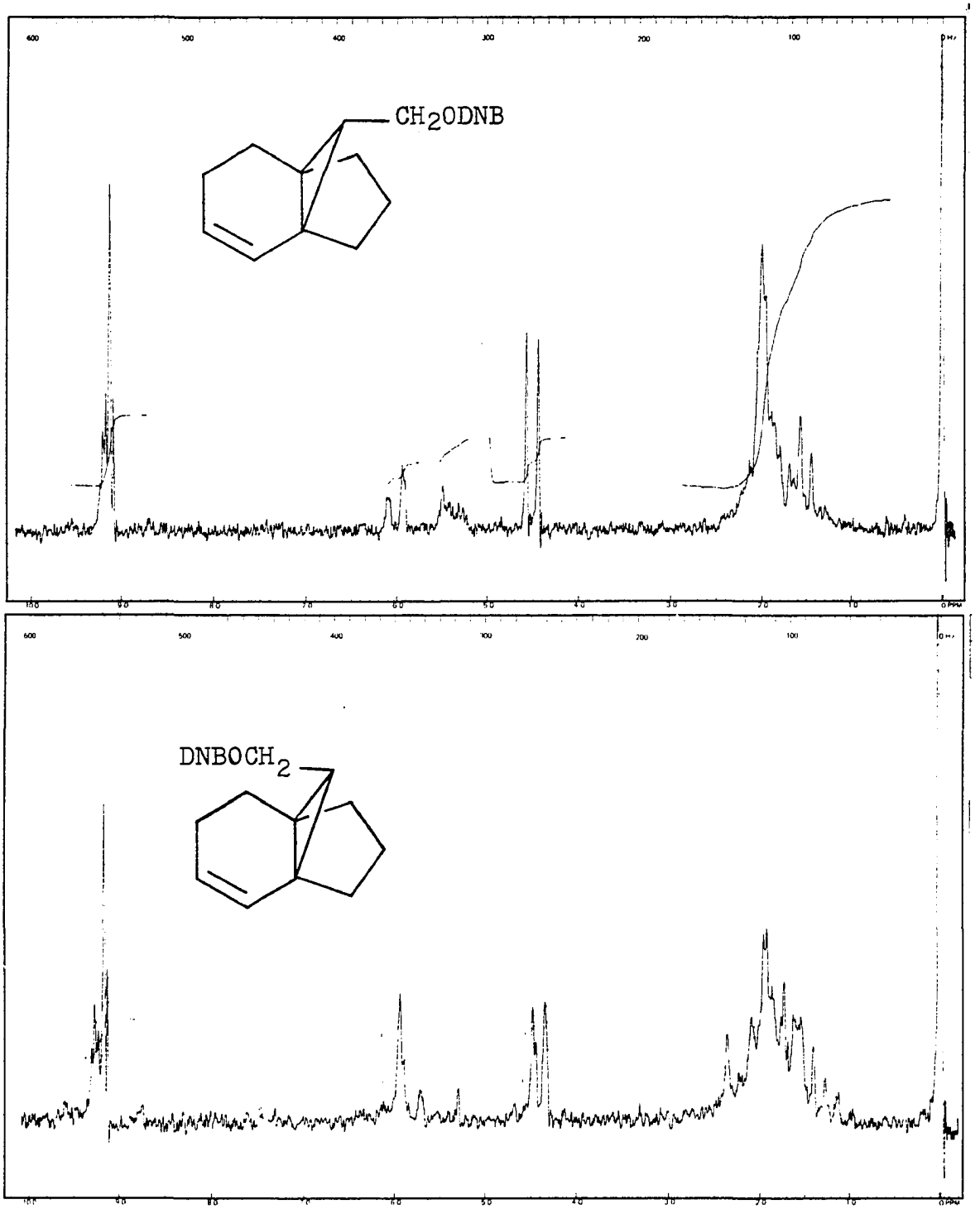


Figure 21. Pmr Spectra of 10-(2,4-Dinitrobenzoyloxymethyl) tricyclo[4.3.1.$0^{1,6}$]dec-2-ene: 43e (Top) and 47e (Bottom).

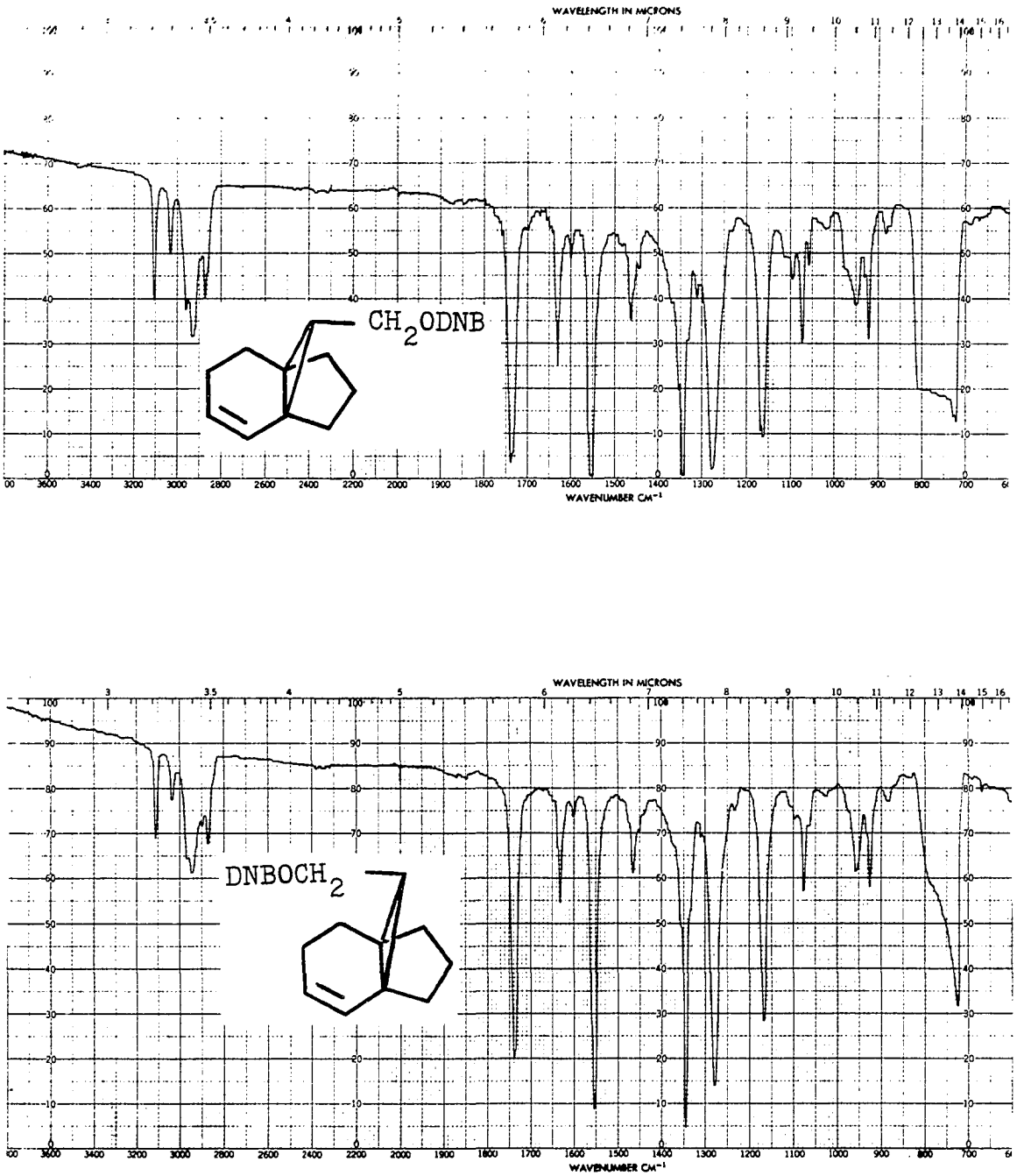


Figure 22. Ir Spectra of 10-(2,4-Dinitrobenzoyloxymethyl)-tricyclo[4.3.1.$0^{1,6}$]dec-2-ene: 43e (Top) and 47e (Bottom).

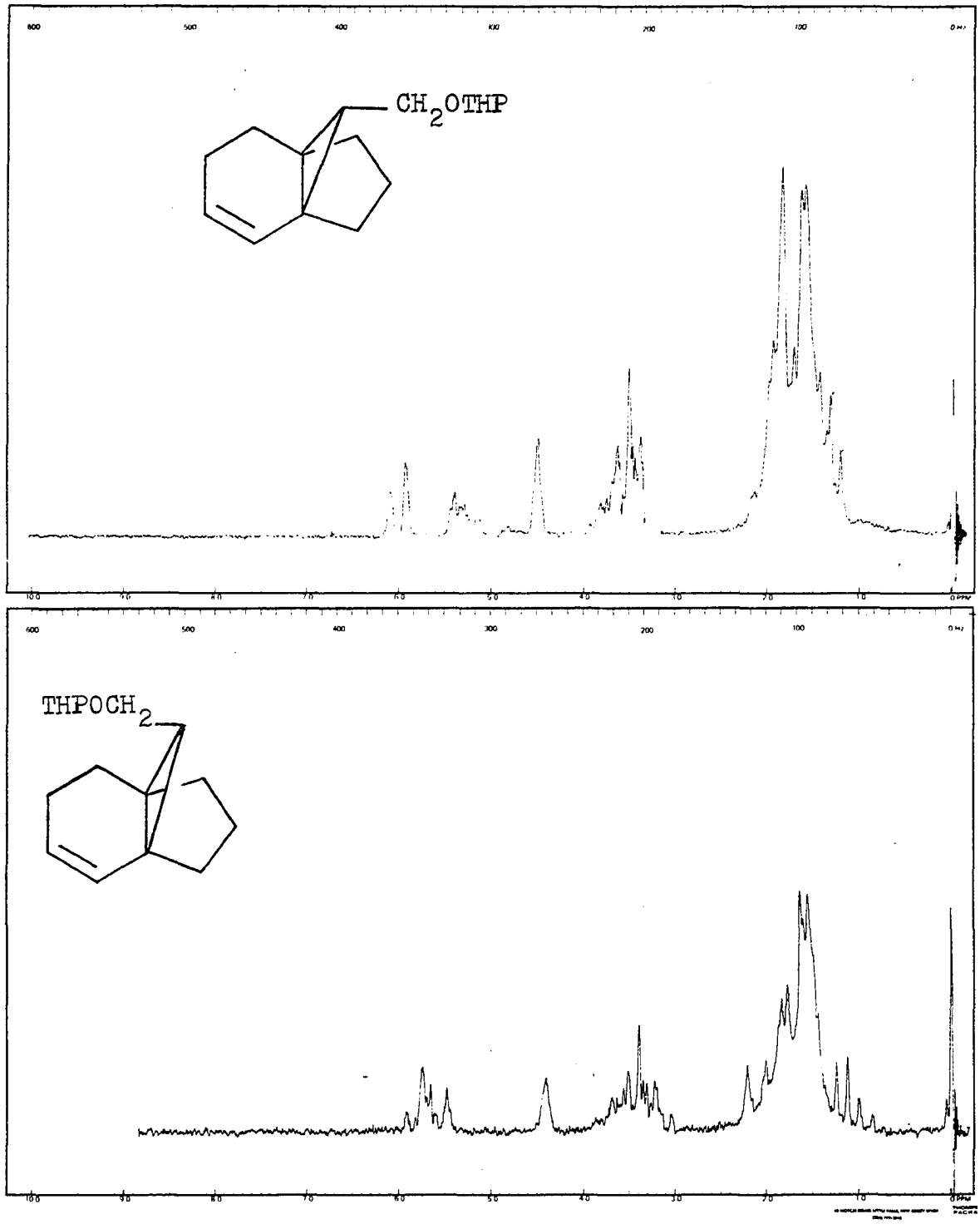
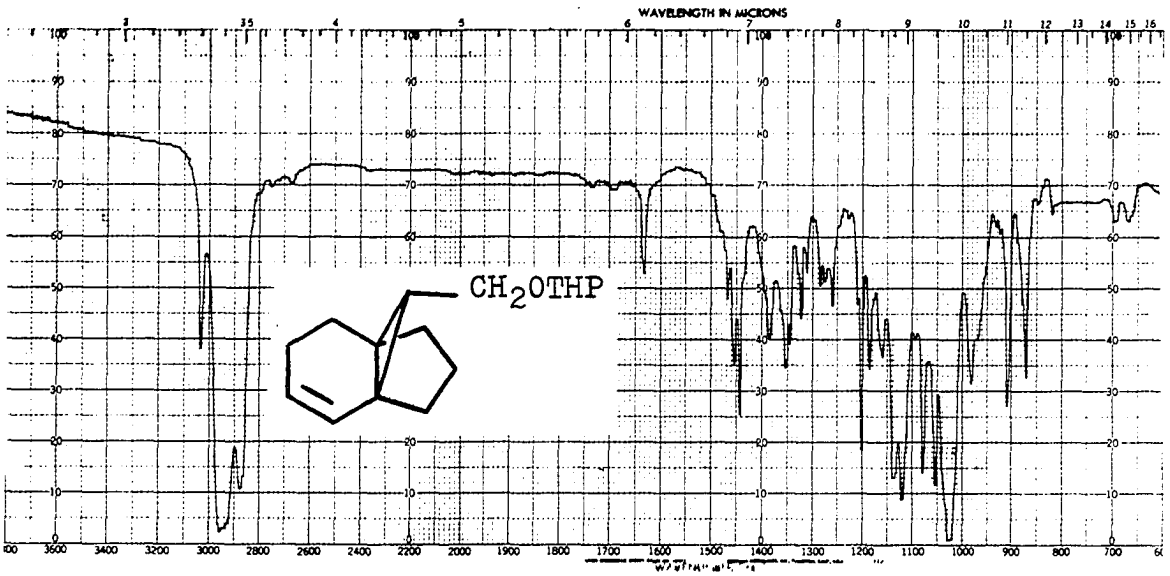


Figure 23. Pmr Spectra of 10-Tetrahydropyranyloxymethyl-tricyclo[4.3.1.$0^{1,6}$]dec-2-ene: 43d (Top) and 47d (Bottom).



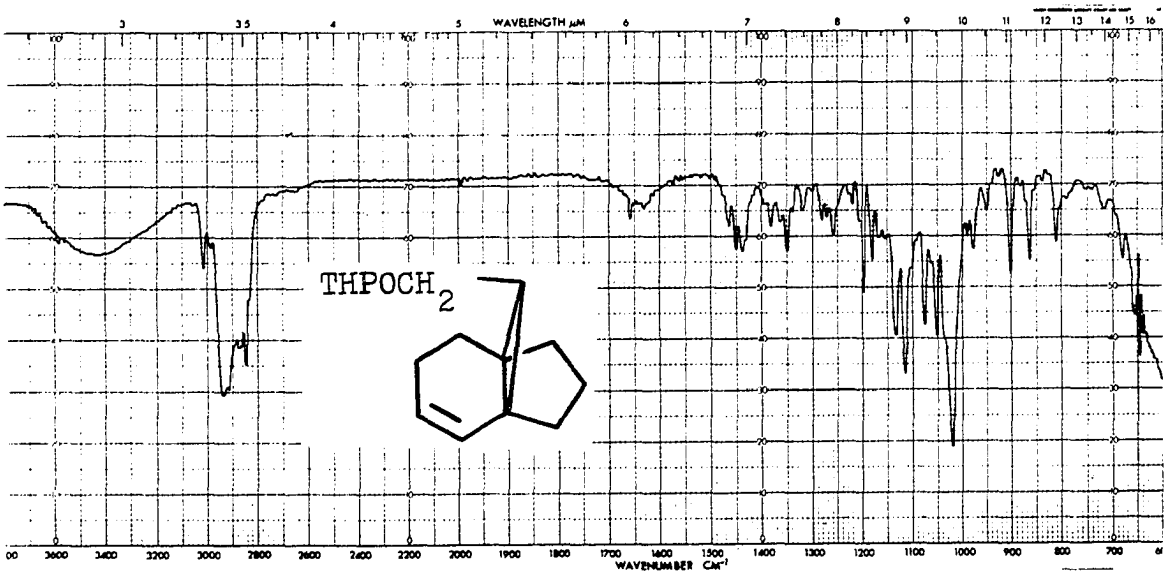


Figure 24. Ir Spectra of 10-Tetrahydropyranyloxymethyl-tricyclo[4.3.1.$0^{1,6}$]dec-2-ene: 43d (Top) and 47d (Bottom).

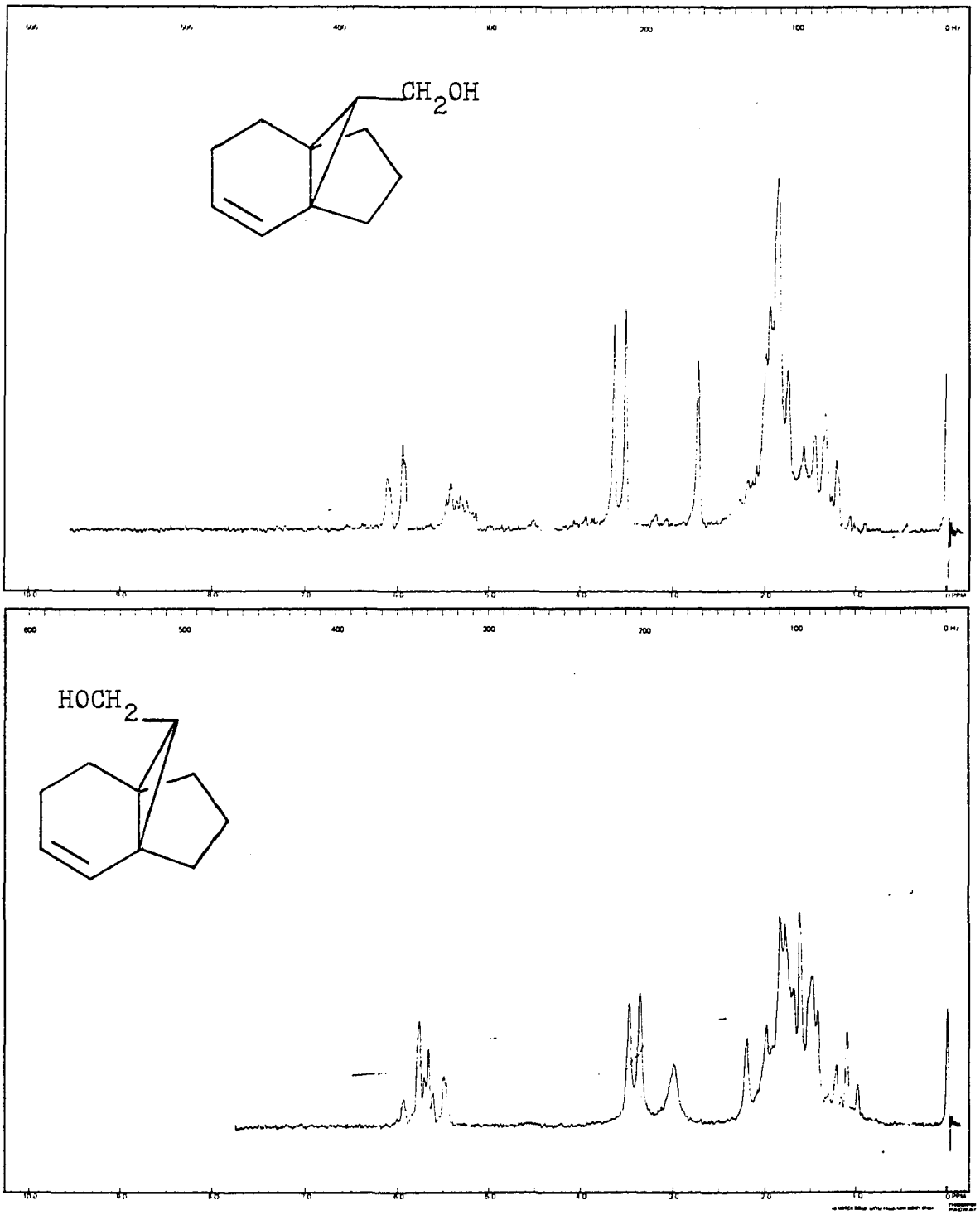
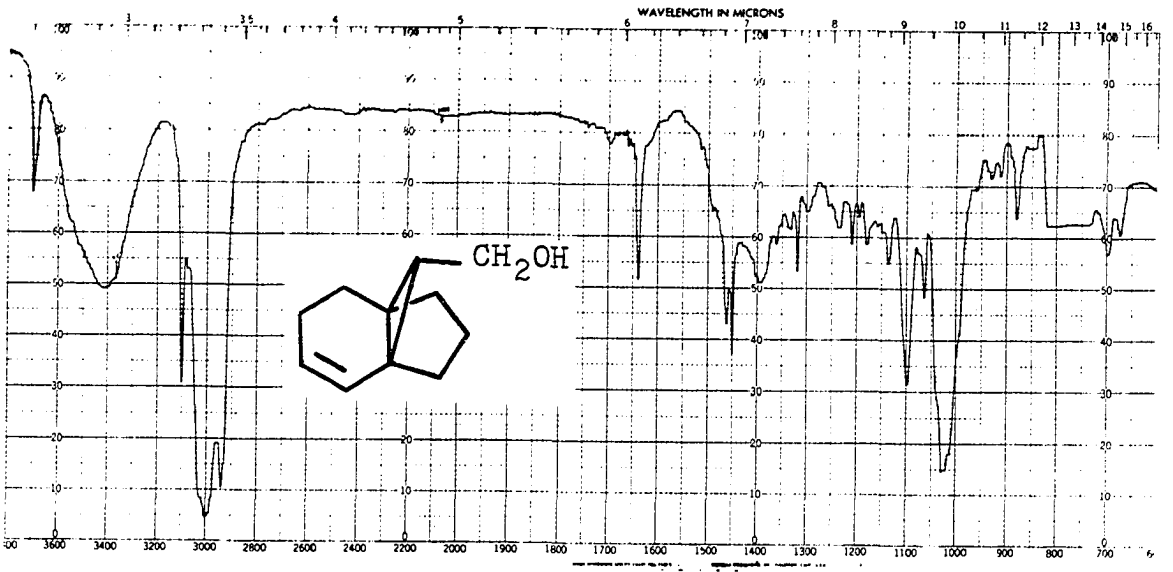


Figure 25. Pmr Spectra of 10-Hydroxymethyltricyclo-[4.3.1.$0^{1,6}$]dec-2-ene: 43c (Top) and 47c (Bottom).



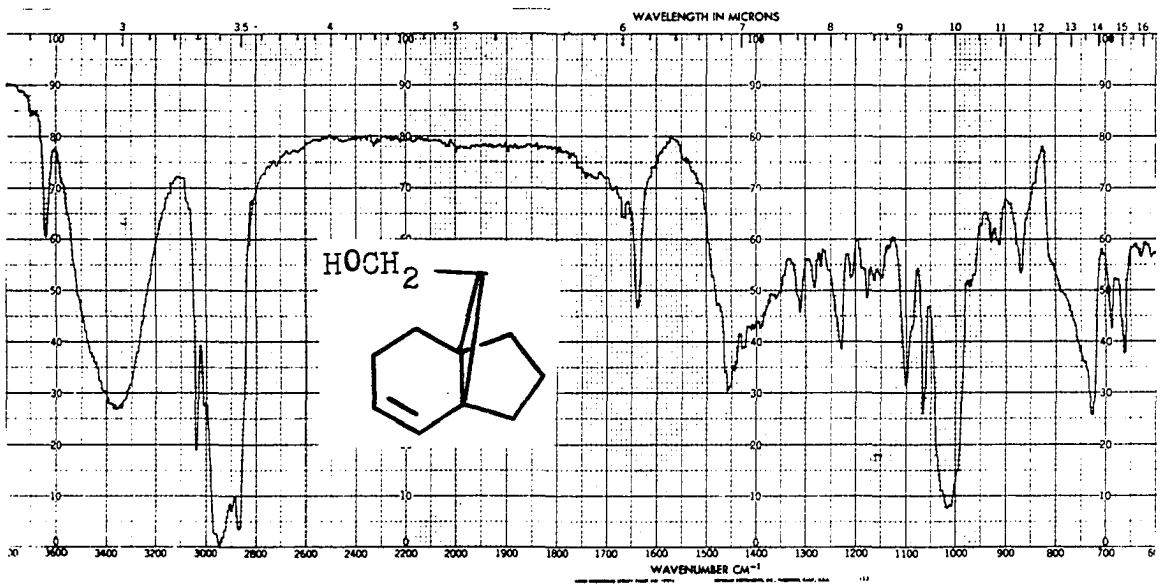


Figure 26. Ir Spectra of 10-Hydroxymethyltricyclo-[4.3.1.$0^{1,6}$]dec-2-ene: 43c (Top) and 47c (Bottom).

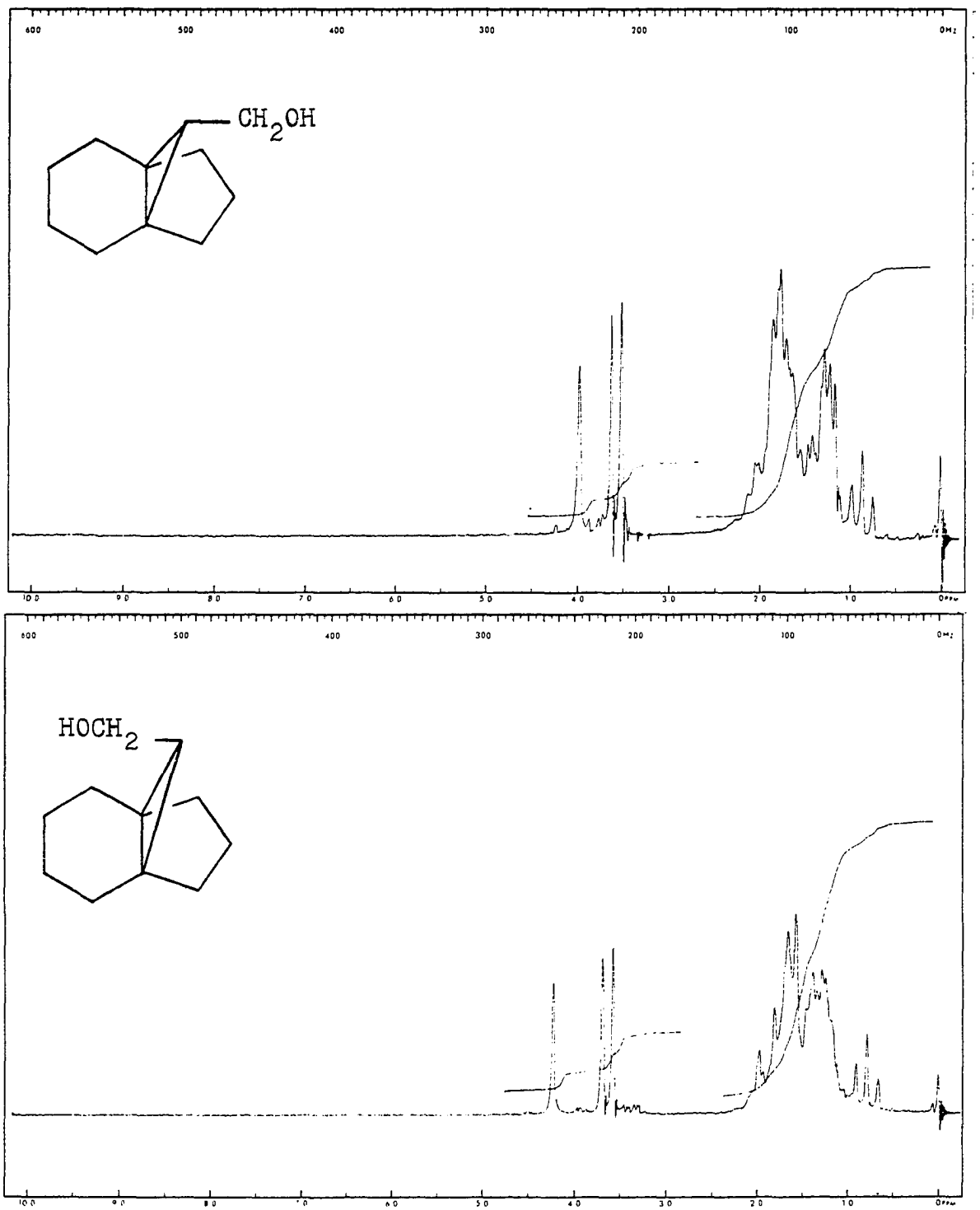


Figure 27. Pmr Spectra of 10-Hydroxymethyltricyclo-[4.3.1.$0^{1,6}$]decane: 41c (Top) and 45c (Bottom).

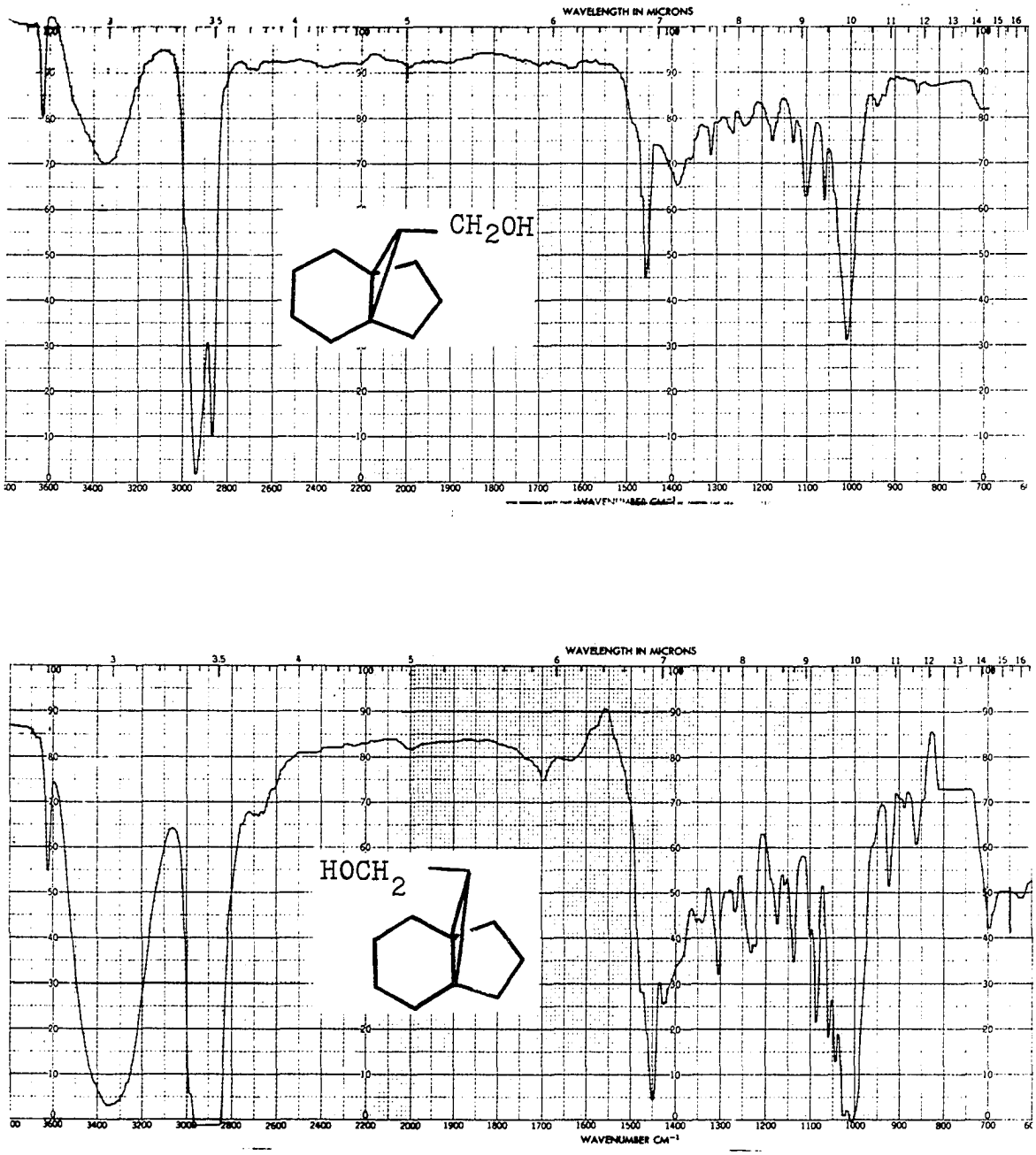


Figure 28. Ir Spectra of 10-Hydroxymethyltricyclo-[4.3.1.$0^{1,6}$]decane: 41c (Top) and 45c (Bottom).

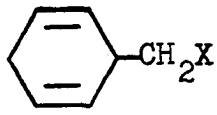
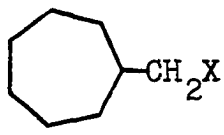
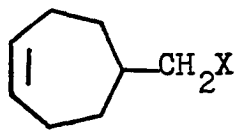
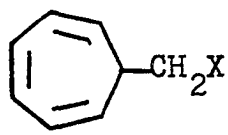
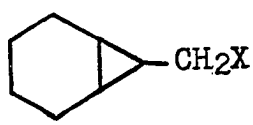
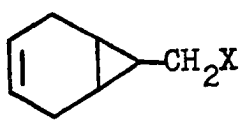
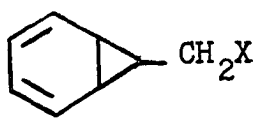
As model compounds, esters 41e, 42e, 43e and their epimers were also prepared according to Scheme 3 (see Fig. 17, 18, 19, 20, 21 and 22). Rearrangement of the symmetrical olefin 42d in a KOtBu-DMSO solution[46] led to a ca. 1:1 mixture of starting ether 42d and the rearranged counterpart 43d. The unsymmetrical olefins 43d and 47d (see Fig. 23 and 24) were separated individually from their symmetrical counterparts via chromatography on silver nitrate-impregnated (12%) silica gel.[47] Finally, hydrolysis afforded the corresponding alcohols 43c and 47c in 28% and 30% yield from 42d and 46d, respectively (see Fig. 25 and 26).

Catalytic hydrogenation (Pt/ether) of 42c and 46c gave 41c and 45c, (see Fig. 27 and 28), respectively. Both were routinely converted to the corresponding dinitrobenzoate esters, 41e and 45e.

Kinetics

Originally, on the basis of the results shown in Table 2, Sargent,[41] et al, proposed that solvolysis of 7-cycloheptatrienylcarbinyl-3,5-dinitrobenzoate 28b involves prior isomerization to the valence tautomer 29b followed by cyclopropyl-assisted ionization. During the progress of this work, Paquette, et al.,[48] published their study of the tetramethylene bridged derivatives 35-39. The observed reacti-

Table 2. Relative Reactivity of Some Cycloalkylcarbinyl Derivatives.

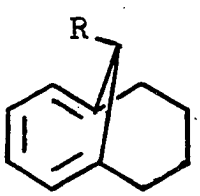
Compound	krel at 100°
	1.0
	5.1×10^{-2}
	3.1
 28	2.8×10^{4}
 30	1.1×10^{6}
	1.6×10^{5}
 29	2.8×10^{8}

vities are shown in Scheme 4.

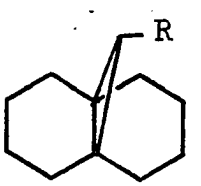
The above data led the authors to conclude that their evidence further supported Sargent's proposal,[41] although the spread of relative rate constants for 35-38 was only a factor of 10. In view of the 3.4-fold enhanced rate for anti-epimer 36, relative to syn-epimer 35, Paquette suggested that 7-cycloheptatrienyl-carbinyl systems solvolyze preferentially through the anti configuration. However, it is not possible to draw a firm conclusion from their studies of 35 and 36, since the solvolyses are dependent upon pre-equilibria, i.e., upon Keq values of unknown magnitude.

Scheme 4

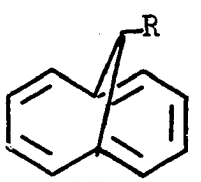
$R=CH_2ODNB$



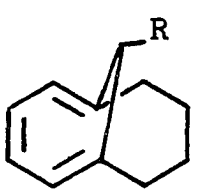
35



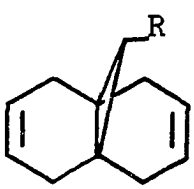
37



39



36



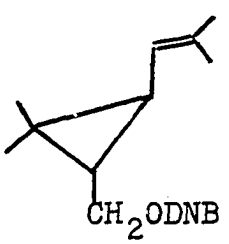
38

krel.	1.0	3.4	8.0	0.8	0.4
at 100°	35	36	37	38	39

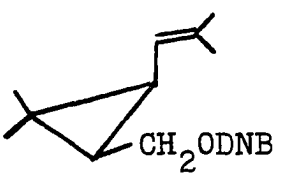
Table 3. Solvolysis Rates for 3,5-Dinitrobenzoates in 70:30 Acetone-Water.

Compd.	T, °C, ±0.1	k_1, sec^{-1}	krel. (70°)	kcal/Mol ΔH	eu ΔS
41e	70.0	$(2.17\pm0.09)\times10^{-5}$	8.6	24.9	-8.0
	100.0	$(4.70\pm0.20)\times10^{-4}$			
42e	70.0	$(5.18\pm0.44)\times10^{-5}$	2.1	27.0	-4.6
	100.0	$(1.45\pm0.02)\times10^{-4}$			
43e	70.0	$(8.49\pm0.26)\times10^{-5}$	3.4	26.0	-6.6
	100.0	$(2.11\pm0.05)\times10^{-4}$			
44e	70.0	$(2.03\pm0.07)\times10^{-4}$	80	25.8	-0.6
	100.0	$(4.98\pm0.17)\times10^{-3}$			
45e	70.0	$(1.04\pm0.02)\times10^{-5}$	4.1	25.1	-8.6
	100.0	$(2.30\pm0.02)\times10^{-4}$			
46e	70.0	$(3.04\pm0.30)\times10^{-5}$	1.2	24.9	-11.8
	100.0	$(6.62\pm0.08)\times10^{-4}$			
47e	70.0	$(3.78\pm0.27)\times10^{-5}$	1.5	28.2	-1.8
	100.0	$(1.21\pm0.03)\times10^{-4}$			
48e	70.0	$(2.53\pm0.13)\times10^{-5}$	1.0	25.5	-10.2
	100.0	$(5.85\pm0.22)\times10^{-4}$			

Our study of the solvolyses of 41e-48e in acetone-water (70:30 by volume) were followed by titrations with standardized NaOH solution. Clean first-order kinetics were observed up to ca. 2-3 half-lives, using calculated infinity titers. The rate constants are given in Table 3. Several conclusions can be drawn from these data.[49] First, it can be seen that, with the exception of the dienes 44e and 48e, the compounds of the anti series (41e, 42e and 43e) solvolyze ca. twice as fast as those of the syn series (45e, 46e and 47e). There is no discernible through-space (field) effect[50] of the double bond of 46e or 47e. The factor of 2 is attributable to steric acceleration in the anti series. Secondly, one may evaluate the conjugative effect of a vinyl group in the β-position of a cyclopropyl-carbinyl cation. This is of interest due to the recently reported chrysanthemyl (cis-40 and trans-40) solvolyses,[51] in which a trans-β-vinyl substituent is five times more accelerative than a cis-β-Vinyl substituent.



trans-40



cis-40

At least in our case, the idea[51] that trans-β-vinyl groups can conjugate better than cis-ones is illusory; the relative rate for the trans case (i.e., 43e/41e = 0.39) is the same as for the cis (47e/45e = 0.36). The absolute rate difference between cis and trans is due to steric factors. Indeed, the cis/trans ratios found by Sasaki et al.[51] are most likely also due to steric effects. Furthermore, with respect to the ability of the cyclopropane ring to transmit the conjugative effect of a vinyl group,[52] it can be seen that our data indicate a very small, but real, effect. This is best noted by comparing the unsymmetrical to symmetrical olefins (i.e. 43e/42e = 1.64 and 47e/46e = 1.24). The blend of inductive and resonance effects are such that both need be stronger in the unsymmetrical cases. In any event, we do not feel the finding of allylcarbinyl-type products requires the postulation of distorted cyclopropylcarbinyl-type ions.[51] Thirdly, it is most interesting to compare the data for the unsymmetrical olefins (43e and 47e) with that for the dienes (44e and 48e). If the effect of the double bonds in the dienes is similar to that of the double bonds in the unsymmetrical monoenes, then the predicted relative solvolysis rates are 1.31 for 44e [43e x 43e/41e] and 0.54 for 48e [47e x 47e/45e]. The actual relative rates are 80.2 and 1.00, corresponding to an "unexpected" acceleration of 61.6 and 1.85. Through the use of extended Hückel

calculations, Stohrer and Daub[53] have recently provided a partial electronic explanation for the greater stability of the anti form of 7-acceptor-substituted norcaradienes relative to the syn-epimer (calculated $\Delta E = 3.9$ kcal/mole for a CH_2^+ substituent). From our data, we can calculate the energy difference between the transition states for the formation of the two norcaradienylcarbinyl cations:

$$\Delta F = -RT \ln \left(\frac{k_{48e}/k_{45e}}{k_{44e}/k_{41e}} \right) = 2.7 \pm 0.1 \text{ kcal/mole.}$$

This method eliminates steric effects and should approximate the electronic energy difference between syn and anti cations. However, since the extended Hückel calculations do not factor out steric effects, it may be more relevant to simply consider the rate difference between 44e and 48e, whereby $\Delta F = -RT \ln (k_{48e}/k_{44e}) = 3.2 \pm 0.1$ kcal/mole. This value is surprisingly close to that obtained by Stohrer and Daub.[53a]

It should be pointed out that a low temperature pmr study of 49 in strong acid has also shown that the norcaradienylcarbinyl cation exists preferentially in the anti-form ($J_{1,7} = 3.5$ Hz). Fourthly, and most importantly, conclusions may be drawn regarding the cycloheptatriene-norcaradiene preequilibria encountered by Sargent,[41] et al., Paquette,[48] et al. Their mechanism can be written as follows:

$$\text{Cycloheptatriene derivative "A"} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \text{Norcaradiene derivative "B"} \xrightarrow{k_2} \text{Products "C"}$$

A steady-state treatment of [B] gives

$$k_1[A] = k_{-1}[B] + k_2[B]$$

$$\text{or } [B]/[A] = k_1/(k_{-1} + k_2)$$

if we assume $k_{-1} \gg k_2$, then $[B] = \frac{k_1}{k_{-1}}[A]$.

Since the rate law is $\frac{d[C]}{dt} = k_2[B] = k_2\frac{k_1}{k_{-1}}[A] =$ $k_{solv}[A]$, one may obtain Keq via the appropriate substitution:

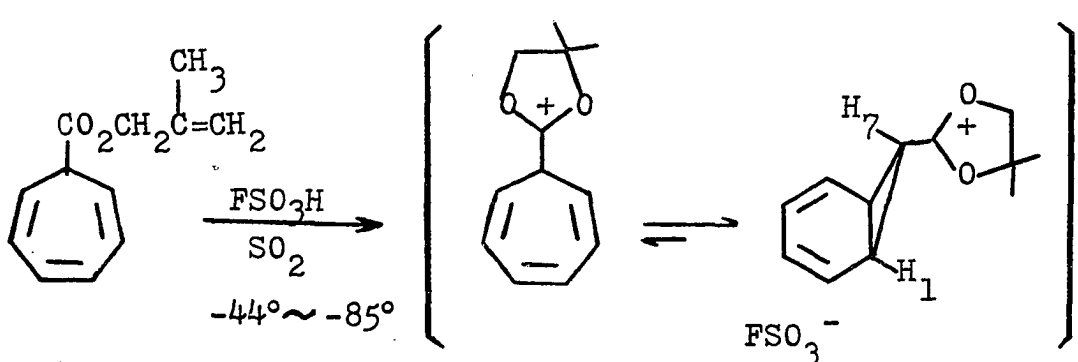
$$k_{solv} = k_2\frac{k_1}{k_{-1}}$$

$$= k_2 Keq \text{ ----------(1)}$$

$$\text{and } \Delta F = -RT\ln Keq \text{ ----------(2)}$$

However, one must obtain a suitable value for k_2.

If one assumes that the preferred conformation of the CH_2ODNB group in 41e-44e is the same as in the bicyclic compounds of Sargent, et al.[41]



49

and the tricyclic ones of Paquette, et al.,[48] k_2 can be obtained by taking the ratio of the rate constant of norcaradiene 44e to an appropriate model compound 41e (or 45e) (this factors out differential steric effects). One then utilizes the observed k_{solv}'s for the triene systems, divided by the k_{solv} for an appropriate reference compound. The equilibrium constants and free energy differences are thus calculated (see equation (1) and (2), and Table 4).

Table 4. Calculated Keq and ΔF for Cycloheptatriene-Norcaradiene Derivatives at 100°.

Compound	Keq	ΔF, kcal/mole
28	2.5×10^{-3} [a]	4.5
	5.0×10^{-3} [b]	4.0
36	3.9×10^{-2} [c]	2.4
35	4.7×10^{-1} [c]	0.57

[a] Calc'd on the basis of $k_2 = k_{44e}/k_{41e}$

[b] Calc'd on the basis of $k_2 = k_{44e}/k_{42e}$

[c] Calc'd on the basis of $k_2 = k_{48e}/k_{45e}$

Interestingly, the equilibrium constant for syn-epimer 35 (Keq = 0.47) is almost the same as the one found for 7-cyano-7-trifluoromethylcycloheptatriene, wherefore it is suggested that at low temperature, both norcaradiene and cycloheptatriene forms should be observable.[26] Unfortunately, neither the valence tautomerism of 35 or 36 could be slowed to the intermediate or slow range on the pmr time scale before crystallization of the solute occurred.[48b] However, it seems certain[48b] that the C_{11} stereochemistry exerts a very marked effect on the valence tautomeric equilibrium, with 36 existing chiefly as a cycloheptatriene derivative and 35 partaking of substantial norcaradiene character, as revealed by low temperature cmr studies.

In conclusion, our results, together with Paquette's data, firmly support the idea that the capability of a 7-cycloheptatrienyl group to stabilize a neighboring cationic center is due to the intermediacy of the norcaradienyl valence tautomer, with the cationic center in the anti-configuration. Furthermore, the calculated free energy difference between bicyclic derivative 36 and its norcaradiene form (as well as for 35 and its counterpart) compared to that for monocyclic compound 28, indicates a significant decrease (ca. 2-4 Kcal/mole) due to the bracketing effect of a tetramethylene bridge.

Product Analysis

The products formed upon hydrolysis of 44e and 48e were identical. When the reactions were carried out in unbuffered 70% aqueous acetone for ten half-lives, the only isolable product was identified as 4-vinylindan 50. The structural assignment of 50 was based, in part, on its non-identity with 5-vinylindan 51, synthesized from the coupling of readily available 5-bromoindan and lithium divinylcopper.[54] Solvolysis product 50 exhibited ir absorption at 725 cm^{-1}, characteristic for three adjacent ring hydrogens in a 1, 2, 3-trisubstituted benzene.[55] On the other hand, 51 displayed two bands at 830 and 870 cm^{-1}, corresponding to two adjacent hydrogens and one lone hydrogen in a 1, 2, 4-trisubstituted benzene.[55] The pmr spectra of 50 and 51 were slightly different with respect to the chemical shifts of the ABX pattern of the vinyl group. (see Fig. 29 and 30).

It was shown that alkyl-oxygen rather than acyl-oxygen cleavage was occurring, since 44c was proven to be stable under the unbuffered solvolysis conditions. Therefore, the 4-vinylindan formed is completely analogous to the products found in Paquette's system[41, 48, 56] and presumably arose via the same mechanism. The major products obtained from the hydrolysis of model compounds 41e, 42e, 43e, 45e, 46e

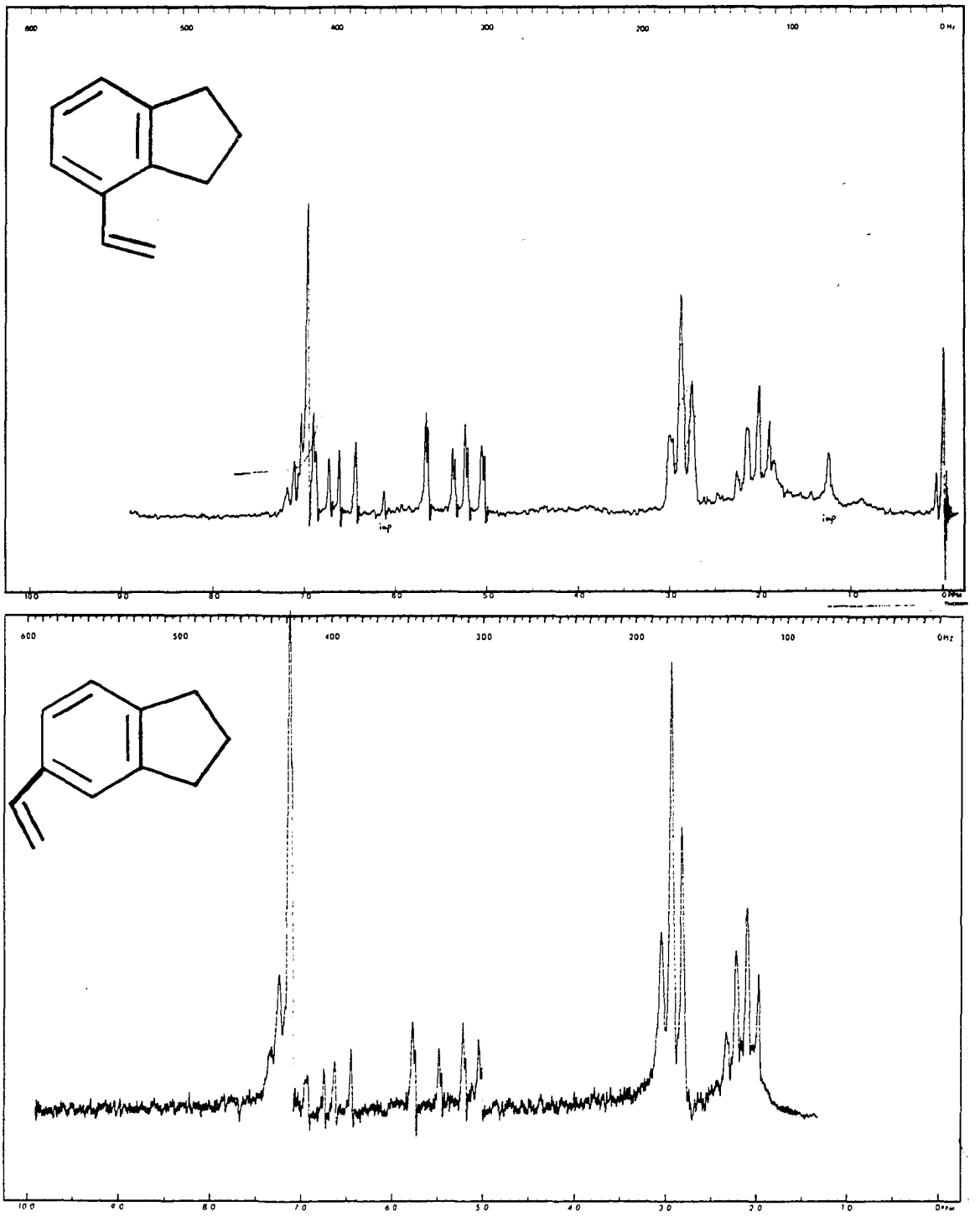


Figure 29. Pmr Spectra of 4-Vinylindan, 50 (Top) and 5-Vinylindan, 51 (Bottom).

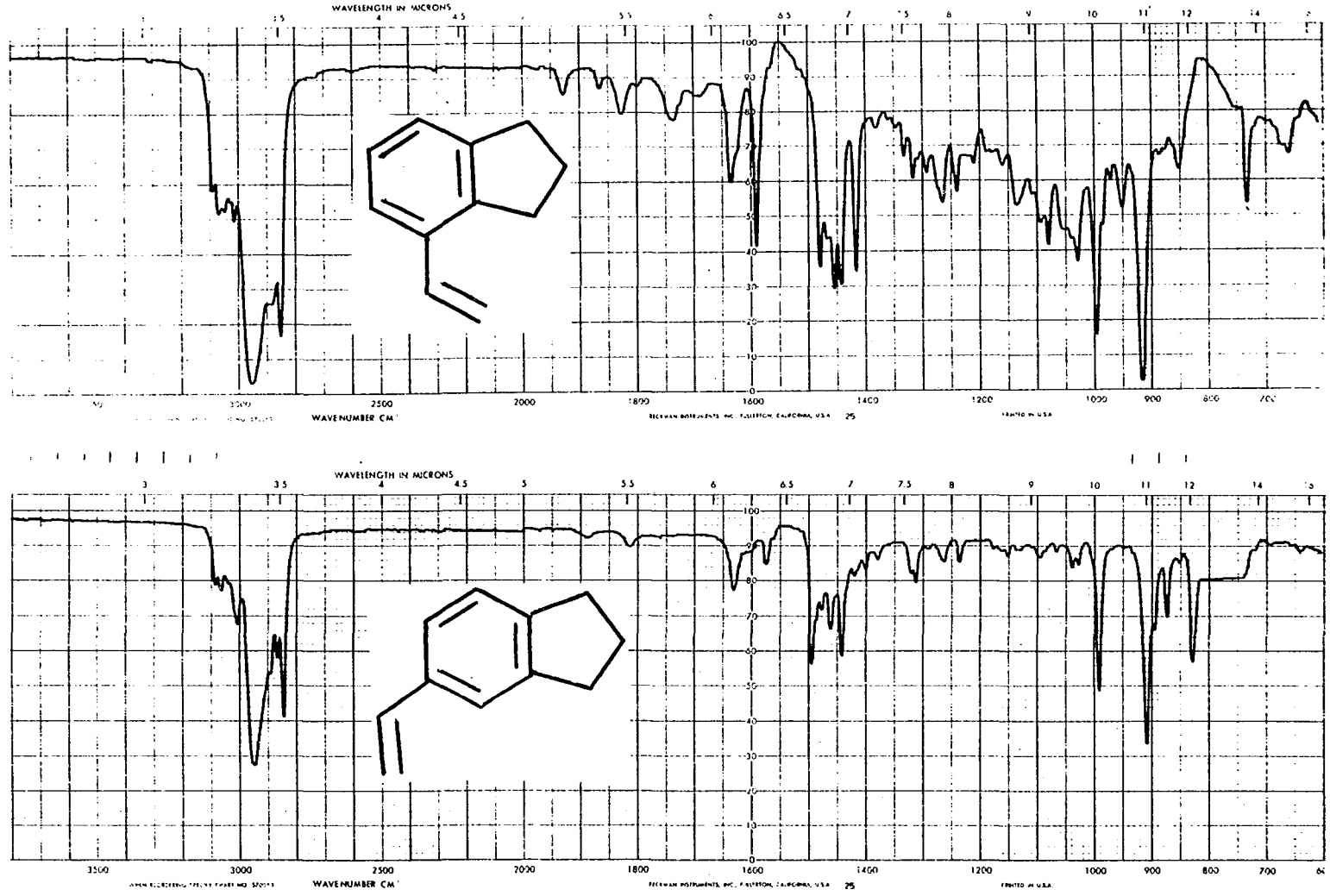
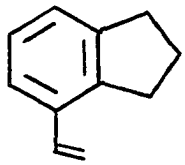
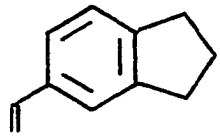


Figure 30. Ir Spectra of 4-Vinylindan, 50 (Top) and 5-Vinylindan, 51 (Bottom).

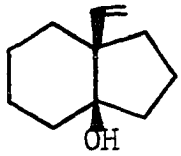
and 47e were homoallylic-type products with ca. 1/3 of products being that of internal return for 41e, 42e, 45e and 46e on the basis of pmr spectra. However, we found no internal return for 43e and 47e, whereby we surmise that the product is allylic alcohol 54.



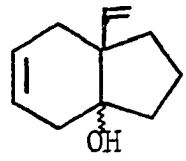
50



51

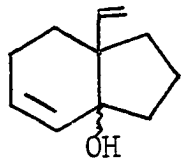


52

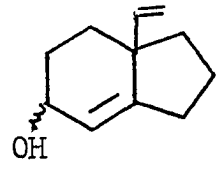


53

The ir spectrum of pure 52 obtained both from 41e and 45e, shows an intramolecularly hydrogen-bound hydroxyl (sharp, 3570 cm^{-1}) as well as the usual hydroxyl absorptions (sharp, 3615 and broad, 3420 cm^{-1}), which allows the assignment of a cis ring fusion to 52. It seems likely that 53 and 54 are also cis fused. While we did not obtain sufficient material for complete analysis, the clean ABX pattern observed in the pmr spectra of 53 and 54 strongly suggests that the material is largely one isomer in each case. Thus 55, a reasonable product from 43e and/or 47e, was not observed.



54



55

EXPERIMENTAL

General

Infrared spectra were recorded on Beckman IR-12, IR-18A and IR-4250 spectrophotometers. The ultraviolet spectra were recorded on a Cary Model 14 spectrophotometer. The proton magnetic resonance spectra were obtained on Varian A-60, and Hitachi Perkin-Elmer R-20B spectrometers, using carbon tetrachloride as the solvent and tetramethylsilane as the internal standard, unless otherwise specified. The carbon magnetic resonance spectra were recorded on a Bruker HX-90 spectrometer equipped with a Nicolet Model 1089 data package. The mass spectral studies were conducted using Altas CH-4, High Resolution MS-9 and Perkin-Elmer 270 GLC-mass spectrometers. Glc analyses were conducted on a Varian Aerograph Model 90-P gas chromatograph. Melting points were taken on a Thomas-Hoover melting point apparatus and are uncorrected. Elemental analyses were performed by the Ilse Beetz Microanalytical Laboratory, Kronach, West Germany and Spang Microanalytical Laboratory, Ann Arbor, Michigan.

The following glc columns were utilized.

A, 10 ft. x 0.125 in., 3% DEGS on chromsorb P.

B, 6 ft. x 0.25 in., 20% DEGS on chromsorb P.

C, 8 ft. x 0.25 in., 20% SE-30 on chromsorb P.

D, 5 ft. x 0.25 in., 3% SE-30 on varaport 30.

E, 6 ft. x 0.25 in., 20% dinonyl phthalate on Chromsorb W.

F, 10 ft. x 0.25 in., 5% carbowax 20 M on chromsorb W.

G, 6 ft. x 0.25 in., 15% FFAP on chromsorb P.

H, 15 ft. x 0.125 in., 12% DC-550 on chromsorb W.

Synthesis

Tricyclo[4, 3, 1, $0^{1,6}$]-deca-3-ene-10-carboxylic acids (42a, 46a) To a refluxing mixture of 6.5 g (0.27 mole) magnesium powder in 26 ml of freshly distilled THF was added a solution of 6.5 ml dibromoethane in 26 ml dry THF. After the evolution of ethylene subsided, a solution of 21.6 g (0.074 mole) of bromides 46f and 42f (3.3 to 1 ratio) in 155 ml dry THF was added dropwise to the slurry over a period of 30 min. The resultant mixture was refluxed for one additional hr., and then cooled to room temperature. Carbon dioxide was bubbled through the mixture overnight. Dilution with 100 ml ether was followed by acidification with 2N HCl solution. The resulting milky suspension was extracted with ether several times, and the combined ethereal layers were then extracted with dilute NaOH solution. Reacidification of the basic solution with 2N HCl, followed by ether extraction, drying over anhy. Na_2SO_4 and concentration in vacuo gave 7.6 g (43%) of the white solid

carboxylic acids, mp 153-156° (hexane). Spectral data for the separate acids are given later.

Anal. Calc'd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92

Found : C, 74.34; H, 8.14

Equilibration of 42a and 46a via their methyl esters

A stirred solution of 5.0 g (28.2 mole) of 42a and 46a in 75 ml ether was titrated with etheral diazomethane[57] solution at room temperature until the yellow color persisted and no further bubbles were evolved. The solution was concentrated to give a yellow oil (5.23 g, 97%). The ratio of esters 42b to 46b was determined by pmr as 91 to 9 (δ, 3.52 for OCH_3 of 42b and δ.3.47 for OCH_3 of 46b). Preparative separation of the epimers was attempted, without success, on the column E and F. A single symmetrical peak was observed in every case.

Anal. Calc'd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39

Found : C, 75.05; H, 8.44

To a solution of 4.33 g (22.5 mmol) of 42b and 46b in 50 ml of absolute methanol was added 12.2 g (225 mmol) sodium methoxide. The resulting brown mixture was refluxed for 46 hr. Upon cooling, the mixture was diluted with 50 ml ether and washed with 5 x 20 ml water. After drying over anhydrous sodium sulfate and removal of solvent, there remained a oil which weighed 0.88 g and contained an equal amount of 42b and 46b. Acidification of the combined aq.

layers yielded the corresponding acids (3.06 g). Saponification of the esters, followed by acidification, produced 42a and 46a (0.81 g). The overall yield (3.87 g) was 78%.

Separation of 42a and 46a via iodolactonization

A solution of 10.1 g (56 mmol) of equilibrated 42a and 46a in 500 ml of 0.5 N sodium bicarbonate solution and a solution of 28.6 g (112 mmol) of I_2 and 56.0 g (337 mmol) KI in 150 ml water were mixed and stirred in a one liter flask which was wrapped with aluminum foil to avoid decomposition of the product. After 24 hr. the dark brown oil was separated from the aq. solution, which was then extracted with 3 x 200 ml chloroform. The combined organic layers were shaken with 2 x 150 ml 10% sodium thiosulfate solution, followed by washing with 2 x 80 ml water and drying over anhy. Na_2SO_4. Finally, removal of solvent yielded 7.90 g of yellow solid. Two recrystallizations from 95% ethanol gave 7.75 g (90% yield based on 46a used) of 34, mp 135-136° (ethanol)

Ir ($CHCl_3$): 1720, 1710, 1365, 1070 and 1030 cm^{-1}

Pmr ($CDCl_3$): δ4.52 (m, 2H), 3.40-2.30 (m, 4H) and 2.25-1.05 (m, 7H); (see Fig. 2)

Mass spec: parent ion at m/e 304.

Anal. Calc'd for $C_{11}H_{13}O_2I$: C, 43.44; H, 4.31

Found : C, 43.39; H, 4.47

The aq. solution separated from the reaction mixture was

treated with 10% $Na_2S_2O_3$ solution until the red color disappeared. After acidification with 2N hydrochloric acid, the resulting mixture was extracted with 3 x 200 ml ether. The etheral layers were combined, dried and concentrated. The white solid (42a) weighed 3.77 g (75%), mp 160-162° (ether),

Ir.(CCl_4): 3500-2400, and 1700 cm^{-1}.

Pmr: δ12.7 (s, 1H) 5.45 (m, 2H) and 2.8-1.4 (m, 11H) (see Fig. 3 and 4).

Mass spec.: parent ion at m/e 178.

Esterfication of 42a with diazomethane gave a quantitative yield of 42b.

Ir (CCl_4): 1735 cm^{-1}.

Pmr: δ5.40 (m, 2H), 3.52 (s, 3H), and 2.7-1.5 (m, 11H) (see Fig. 5 and 6).

Mass spec.: parent ion at m/e 192.

The procedure was repeated except 0.90 g of the nonequilibrated acid mixture eas used. The products were 0.21 g of 34 and 0.76 g of 42a.

syn-Carboxylic acid 46a from iodolactone 34 To a solution of 7.5 g (2.46 mmol) 34 in 12 ml glacial acetic acid was added 2.0 g zinc dust. The mixture was stirred at 90° for 6.5 hr. The resulting mixture was filtered and washed with 2 x 10 ml hot water. After cooling to room temperature, the filtrate was extracted with 3 x 30 ml

ether. Evaporation of the ether gave a white solid (46a) which was redissolved in 5% potassium hydroxide and acidified with 2N hydrochloric acid. Filtration and drying left 3.97 g (91%) 46a, mp 145-147° (ether)

Ir (CCl_4): 3500-2400 and 1710 cm^{-1}.

Pmr: δ12.6 (s, D_2O exchangeable, 1H) 5.40 (m, 2H) and 2.7-1.3 (m, 11H); (see Fig. 3 and 4).

Mass spect.: parent ion at m/e 178.

anti-10-hydroxymethyl-tricyclo-[4.3.1.$0^{1,6}$]deca-3-ene (42c) To 1.95 g (51.5 mmol) lithium aluminum hydride suspended in 30 ml anhydrous ether in a 250-ml two-necked flask equipped with magnetic stirrer, addition funnel and a drying tube on the top of the reflux condenser, was added 3.00 g (16.9 mmol) 42a in 80 ml ether at such a rate as to produce gentle reflux. The mixture was allowed to stir for 24 hr. The excess hydride was decomposed by adding 25 ml of 20% sodium potassium tartrate solution. The layers were separated, and the aqueous layer extracted with 3 x 10 ml ether. The combined etheral layers were dried over anhydrous sodium sulfate and concentrated. The colorless oil solidified upon cooling, and recrystallization from hexane gave 2.18 g (79%) 42c. The solid was hygroscopic.

Ir (CCl_4): 3635, 3340, 3040, 1660, 1115, 1060, and 1020 cm^{-1}.

Pmr: δ5.40 (m, 2H), 3.72 (Br. d, OH), 3.35 (d, 2H,

J = 7Hz), 2.20-1.20 (m, 10H), and 1.03 (t, 1H, J = 7Hz) (see Fig. 7 and 8).

Anal. Calc'd for $C_{11}H_{16}O$: m/e = 164.1201.
Found : 164.1202.

syn-10-hydroxymethyl-tricyclo [4.3.1.$0^{1,6}$]deca-3-ene 46c Treatment of the syn-carboxylic acid (46a) (3.97 g) as described for 42a gave a 92% yield (3.36 g) of the syn-alcohol (46c), which solidified when cooled.
Ir (film): 3340, 3020, 1660, 1100, 1030 and 1010 cm^{-1}.
Pmr: δ5.47 (m, 2H), 3.88 (Br. s, OH), 3.38 (d, 2H, J = 7Hz), 2.50-1.00 (m, 10H), and 0.81 (t, 1H J = 7Hz) (see Fig. 7 and 8).

Anal. Calc'd for $C_{11}H_{16}O$: m/e = 164.1201.
Found : 164.1202.

anti-10-tetrahydropyranyloxymethyltricyclo[4.3.1.$0^{1,6}$] deca-3-ene (42d) To 2.88 g (17.6 mmol) 42c was added 1.50 g (17.9 mmol) 3,4-dihydropyran, to which had been added five drops conc. hydrochloric acid. The mixture was allowed to stir at room temperature for 5 hr. Dilution with 20 ml ether was followed by extraction with 2 x 5 ml saturated sodium bicarbonate solution and then 2 x 5 ml water. The ethereal layer was dried over anhy. magnesium sulfate, filtered and evaporated. The yellow oil was chromatographed on silica gel and eluted with a hexane/ether mixture, to yield 3.58 g (82%) 42d as a colorless oil.

The sample was suitable for analysis.

Ir (CCl_4): 3020, 1650(w), 1075, and 1020 (s) cm^{-1}.

Pmr: δ5.42 (m, 2H), 4.48 (Br. s, 1H), 3.90-3.15 (m, 4H), 2.70-1.20 (m, 16H), and 1.03 (t, 1H, J = 7Hz) (see Fig.9 and 10).

Mass spec: parent ion at m/e 248.

Anal. Calc'd for $C_{16}H_{24}O_2$: C, 77.38; H, 9.74.

Found : C, 77.36; H, 9.53.

syn-10-tetrahydropyranyloxymethyltricyclo[4.3.1.$0^{1,6}$]deca-3-ene (46d) Treatment of the syn-alcohol 46c (3.30 g) as described for 42c gave a brownish oil which was purified by column chromatography to yield 4.25 g (85%) of 46d.

Ir (CCl_4): 3010, 1655 (w), 1075, 1050, and 1020 (s) cm^{-1}.

Pmr: δ5.50 (m, 2H), 4.41 (Br. s, 1H), 3.80-3.05 (m, 4H), 2.75-1.10 (m, 16H), and 0.87 (t, 1H, J = 7Hz) (see Fig. 9 and 10).

Mass spect.: parent ion at m/e 248.

Anal. Calc'd for $C_{16}H_{24}O_2$: C, 77.38; H, 9.74.

Found : C, 77.36; H, 9.53.

anti-10-tetrahydropyranyloxymethyltricyclo[4.3.1.$0^{1,6}$]deca-2,4-diene (44d) To a solution of 2.55 g (10.3 mmol) 42d in 10 ml methylene chloride which was cooled to -78° was slowly added a solution of 1.65 g (10.3 mmol) bromine in 1.5 ml methylene chloride. After stirring at -78° for 30

min, the mixture was warmed to room temperature. Removal of solvent under vacuum at less than 35° resulted in a brownish oil which was used for dehydrobromination without further purification. The dibromo compound was dissolved in 10 ml freshly distilled THF which was predried over lithium aluminum hydride. Under nitrogen, 15 ml of a dry THF solution containing 5.0 g (33 mmol) 1.5-diazabicyclo[5.4.0]undeca-5-ene (DBU) was slowly syringed into the solution of the dibromo compound. A brown ppt. formed as soon as the DBU was added. The resulting mixture was heated at 45° for 48 hr. After cooling, 5 ml water was added, followed by extraction with 4 x 15 ml ether. The combined ethereal layers were dried, filtered and stripped of solvent. The resulting brown oil was chromatographed on silica gel using 1% ether in hexane as the eluent. Analytically pure 44d (1.72 g, 68%) was obtained as a slightly yellow oil.

Ir (film): 3040, 1080, and 1028 cm^{-1}.

Pmr: δ6.30-5.60 (m, 4H,AA'BB'),4.60 (Br. s, 1H), 4.10-3.25 (m, 4H), 2.40-0.90 (m, 12H), and 0.31 (t, 1H, J = 7Hz) (see Fig. 11 and 12).

Mass spect.: parent ion at m/e 246.

Anal. Calc'd for $C_{16}H_{22}O_2$: C, 78.01; H, 9.00.
Found : C, 77.88; H, 8.76.

syn-10-tetrahydropyranyloxymethyltricyclo[4.3.1.$0^{1,6}$]deca-2, 4-diene (48d) Treatment of the syn-THP ether

46d (2.50 g) as described for 42d gave a yellow oil which was chromatographed to yield 65% (1.63 g) of 48d.

Ir (film): 3040, 1064, and 1035 cm^{-1}.

Pmr: δ5.90 (m, olefinic 4H), 4.36 (s, 1H), 3.90-3.30 (m, 2H), 3.05 (d. of d. 1H, J = 12Hz, J = 7Hz), 2.65 (d. of d. 1H, J = 12Hz, J = 7Hz), and 2.40-1.10 (m, 13H) (see fig. 11 and 12).

Mass spect.: parent ion at m/e 246.

Anal. Calc'd for $C_{16}H_{22}O_2$: C, 78.01; H, 9.00.

Found : C, 77.88; H, 8.76.

syn-10-tetrahydropyranyloxymethyltricyclo[4.3.1.$0^{1,6}$]deca-2-ene (47d)) In a 100-ml 3-necked flask, 3.90 g (34.8 mmol) of potassium t-butoxide in 25 ml DMSO was heated to 70° under nitrogen. A 20 ml DMSO solution containing 2.80 g (11.3 mmol) 46d was syringed into the mixture. The resulting mixture became dark brownish immediately. After heating at 75° for 14 hr, the mixture was poured into 50 ml H_2O and extracted with 4 x 50 ml ether. The combined ethereal layers were seqentially washed with 2 x 10 ml of 10% hydrochloric acid solution, 2 x 10 ml of 0.5N sodium bicarbonate solution and 2 x 10 ml water. The organic layer was dried over anhy. Na_2SO_4, filtered and concentrated to give a crude product which was chromatographed on silica gel. Elution with 2% ether in hexane gave a mixture of

46d and 47d (1.90 g, 68%). Separation of the mixture (0.45 g) was achieved by column chromatography, using a 12% silver nitrate-impregnated silica gel packing on a 1/2 x 20 in. column and eluting with 500 ml hexane, then 1% Et_2O/hexane, and finally ether. 15 ml fractions were collected; fractions 31-59 (0.18 g) were identified as containing 46d and fractions 65-68 (0.18 g) as containing 47d (pmr analysis).

Ir (film): 3020, 1660 (w), 1050, and 1020 cm^{-1}.

Pmr: δ5.95-5.40 (m, 2H), 5.40 (s, 1H), 3.90-3.00 (m, 4H), 2.30-1.20 (m, 16H), 1.12 (t, 1H, J = 7Hz) (see Fig. 23 and 24).

Mass spect.: parent ion at m/e 248.

Anal. Calc'd for $C_{16}H_{24}O_2$: C, 77.38; H, 9.74.

Found : C, 77.27; H, 9.61.

anti-tetrahydropyranyloxymethyltricyclo[4.3.1.$0^{1,6}$]deca-2-ene (43d) Treatment of the anti-THP ether 42d (2.36 g) as described for 46d gave a 79% (1.86 g) yield of a mixture of 42d and 43d. Separation was accomplished over a 12% silver nitrate-impregnated silica gel 60 dry column (1 x 60 in). Two spots (R_f = 0.11 and 0.34) were found via TLC, where the TLC plate was pretreated with an acetonitrile solution containing silver nitrate (developing solvent 8% ether/hexane).

Ir (CCl_4): 3035, 1630 (w), 1055, and 1020 cm^{-1};

Pmr: δ6.00 (d, 1H, J = 10Hz), 5.50-5.10 (m, 1H), 4.50 (s, 1H), 4.00-3.15 (m, 4H), and 2.20-1.10 (m, 17H) (see Fig. 23 and 24).

Mass spect.: parent ion at m/e 248.

Anal. Calc'd for $C_{16}H_{24}O_2$: C, 77.38; H, 9.74.

Found : C, 77.38; H, 9.73.

syn-10-hydroxymethyltricyclo[4.3.1.$0^{1,6}$] decane (45c)

A mixture of 0.59 g (3.6 mmol) 46c and 0.15 g 5% pt/C in 30 ml ether was stirred at room temp. under a 15 psi hydrogen atmosphere for one hr. The catalyst was then filtered off and washed with 2 x 10 ml ether. After removal of solvent, the crude product was recrystallized from pentane (0.57 g, 97%), mp 41-42°.

Ir (CCl_4): 3620, 3350, 1085, 1060, 1045, and 1010 cm^{-1}.

Pmr: δ4.22 (s, OH), 3.64 (d, 2H, J = 7Hz), 2.10-1.00 (m, 14H), and 0.78 (t, 1H, J = 7Hz) (see Fig. 27 and 28).

Mass spect.: parent ion at m/e 166.

Anal. Calc'd for $C_{11}H_{18}O$: C, 79.47; H, 10.91

Found : C, 79.50; H, 10.91

anti-10-hydroxymethyltricyclo[4.3.1.$0^{1,6}$]decane (41c)

Hydrogenation of 42c (0.52 g) as described for 46c gave a 94% (0.49 g) yield of 41c which failed to crystallize.

Ir (CCl_4): 3640, 3350, 1100, and 1010 cm^{-1}.

Pmr: δ4.00 (s, OH), 3.56 (d, 2H, J = 7Hz), 2.3-1.0 (m, 14H), 0.86 (t, 1H, J = 7Hz) (see Fig. 27 and 28).

Mass spect.: parent ion at m/e 166.

Anal. Calc'd for $C_{11}H_{18}O$: C, 79.47; H, 10.91.

Found : C, 79.40; H, 10.87.

anti-10-hydroxymethyltricyclo[4.3.1.$0^{1,6}$]deca-2, 4-diene (44c) To 0.60 g (2.44 mmol) 44d in 2 ml 95% ethanol was added 5 mg p-toluenesulfonic acid. The mixture was stirred at 55° for one hr. and then poured into a mixture of 4 ml water and 60 ml ether. After separation of the layers, the ether layer was washed with 2 x 5 ml 0.5N sodium bicarbonate solution, 2 x 5 ml water, dried and stripped of solvent. The yellow oil thus obtained failed to crystallize. Column chromatography on silica gel (methylene chloride elution) produced 0.28 g (71%) of pure 44c.

Ir (benzene): 3600, 3450, 1090, and 1010 cm^{-1}.

Pmr ($CDCl_3$): δ6.40-5.60 (m, 4H of AA'BB'), 4.60 (s, 1H, OH), 3.95 (d, 2H, J = 7Hz), 2.70-1.30 (m, 6H), and 0.35 (t, 1H, J = 7Hz) (see Fig. 13 and 14).

Uv (cyclohexane): 272 (4170), 254 (3960), and 248 (4000) nm

Mass spect.: parent ion at m/e 162.

Anal. Calc'd for $C_{11}H_{14}O$: C, 81.44; H, 8.70.

Found : C, 81.22; H, 8.73.

<u>syn-10-hydroxymethyltricyclo[4.3.1.$0^{1,6}$]deca-2, 4-diene (48c)</u> Treatment of 0.54 g of <u>48d</u> as described for <u>44d</u> gave 68% (0.23 g) of <u>48c</u> after column chromatography.

Ir (film): 3410, 3040, 1090, 1070, and 1020 cm^{-1}.

Pmr: δ5.95 (Br. s, 4H), 4.50 (s, 1H of $\ddot{O}\ddot{H}$), 2.88 (d, 2H, J = 7Hz), 2.70-1.20 (m, 6H), and 1.18 (t, 1H, J = 7Hz) (see Fig. 13 and 14).

Uv (cyclohexane): 246 (3230), 252 (4040), and 257 (3230).

Mass spect.: parent ion at 162.

Anal. Calc'd for $C_{11}H_{14}O$: C, 81.44; H, 8.70.

Found : C, 81.22; H, 8.73.

<u>anti-10-hydroxymethyltricyclo[4.3.1.$0^{1,6}$]deca-2-ene (47c)</u> Treatment of 0.40 g of <u>47d</u> as described for <u>44d</u> gave 68% (o.18 g) of <u>47c</u> after column chromatography (elution with CH_2Cl_2).

Ir (CCl_4): 3630, 3330, 3030, 1640, 1100, 1065, and 1025 cm^{-1}.

Pmr (CCl_4): δ6.02 (Br. s, 1H), 5.50-5.10 (m, 1H), 3.57 (d, 2H, J = 7Hz), 2.70 (s, 0H), 2.50-1.30 (m, 10H), and 1.33 (t, 1H, J = 7Hz) (see Fig. 25 and 26).

Anal. Calc'd for $C_{11}H_{16}O$: m/e 164.1201.

Found : m/e 164.1194.

syn-10-hydroxymethyltricyclo[4.3.1.$0^{1,6}$]deca-2-ene (43c) Treatment of 0.35 g of 43d as described for 44d gave 65% (0.15 g) of 43c.

Ir (CCl_4): 3640, 3040, 1635, 1100, 1065, and 1020 cm^{-1}.

Pmr: δ6.00-5.40 (m, 2H), 3.40 (e, 2H, J = 7Hz)
3.00 (s, 1H), 2.30-1.30 (m, 10H), and
1.10 (t, 1H, J = 7Hz) (see Fig. 25 and 26).

Mass spect.: parent ion at m/e 164.

Anal. Calc'd for $C_{11}H_{16}O$: C, 80.49; H, 9.82.
Found : C, 80.19; H, 9.87.

General Procedure for the 3,5-dinitrobenzoates (41e-48e)

To a solution of 0.20 g (1.22 mmol) of alcohol in 10 ml dry pyridine was added 0.40 g (1.74 mmol) of 3,5-dinitrobenzoyl chloride (which was previously recrystallized twice from ether and hexane). The mixture was stirred at room temperature for 2 hr. and then left in the refrigerator overnight. The resulting mixture was poured onto ice-water. After ether extraction, the combined ether layers were washed with 10% HCl solution, then 0.5N $NaHCO_3$ solution, and finally saturated NaCl solution. After drying over anyh Na_2SO_4 and removal of solvent, the remaining solid was recrystallized from CCl_4/hexane to give the pure 3,5-dinitrobenzoate. The data for the various 3,5-dinitrobenzoates (41e-48e) are collected in Table 5 (see Fig. 15-22 for pmr and ir spectra).

Table 5. The Physical Properties and Analyses for some 3,5-dinitrobenzoates.

comp	mp	yield (%)	Mass spect. m/e, at 70ev		Elemental Analysis			
			calc'd	found	calc'd %C	calc'd %H	found %C	found %H
41e	104-105°	54	360	360	55.99	5.59	59.82	5.53
42e	81-82.5°	74	358	358	60.33	5.06	60.44	4.93
43e	84-85°	69	358	358	60.33	5.06	60.38	5.05
44e	113-114°	36	356	356	60.67	4.53	60.64	4.69
45e	86-87°	77	360	360	59.99	5.59	60.00	5.70
46e	98-99°	52	358.1165	358.1159	-		-	
47e	104-105°	66	358.1165	358.1144	-		-	
48e	92-94°	38	356.1008	356.0983	-		-	

Kinetic Studies

A stock solution of 70:30 (by volume) acetone-water was prepared from purified acetone (distilled from $KMnO_4$) and distilled water. Solvolyses were carried out in sealed ampoules, into which 3.5 ml of 0.0100 M 3,5-dinitrobenzoate solution had been transferred. A set of ampoules was immersed in a constant temperature bath at the appropriate temperature. After allowing 3 min for temperature equilibration, the zero point was taken and an accurate timer was

started. After the appropriate times, the ampoules were withdrawn, cooled in ice, brought to room temperature and opened. A 2.99 ml aliquot was pipetted and titrated with standardized 0.0142 M sodium hydroxide solution (the concentration changed after several weeks, thus necessitating restandardization) with bromothymol blue as indicator. In each case, good first order kinetics were observed and average rate constants for duplicate runs were calculated according to equation (3).[58] The calculated infinity titer values (V_∞) were used.

$$\log\frac{V_\infty - Vo}{V_\infty - Vt} = \frac{k_1}{2.303} t \qquad (3)$$

All kinetic data are summarized in Tables 6 and 7.

Product Studies - General Procedure

Samples of the 3,5-dinitrobenzoates were solvolyzed in 70% aqueous acetone for ~10 half-lives. The work-up consisted of removal of organic solvent under reduced pressure, extraction with ether, combination of the ether layers, and washing with 2N $NaHCO_3$ and saturated NaCl solution. After drying over anhy. Na_2SO_4, the solution was concentrated under reduced pressure. Products were analyzed by the usual methods.

Solvolysis of 44e and 48e Only one product was isolated and it was identified as 4-vinylindan 50 (see results and discussion) in 84% and 86% yield from 44e and 48e respectively. Anal. Calc'd for $C_{11}H_{12}$: m/e 144.0939; found: 144.0938. Pmr and ir spectra are shown in Fig. 29 and 30.

Solvolysis of 41e and 45e Only alcohol 52 was isolated in ca. 40% yield after column chromatography (silica gel, eluant: 4% ether in hexane). Ir (CCl_4): 3615 (sharp, free OH), 3570 (sharp, intramolecularly H-bound OH), 3420 (broad, intermolecularly H-bound OH), 1632 (w, C = C), 1190 cm^{-1} (s, tert. alcohol C-O); Pmr: δ6.11 (4 lines, X part of ABX, J_{AC} = 16 Hz, J_{BC} = 12 Hz), 5.21, 5.05, 4.92 (5 lines, AB part of ABX, J_{AB} = 2 Hz), 2.3-1.0 (m, with a broad s. centered at 1.42, 15 H).

Anal.: calc'd for $C_{11}H_{18}O$ m/e, 166.1358.

Found: 166.1354.

Solvolysis of 42e and 46e The pmr and ir spectra of the crude products from either 42e or 46e showed one major product, identified as 53. Ir (CCl_4): 3600, 3460 (OH), 3030 (olefinic C - H), 1640 (C = C) cm^{-1}, and Pmr: δ5.80 (4 lines, X part of ABX, J_{AX} = 17 Hz, J_{BX} = 10 Hz), 5.65 (m, 2H), 5.12, 4.94, 4.84 and 4.78 (8 lines AB part of ABX, J_{AB} = 2 Hz), 2.5-1.2 (m, 11 H).

Solvolysis of 43e and 47e The pmr and ir spectra of the crude product indicated one major product, assigned as 54. Ir: 3620, 3600, 3410 (OH), 3020 (olefinic C -H), 1630 (C = C)$cm.^{-1}$ Pmr: δ6.02 (4 broad lines, X part of ABX J_{AX} = 17 Hz, J_{BX} = 11 Hz), 5.56 (m, 2 H), 4.98, 4.90, 4.81 and 4.62 (8 lines, AB part of ABX, J_{AB} = 2 Hz), 2.5-1.1 (m, 11 H).

Synthesis of 5-vinylindan 51 5-Bromoindan was synthesized via bromination of indan in acetic acid according to the procedure described by Bruce[59] bp. 113-115°/16 torr (lit[60] 110-112°/15 torr).

To 150 ml ether and 5.8 g (30.4 mmol) cuprous iodide was added 20 ml of 3.1 M (60.2 mmol) vinyllithium, and the mixture allowed to react for a period of 15min. under, nitrogen at -20°. The resultant dark brown mixture was stirred for an additional 20 min. at -20°. After cooling to -78°, 2.47 g (12.5 mmol) of 5-bromoindan was added dropwise. After stirring for two hr., the flask was allowed to warm to room temperature. Addition of water (50 ml) was followed by ether extraction, drying of the extract and solvent evaporation. 5-Vinylindan (0.32 g, 18%) was obtained as a colorless oil after vacuum distillation, bp 116-121°/17torr (lit[54b] 95-100°/10 torr). The pmr and ir spectra are shown in Fig. 29 and 30.

Control reactions When 0.10 g (0.282 mmol) of 44e was dissolved in 5 ml of 70% aqueous acetone containing 0.0225 g (0.282 mmol) of urea, and solvolyzed for ten half lives, 4-vinylindan was obtained in 88% yield.

When alcohol 44c, (50 mg) was heated under the solvolysis conditions (i.e., in the presence of one equiv. of 3,5-dinitrobenzoic acid) for ten half lives, 58% of starting material was recovered; no 4-vinylindan could be detected by pmr spectroscopy.

Table 6. Kinetic Data for Solvolysis of 3,5-Dinitrobenzoates in 70:30 Acetone-Water at 70°.

Compound	t, min.	Titer,[a] ml.	$10^6 K_1$,[b] sec^{-1}	
41e	0	0.02	-	
	185	0.47	21.6	
	300	0.69	19.4	
	420	0.92	22.4	
	540	1.09	21.8	
	660	1.26	22.6	
	1680	1.90	22.1	Ave. 21.7 ± 0.9
42e	0	0.03	-	
	60	0.09	5.16	
	240	0.19	4.52	
	780	0.52	5.52	
	1500	0.77	4.76	
	2220	1.14	5.60	
	2940	1.34	5.52	Ave. 5.18 ± 0.44
43e	0	0.02	-	
	360	0.34	7.67[c]	

[a]Average values for two runs.

[b]The calculated infinity (V_∞ = 2.12 ml) was utilized.

[c]Discarded value is not included in the average.

Table 6 (Continued)

Compound	t, min	Titer,[a] ml.	10^6K,[b] sec^{-1}	
43e	1080	0.94	8.90	
	1440	1.09	8.25	
	2580	1.53	8.20	
	3300	1.74	8.60	Ave. 8.49 ± 0.26
44e	0	0.04	-	
	1.5	0.54	201	
	30	0.80	202	
	40	0.98	220	
	50	1.08	200	
	60	1.20	202	
	180	1.88	191	Ave. 203 ± 7
45e	0	0.02	-	
	180	0.29	10.2	
	300	0.42	10.7	
	540	0.64	10.0	
	720	0.81	10.4	
	840	0.91	10.4	
	1680	1.40	10.3	Ave. 10.4 ± 0.2

Table 6 (Continued)

Compound	t, min.	Titer,[a] ml.	10^6K,[b] sec^{-1}	
46e	0	0.03	-	
	240	0.14	3.02	
	960	0.42	3.64	
	1680	0.60	3.04	
	2940	0.84	2.70	
	4080	1.08	2.79	Ave. 3.04 ± 0.30
47e	0	0.02	-	
	1080	0.52	4.16	
	2580	1.03	4.25[c]	
	3300	1.16	3.96	
	4380	1.26	3.40	
	7200	1.68	3.60	Ave. 3.78 ± 0.27
48e	0	0.02	-	
	300	0.22	2.50	
	1020	0.42	2.62	
	1680	0.60	2.70	
	2940	0.82	2.38	
	4080	1.03	2.44	
	10080	1.89	3.60[c]	Ave. 2.53 ± 0.13

Table 7. Kinetic Data for Solvolysis of 3,5-Dinitrobenzoates in 70:30 Acetone-Water at 100°.

Compound	t, min.	Titer ml.	$10^6 K$, sec^{-1}	
41e	0	0.02	-	
	25	1.15	450	
	50	1.80	490	Ave. 470 ± 20
42e	0	0.02	-	
	120	1.50	143	
	180	1.85	147	Ave. 145 ± 2
43e	0	0.02	-	
	50	1.12	216	
	120	1.80	206	Ave. 211 ± 5
44e	0	0.02	-	
	2.5	1.26	5150	
	5.0	1.78	4800	Ave. 4980 ± 170
45e	0	0.02	-	
	50	1.16	228	
	100	1.75	232	Ave. 230 ± 2
46e	0	0.02	-	
	120	0.88	65.3	
	180	1.20	67.0	Ave. 66.2 ± 0.8

Table 7 (Continued)

Compound	t, min.	Titer ml.	10^6K, sec^{-1}	
47e	0	0.02	-	
	120	1.34	118	
	180	1.71	124	Ave. 121 ± 3
48e	0	0.02	-	
	120	0.84	60.6	
	180	1.05	56.3	Ave. 58.5 ± 2.2

PART II:

SOLVOLYTIC FORMATION OF BRIDGEHEAD OLEFINS

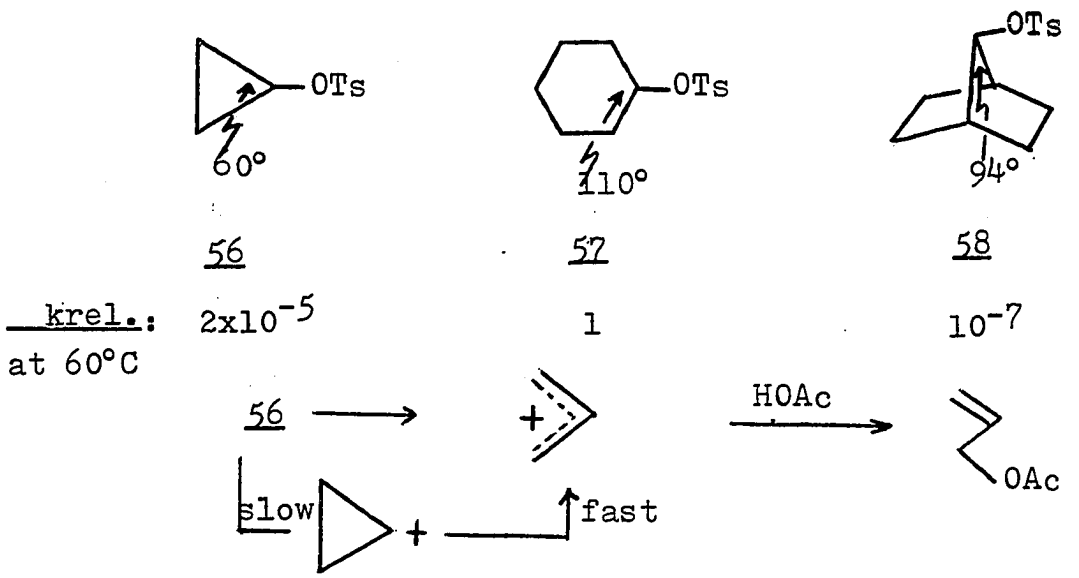
INTRODUCTION

Cyclopropyl Cation Problem

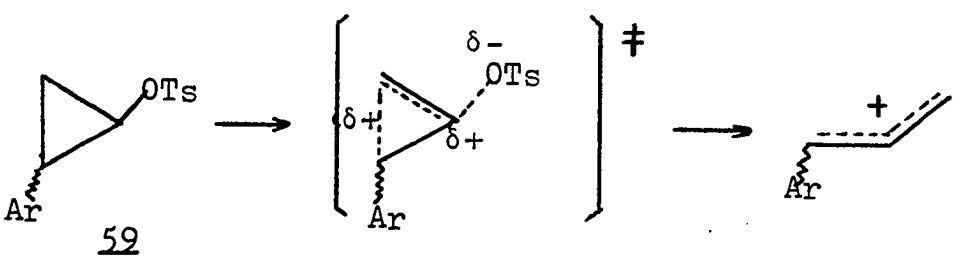
In 1951, Roberts and Chambers[61] first reported the solvolysis of cyclopropyl derivatives wherein they showed that the acetolysis of cyclopropyl tosylate (56) proceeded some 10^5 times slower than the acetolysis of cyclohexyl tosylate (57), and gave allyl acetate as the only isolable product. Based on the kinetic data, the authors proposed a two-step mechanism: slow ionization to the cyclopropyl cation, a process involving an unfavorable increase in bond angle strain at the cation center, followed by fast ring opening to the allyl cation. This conclusion was later questioned by Schleyer and Nicholas[62] who noted that the acetolysis rate of 56 was 100 times faster than that of 7-norbornyl tosylate (58) despite larger bond angles at the cationic center of 58.

Foote[63] and Schleyer[64] have published more quantitative analyses of the solvolysis of 56 which showed that the rate was actually enhanced; they suggested that ionization and ring opening were concerted.

The question of whether ring openings of cyclopropyl systems involve discrete cyclopropyl cations or concerted ionizations to allyl cations has subsequently attracted much attention.



Depuy and coworkers[65] discovered that either cis or trans-2-arylcyclopropyl tosylate (59) was more readily solvolyzed than the parent compound 56. To account for these results the authors postulated that the cyclopropyl cation was not an intermediate in these solvolyses, but that ring opening occurred simultaneously with loss of tosylate, leading to a partial positive charge on the benzyl carbon atom in the transition state.



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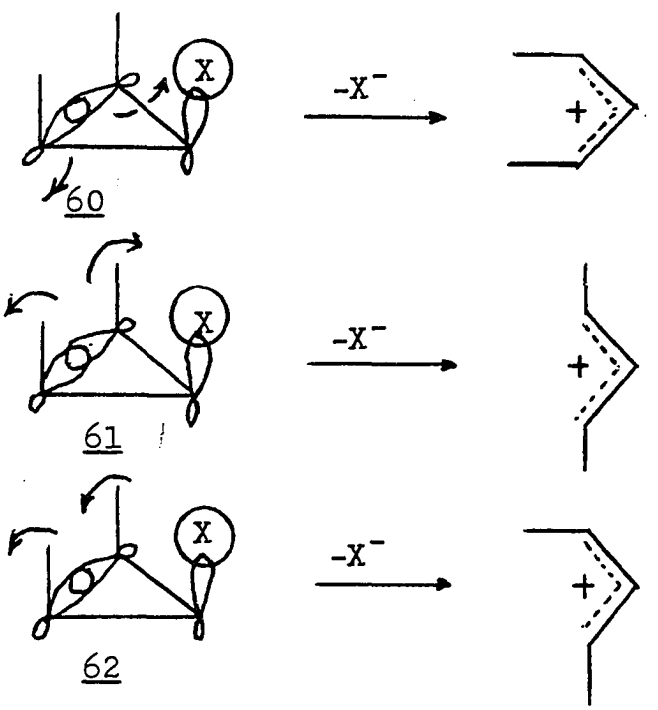
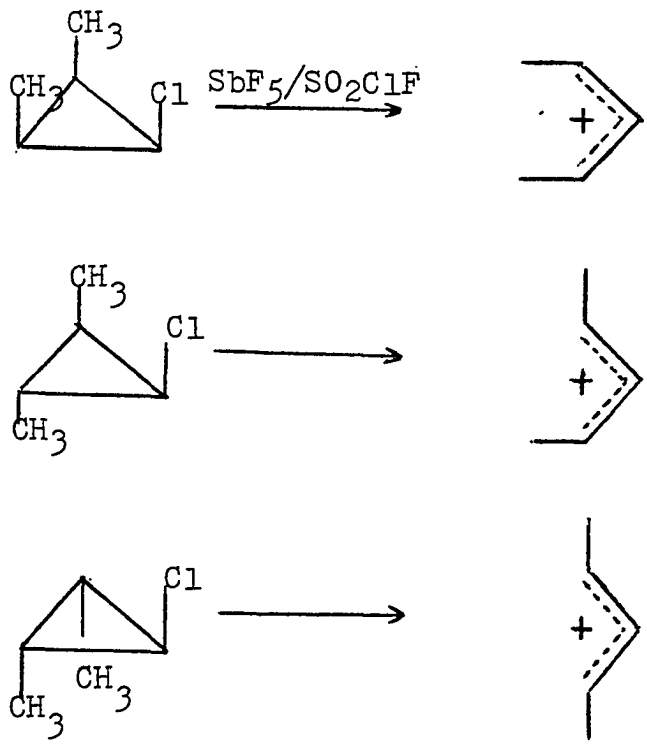
The rearrangement of a cyclopropyl cation to an allyl cation can be treated as an electrocyclic ring opening, subject to orbital symmetry rules,[66] and is thus predicted to be a stereospecific disrotatory process(60 and 61)rather than a conrotatory process(62). Extended Hückel calculations[67] by Woodward and Hoffmann favor mode 60, in which substituents cis to the leaving group rotate inwardly. These predictions have been confirmed by other calculations and have received widespread experimental support based chiefly on indirect kinetic evidence from the solvolyses and thermolyses of cyclopropyl systems.[68]

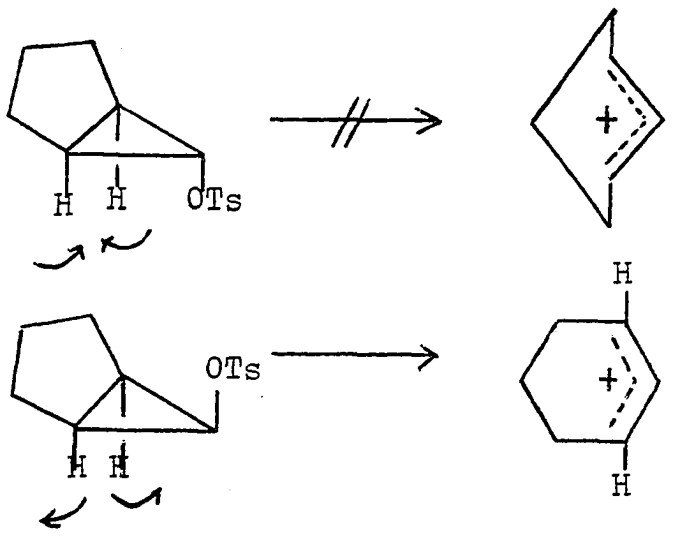


Furthermore, direct and complete stereochemical verification of the prediction was obtained through the study of the isomeric 2,3-dimethylcyclopropyl chlorides in strong acid media (SbF_5, SO_2ClF at -100°).[69] On the basis of the pmr spectra, the steroisomeric allyl cations were observed.

For β-substituted cyclopropyl derivatives, the rates of solvolysis for the trans isomers are ca. 4.5×10^3 times



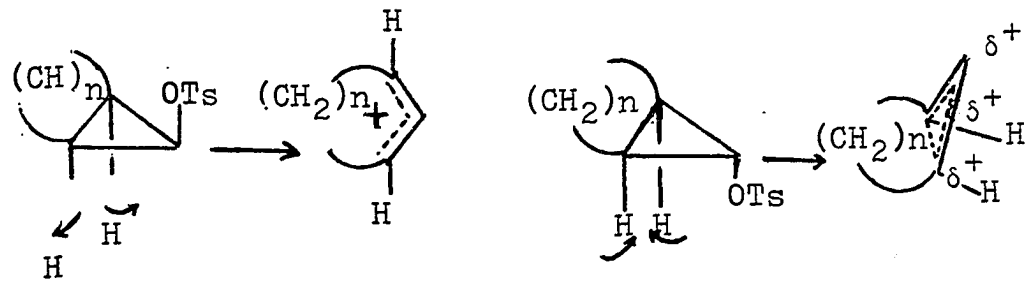
faster than those for the all cis isomers.[70] However, the order of reactivity can be reversed by simply joining the two substituents to form a ring.[71] If the ring is small, a trans, trans allylic cation can not easily be accommodated, but a cis, cis cation can.



Ring size dependence on the stability of bicyclic cyclopropyl tosylates has been studied more quantitatively by Schöllkopf, et al.[71] A series of endo- and exo- bicyclo-[n. 1. 0] alkyl tosylates gave the relative acetolysis rates shown in Table 8.

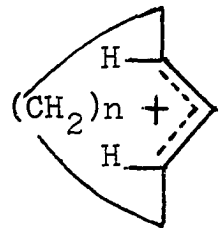
The authors suggested that the rate decrease with increasing ring size in the endo series might indeed be a result of decreasing stability of the cis-cycloalkenyl cation intermediates, 63. As judged from Dreiding models, the cyclohexenyl cation (n = 3 in 63) is almost strain-free, while the cycloheptenyl and cyclooctenyl cations (n = 4 and 5, respectively, in 63) exhibit both torsional and trans-annular strain. Wiberg and Nakahira's[72] experimental results for the solvolysis of cis-cycloalkenyl allylic systems are in accord with this reasoning. The cyclonon cyclononenyl cation (n = 6 in 63)

Table 8. Relative Acetolysis Constants of endo- and exo-Bicyclo[n.1.0]alkyl p-toluenesulfonates.



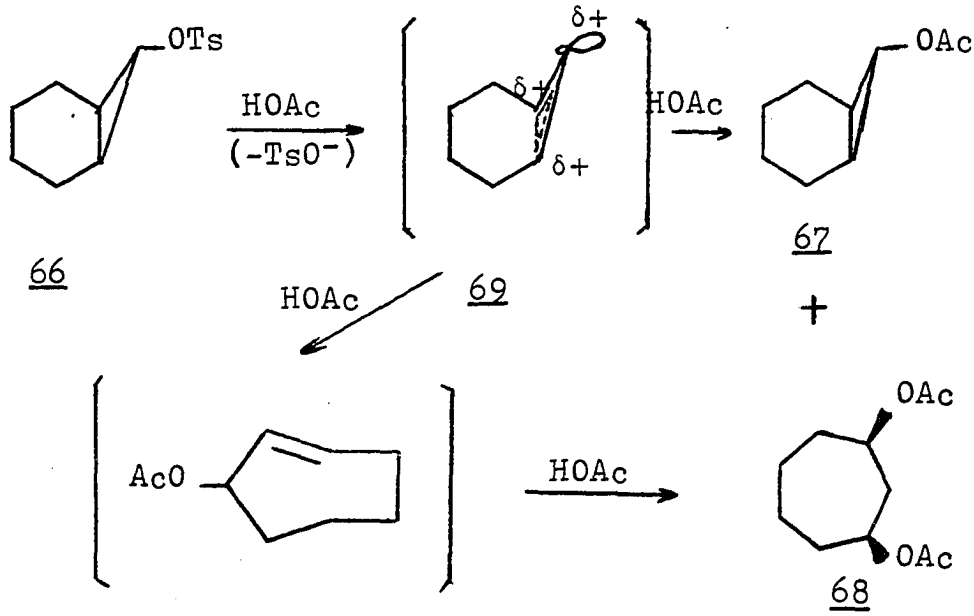
n	krel at 100°	n	krel at 100°
3	25,000	3	0.01
4	62	4	1.7
5	3.1	5	2,500
6	3.5	6	10,000

is, according to models, more flexible than its 7- and 8-membered homologs. The opposite order of reactivity in the exo-series was attributed to the increasing ease in forming the trans, trans-allylic cations as the ring size increased. However, intermediates as simplistic as 65 were ruled out, since these give strain-free Dreiding models only beyond the 12 and 13-membered rings.

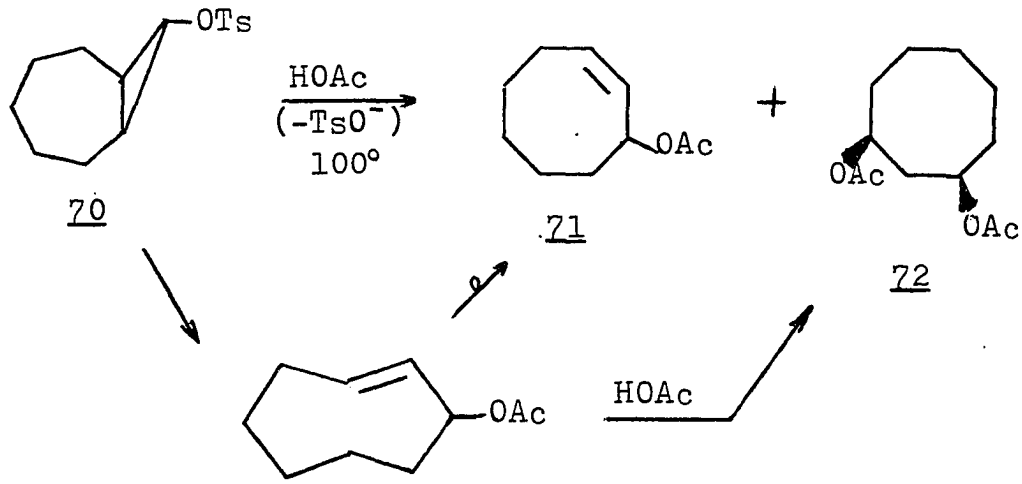


65

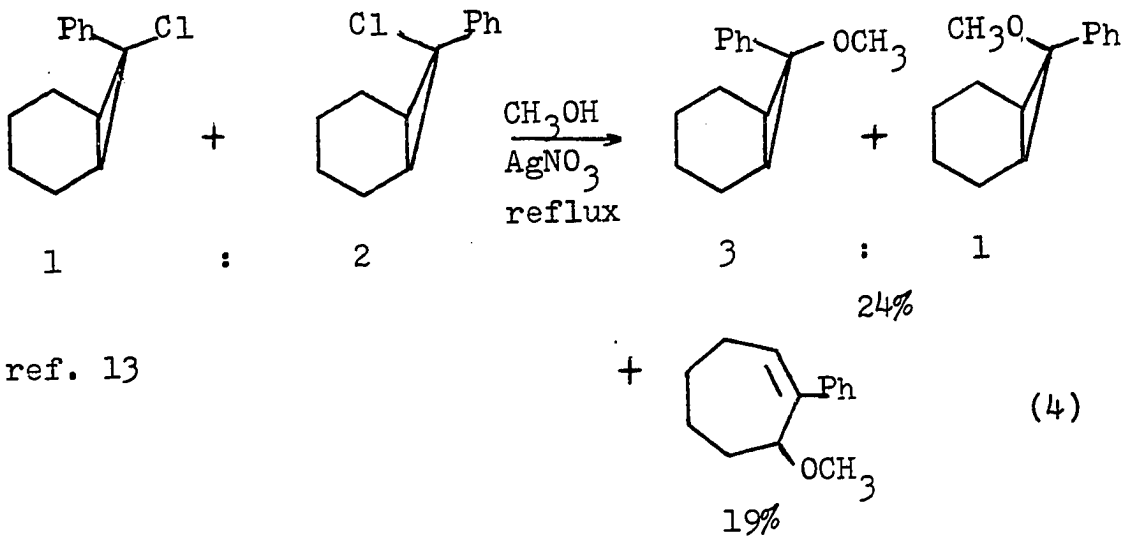
Schöllkopf, et al.[71] -- therefore proposed that the intermediates were somewhere between a cyclopropyl and an allyl cation, i.e. the partially-opened cyclopropyl cation (see 64), wherein positive charge was distributed among the three cyclopropyl carbons, with the cyclopropyl character increasing with decreasing n. For instance, the solvolysis of exo-7-norcaryl tosylate (66) (n = 4) results in an equal mixture of 67 and 68, which can be explained on the basis of cation 69.



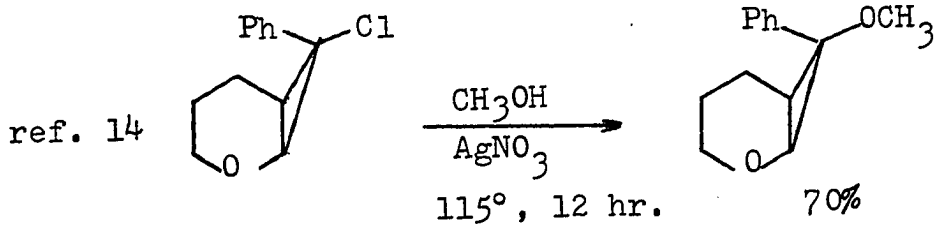
The high stereoselectivity of the formation of 67 suggests that the orbital on C-7 may have a pyramidal configuration.[73] However, when n > 4 in the exo-series,[71] e.g., 70, the allyl character of the cation predominates, leading only to monocyclic products 71 and 72 (the ratio of 71 to 72 is 2).



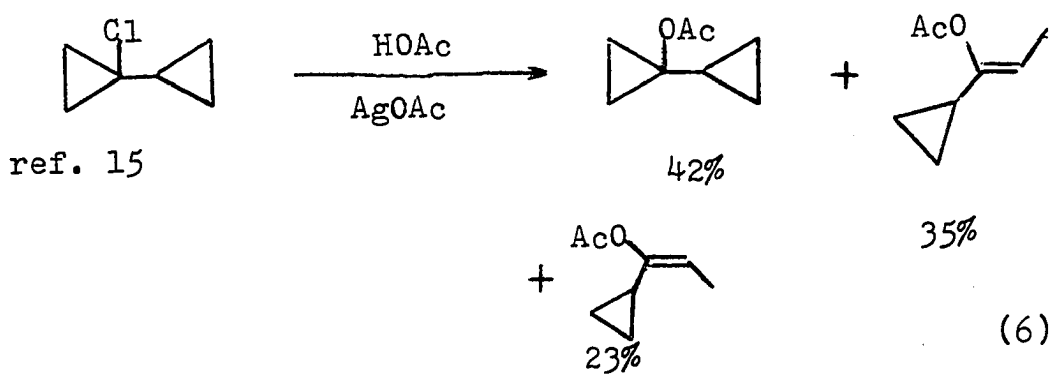
In any event, when the cyclopropyl derivatives possess a substituent (e.g., cyclopropyl[74], phenyl[75, 76, 77] group) which would stabilize a positive charge at the site of the leaving group, primarily products without ring opening result. Evidence has been presented which is consistent with the formation of a classical cyclopropyl cation intermediate in these cases. The results are summarized in equations 4, 5 and 6.


Ph
Cl
Cl
Ph
CH3OH
AgNO3
reflux
Ph
OCH3
CH3O
Ph
1 : 2
3 : 1
24%
ref. 13
Ph
OCH3
19%

(4)


ref. 14
Ph
Cl
O
CH3OH
AgNO3
115°, 12 hr.
Ph
OCH3
O
70%

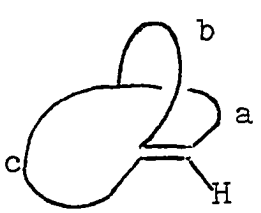
(5)


Cl
HOAc
AgOAc
OAc
AcO
ref. 15
42%
35%
AcO
23%

(6)

Bridgehead Olefins

During the past few years, bridgehead olefins have attracted rapidly increasing attention. Several excellent reviews have been published in this area.[78-80] An early attempt to define the limits of Bredt's rule[81] was made by Fawcett,[82] who proposed that compounds with bridgehead double bonds should be isolable for $S \geq 9$, and that compounds with bridgehead double bonds could be transient intermediates for $S \geq 7$, where S was defined as the sum of the number of carbon (or other) atoms in the bridges of a bicyclic system. Another approach, suggested by Wiseman[83] in 1967, noted that a bridgehead double bond in any bicyclic alkene 73 is endocyclic to two of the rings and must lie trans within one of these. He thus postulated that the strain of a bridgehead alkene is closely related to the strain of the corresponding trans-cycloalkene. On this basis, he forecast that bridgehead alkenes incorporating a trans-cycloheptene might be isolable and would be detectable as transient intermediates.



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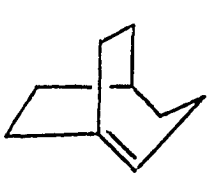

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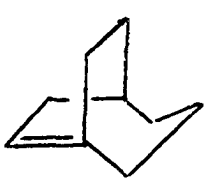
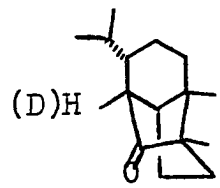


75

Wiseman and Chong[84] reported that they were able to synthesize a mixture of the bicyclononenes 74 and 75 (S = 7), although they dimerized after being isolated. In addition, the base-catalyzed H/D exchange at the bridgeheads of 76[85] and 77[86] implied the existence of enolates related to 78. Recently, Nickon and coworkers[87] reported a remarkably easy bridgehead exchange at C-3 in brendan-2-one, 79, in which the corresponding anti-Bredt enolate also contains a transoid olefin in a seven-membered ring.



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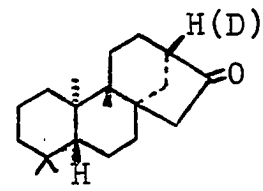

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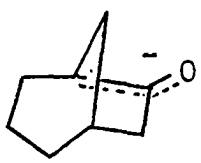
However, so far there is no firm data for the existence of trans-cyclohexene. Consequently, the detection of related bridgehead alkenes is significant. The first example of this type, reported by Campbell, et al.,[88] in 1965, involved the elimination of LiF from 80 to give perfluorinated 1-norbornene, 81, which was trapped by furan to give two stereo isomeric adducts. The parent hydrocarbon of 81 was shown to exist transiently by Keese and Krebs,[89, 90] who treated 1,2-dihalonorbornanes (82) with n-butyllithium in the presence of furan to afford two cycloadducts.

In a similar study, adamantene, 83, was presumed to be the transient intermediate in the dehalogenation[91, 92, 93] of 84 and thermally induced fragmentation[94] of 85 in order to account for the formation of dimers and cycloadducts.



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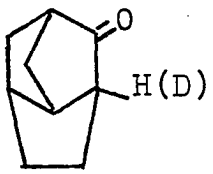

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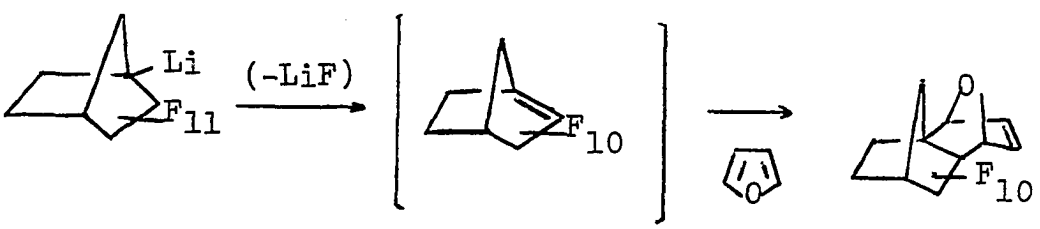
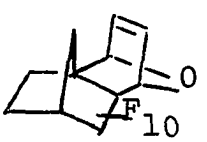
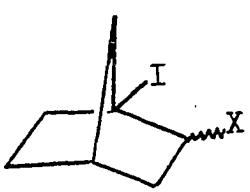
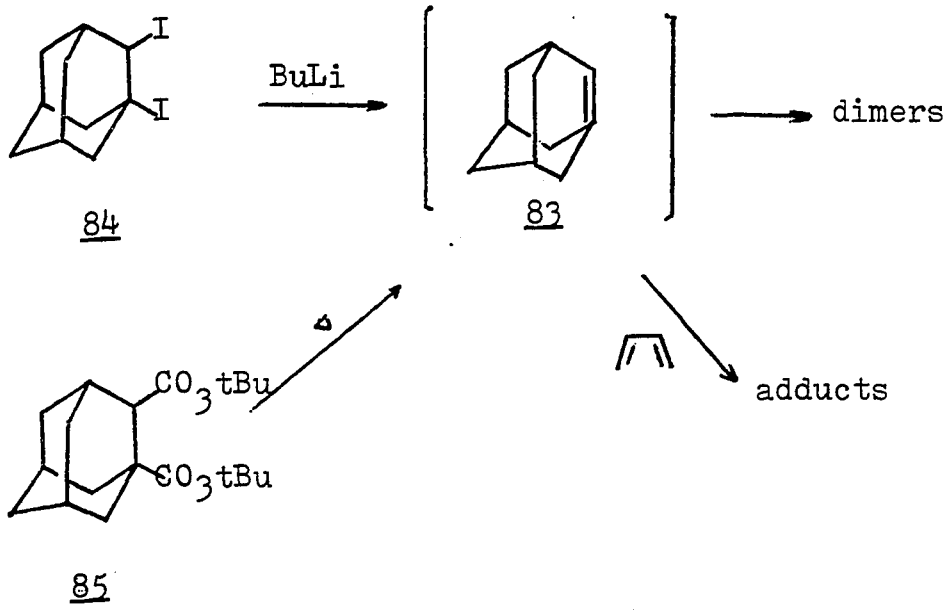


80 81 +



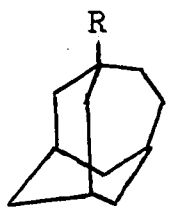


82 X=Cl, Br

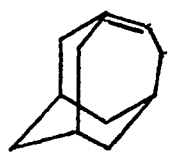


84 83 85

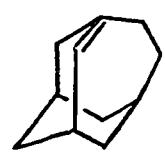
The transient generation of homoadamantene during the pyrolysis of 86 was used to rationalize the ca. 10% yield of a mixture of dimers.[95] Kovacic and Adams suggested that either the reaction proceeded preferentially via 87 or else that 88 rapidly rearranged to 87.



86



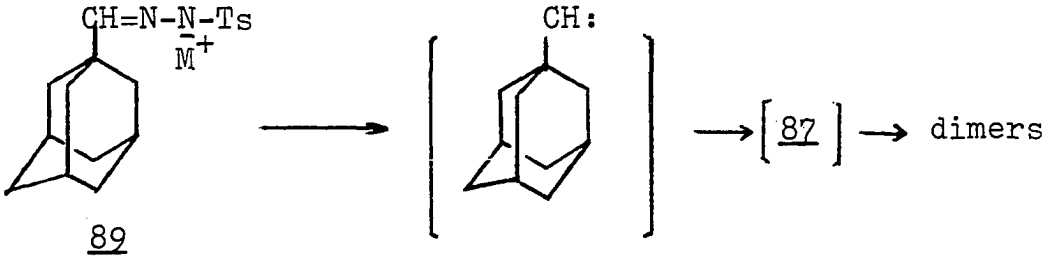
87



88

R = $N(CH_3)_3^+OH^-$
or $NO(CH_3)_2$

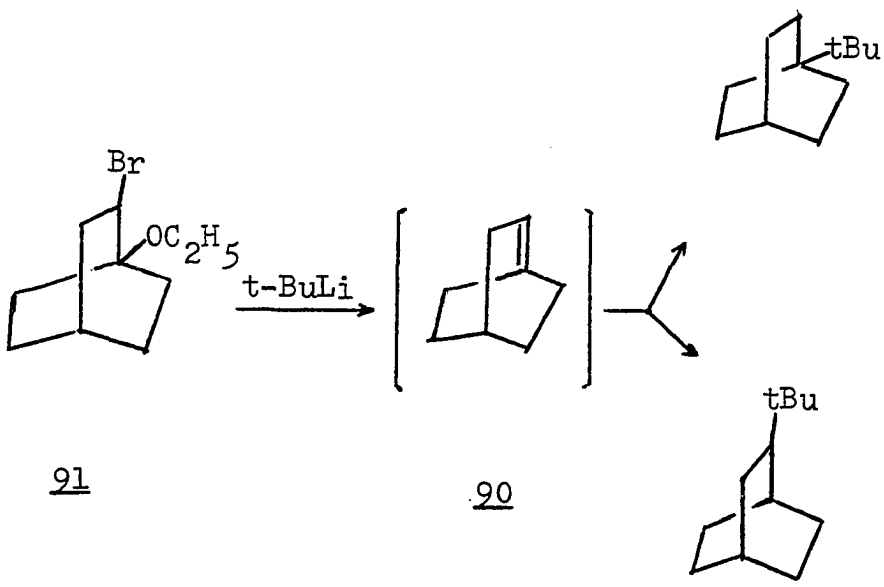
In connection with homoadamantene, Farcasiu and co-workers[96] reported their results involving carbene ring expansion as a source of anti-Bredt olefins. Pyrolysis of 89 did not give unsaturated compounds but rather afforded five hydrocarbons (22% yield) of which three were regarded as direct dimerization products of 87.



89

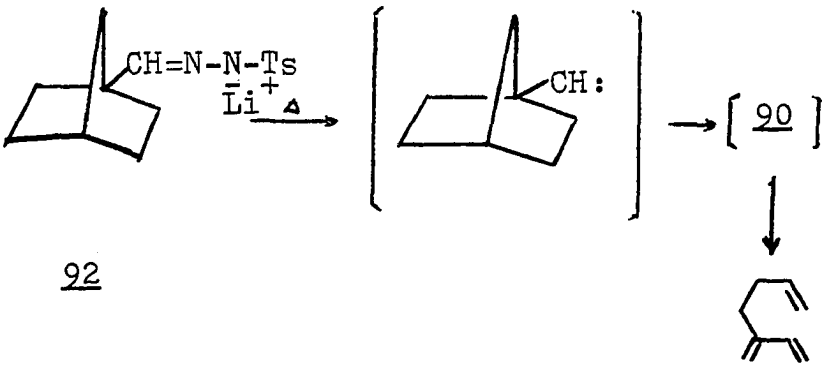
M=Li or Na

Recently, bicyclo[2.2.2]oct-1-ene, 90, was proposed as the transient intermediate to account for the results obtained from the reaction of 91 with an excess of t-butyllithium.[97]



91 90

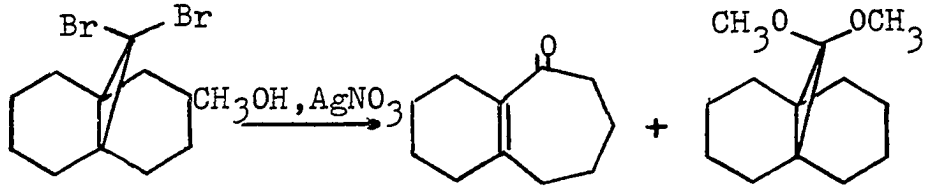
The pyrolysis of the dried tosylhydrazone salt 92 led to 3-methylene-1, 6-heptadiene.[98] On the basis of a deuterium labeling experiment, the formation of the diene could be explained as arising via a retro Diels-Alder cleavage of 90.



92

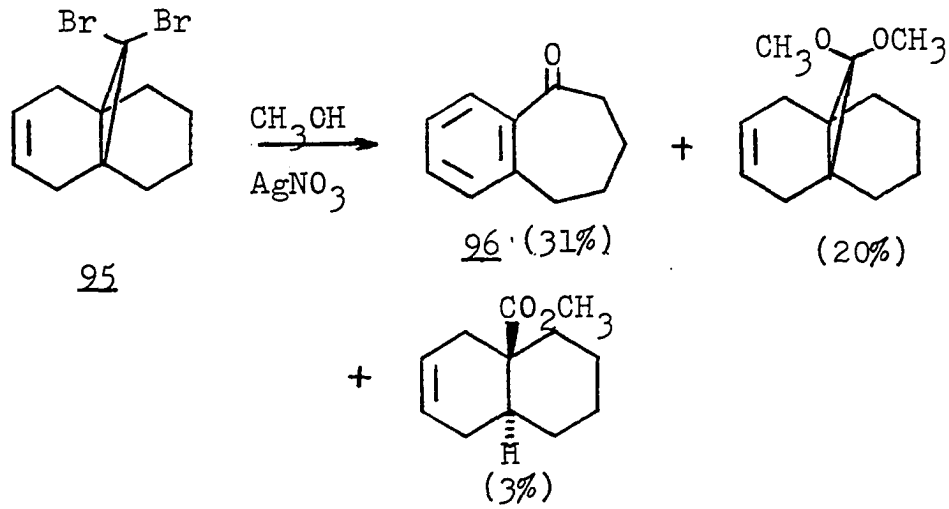
Propellanic Cyclopropyl Cations

Ledlie[99, 100, 101] has studied the Ag^+-assisted methanolysis of 93, in which the dihalocyclopropane unit is constrained in a propellane structure, making normal disrotatory ring opening to a fully opened allyl cation seem prohibitive. With this in mind, the author rationalized the major product, 94, as having arisen via a Wagner-Meerwein rearrangement of the initially formed cationic species (see Discussion for details).

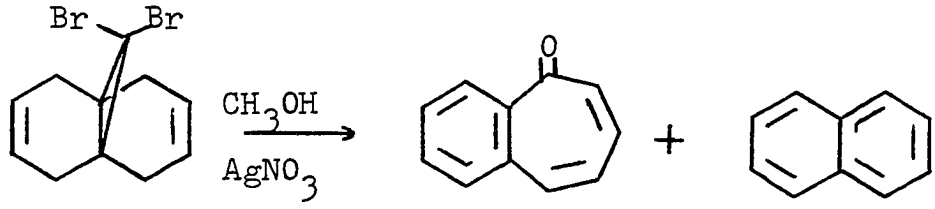


93 94 43% 22%

In addition, comparable products were also isolated by Ledlie et al.[101] from the solvolysis of unsaturated systems 95 and 97.

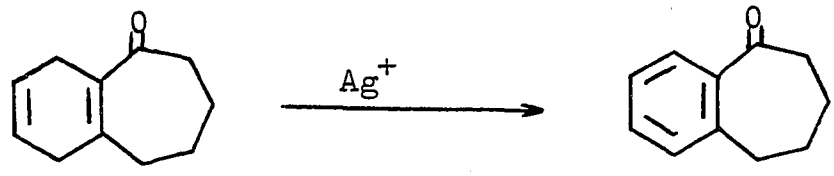


95 96 (31%) (20%) (3%)

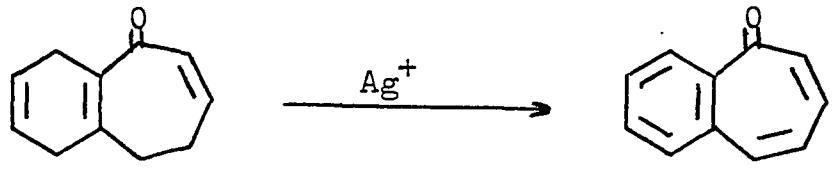


97 98 (2-5%) (2-5%)

Aromatization of diene 99 and 100 by silver ion, as explained by these authors, resulted in the formation of the corresponding ketones 96 and 98.



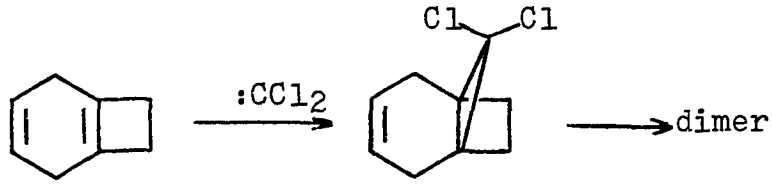
99 96



100 98

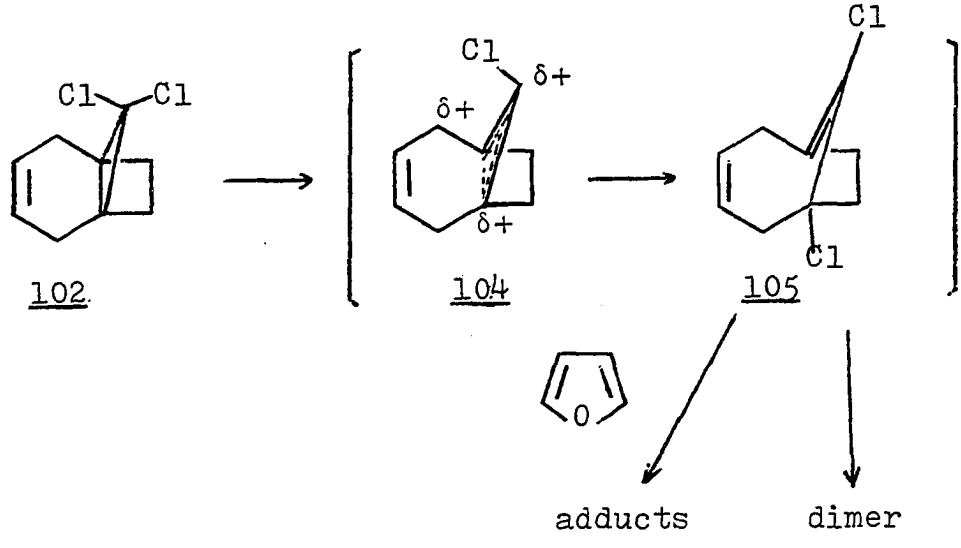
However, Warner, et al.[102] recently found that when dichloro carbene was added to 101 the initial adduct, 102 was thermally labile in dipolar aprotic solvents. The oil (102) obtained after evaporation of the solvent underwent an exothermic reaction upon warming to room temperature. A white, crystalline material 103 (ca. 80% isolated) was deposited in the flask. Mass spectrometry indicated a formula of $C_{18}H_{20}Cl_4$, i.e., a dimer of 102.

An X-ray analysis of the crystalline dimer showed that only one stereoisomer was formed, although there are eleven

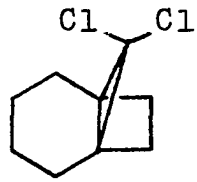


101 102 103

possible stereoisomeric structures for the dimer of 102. Upon dissolving cold 102 in furan, and warming the solution to room temperature, there resulted a mixture of 1:1 adducts. Therefore, Warner and Larose concluded that the formation of dimer 103 occurred via the intermediacy of a partially opened cyclopropyl cation, 104 wich collapsed to transient species 105, which has a bridgehead double bond in a seven-membered ring-the first example of a bridgehead double bond in a one-carbon bridge in this ring system.

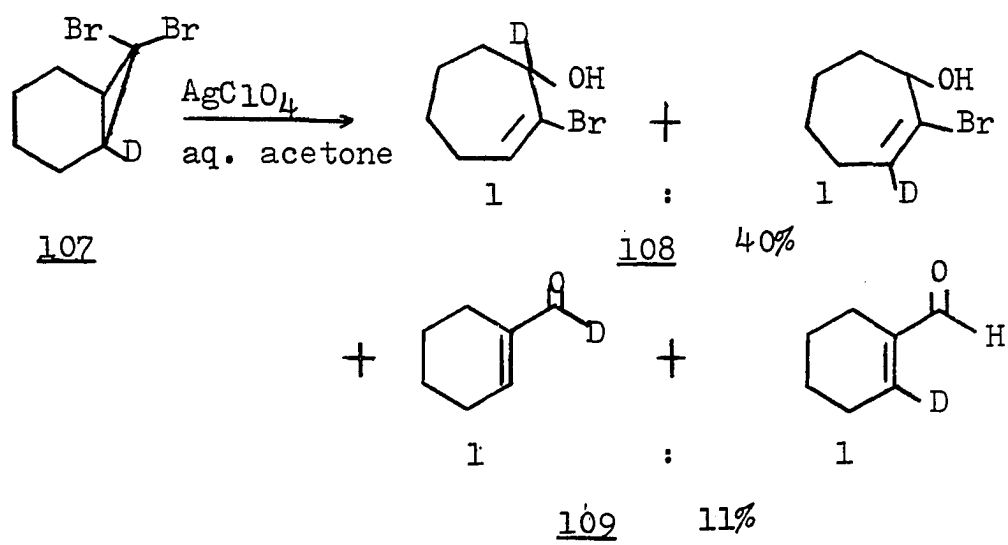


The effect of the double bond of 102 on the dimerization was also investigated.[103] It was observed that the saturated analog 106 was even more labile than 102, i.e., 106 was more reactive toward ionization and ring opening than was 102.

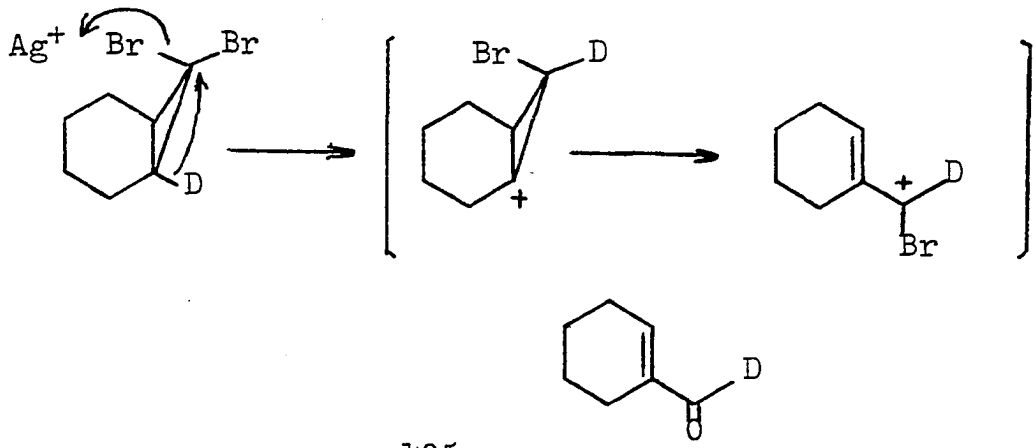


106

In an independent study of the solvolysis of 93 in aqueous acetone in the presence of silver perchlorate at 20°, Reese and Stebles[104] reported that 94 was the only isolable product (62% yield). These authors suggested the same mechanism as did Ledlie. An accompanying hydrolytic study of 1-deuterio-7,7-dibromobicyclo[4.1.0] heptane, 107, wherein pmr spectroscopy revealed that the deuterium atoms in the products (108 and 109) were equally distributed between two positions, led to the postulation of a hydride shift mechanism, as follows:

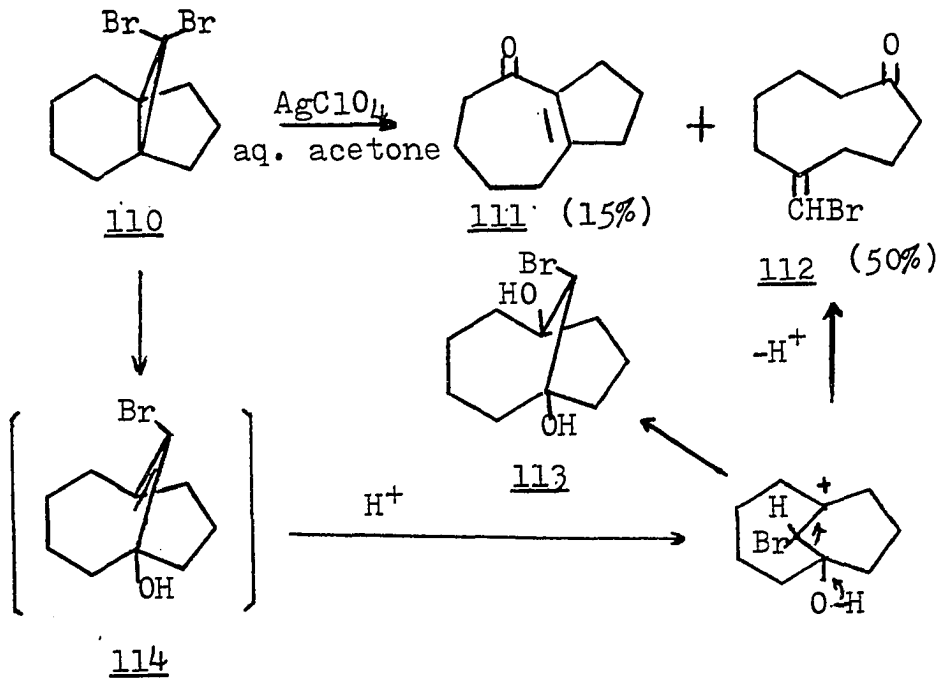


107 108 109

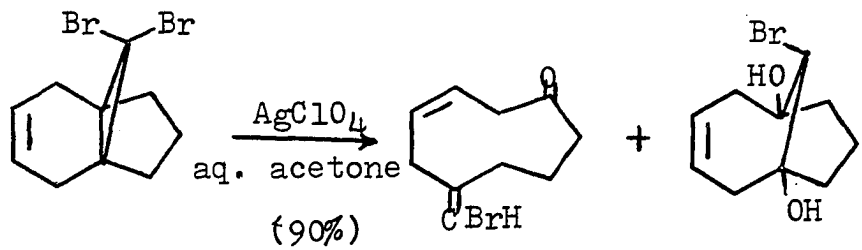


In a similar study,[105] when compound 110 was subjected to silver-assisted solvolysis in aqueous acetone(5:95, v/v), the products were 111, 112 and some unidentified products, one of which was later shown by Warner, et al.,[106] to be diol 113. Since only the formation of 111 could be explained by the Wagner-Meerwein rearrangement mechanism, Reese[105] postulated that 112 arose from bridgehead olefin 114 via protonation and fragmentation. Indeed, the isolation of diol 113 further supported the existence of 114.[106]

The solvolysis of the unsaturated analog of 110, 33 was also examined by two groups. Ketone 115 was the only product identified by Reese and Stebles,[105] who felt that 115 and 112 were both pure geometrical isomers on the basis of the sharpness of the bromomethylene proton signals in the pmr spectra. Further pmr studies of 112, utilizing shift reagents, confirmed this assertion.[107] However, Warner and coworkers[106] found that a diol, 116, was isolated in 44% yield



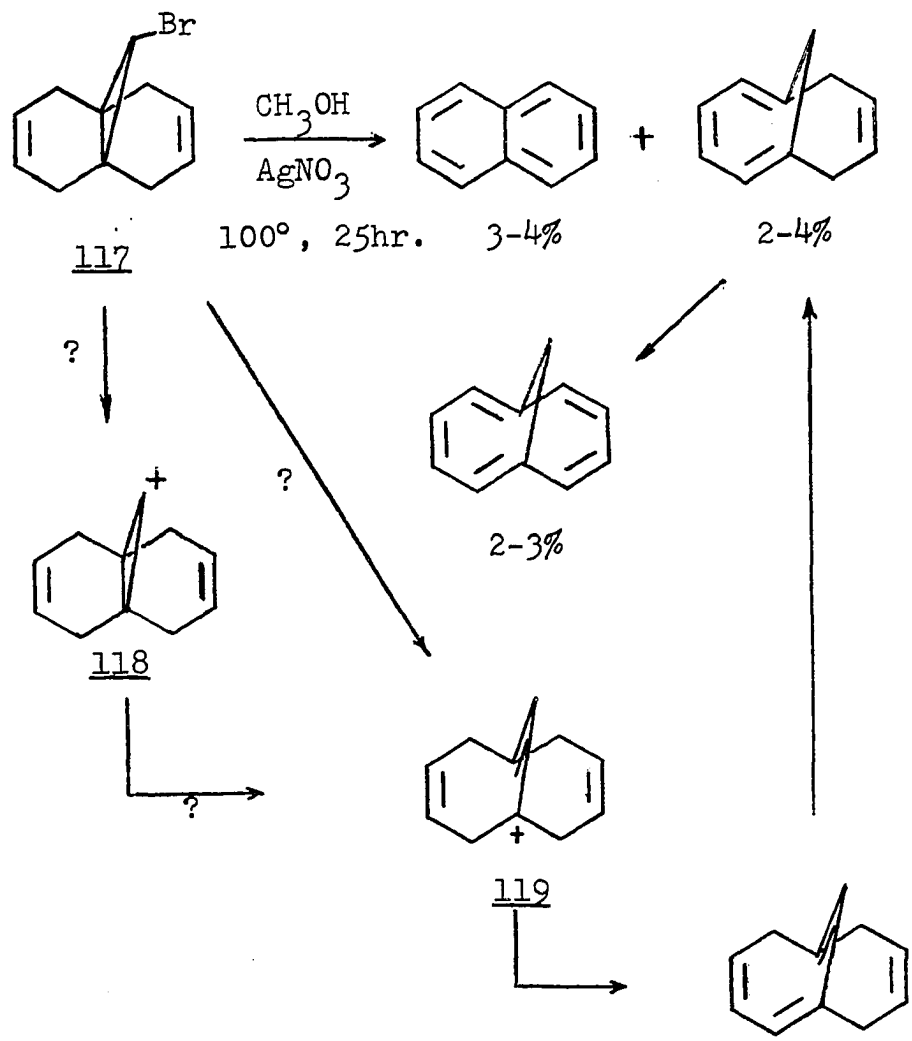
in the Ag^+-assisted solvolysis of 33 in 90% aqueous acetone, along with 115 in 27% yield. A single crystal X-ray analysis of diol 116 showed that stereospecific protonation had occurred.



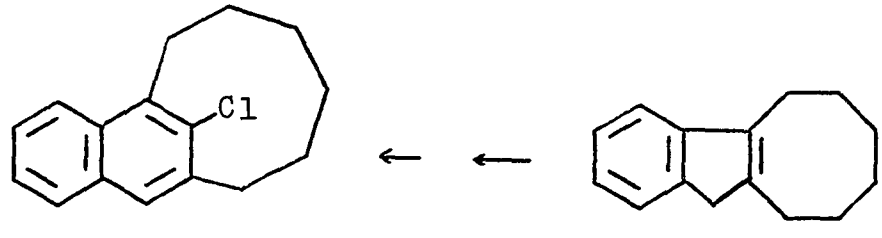
33 115 116

27% 44%

More recently, Ledlie and Bowers[108] investigated the methanolysis of 117 in the presence of silver nitrate at 100° and found that three volatile products were obtained in ca. 10% yield. The authors proposed the following pathway for the formation of the volatile products. The intermediacy of 118 or 119 is at best problematical.

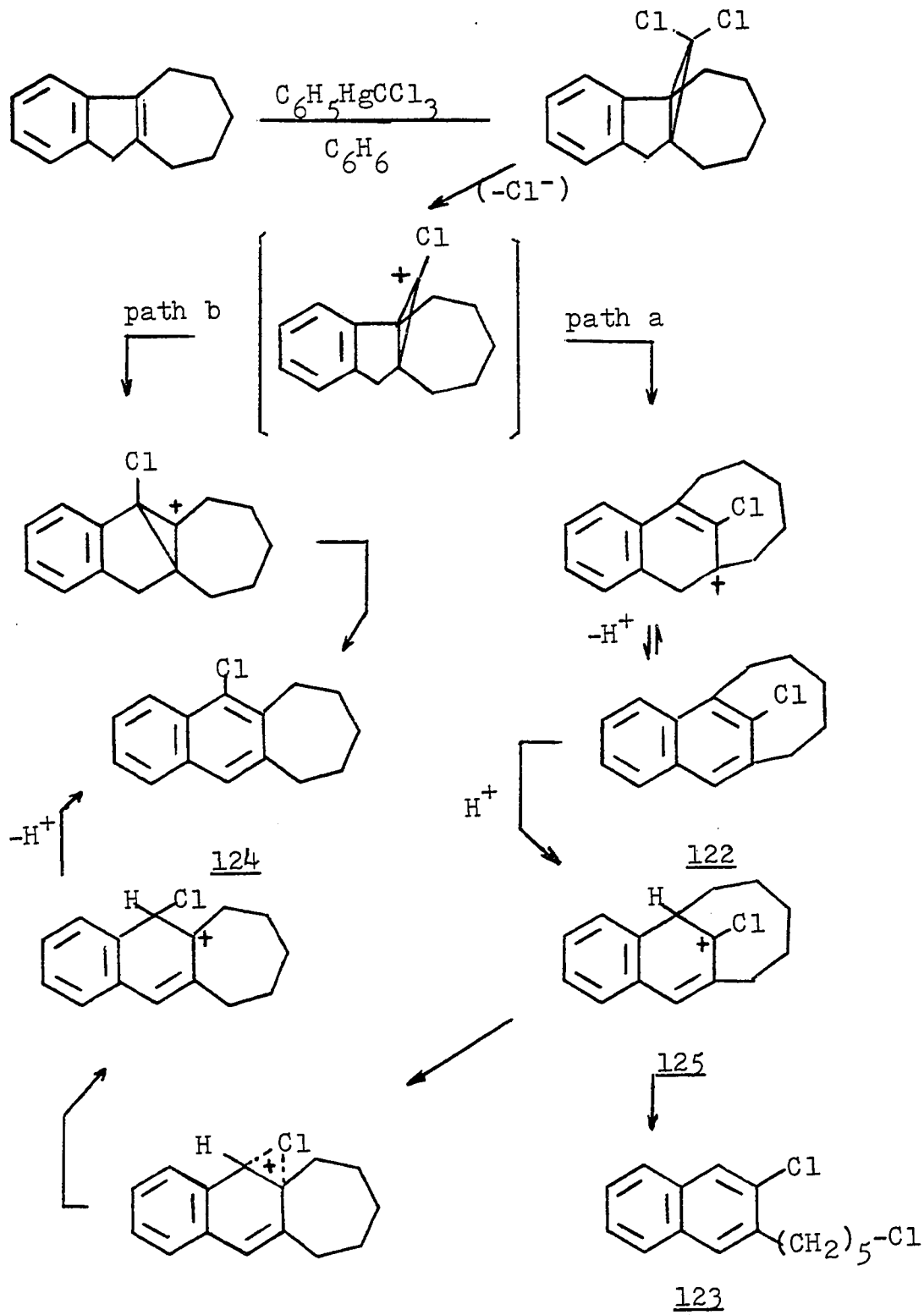


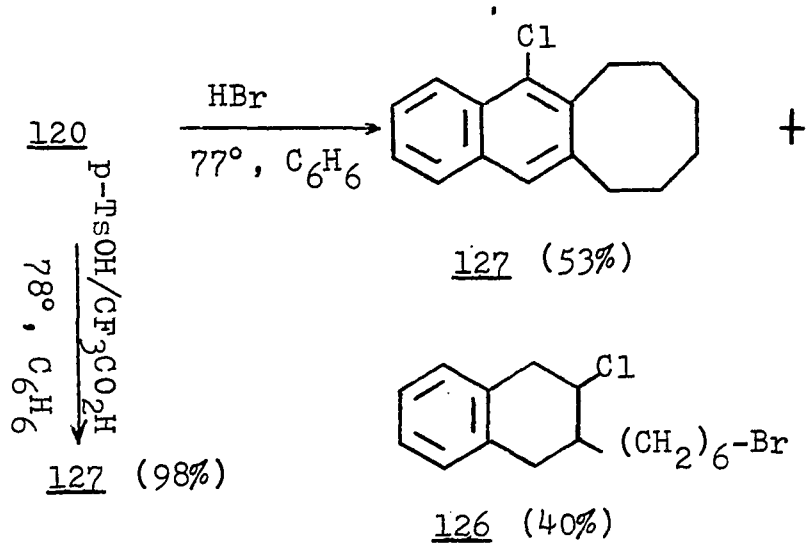
The synthesis of metacyclophane 120 was achieved by treating 121 with phenyl (trichloro methyl) mercury in hot benzene (74% yield).[109] On the other hand, its lower homolog, 122. was not obtained utilizing the same procedure. Instead, a mixture of 123 (8.4% yield) and 124 (66% yield) was produced.[110] Parham considered two pathways for formation of 124: (1) a route involving a bridged allylic ion, which also gave rise to 123 (path a in Scheme 5) and (6) a separate route to 124 involving a phenyl migration (path b in Scheme 5 . Evidence mitigating against path b came from the authors' demonstration that 120 reacted readily with HBr in hot benzene to give a mixture of 126 (40% yield) and 127 (53% yield). Additionally, when 120 was heated in benzene containing a mixture of p-toluenesulfonic acid and trifluoro-acetic acid, 127 was produced quantitatively.[110]



120 121

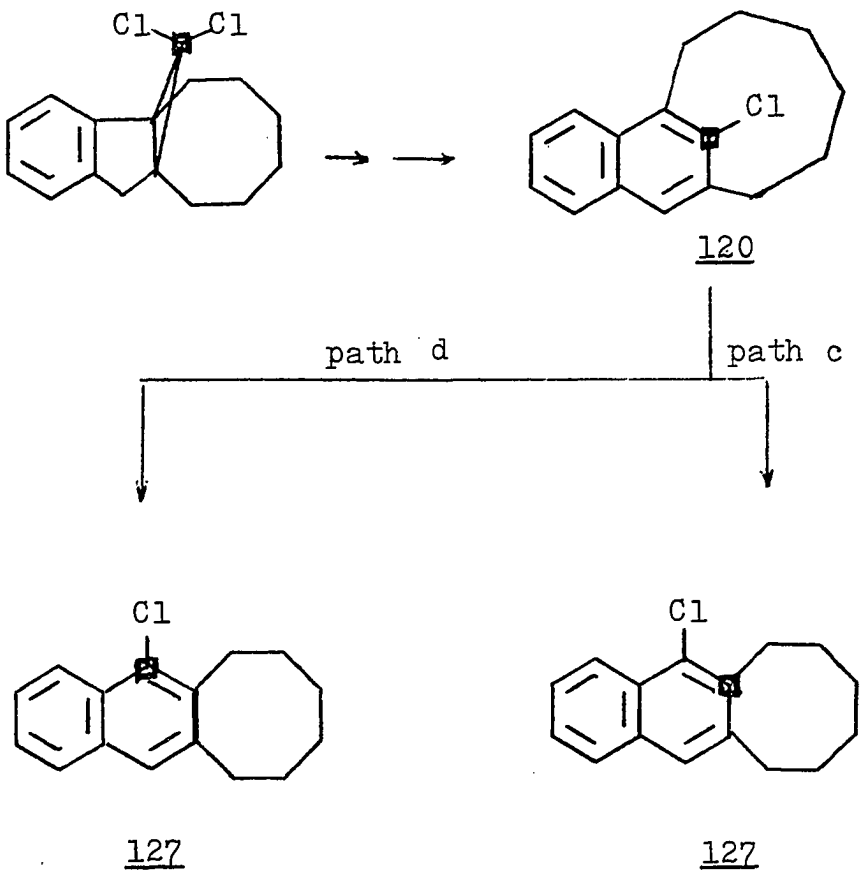
Scheme 5


Cl
Cl
$C_6H_5HgCCl_3$
C_6H_6
(-Cl⁻)
Cl
path b
path a
Cl
Cl
$-H^+$
Cl
Cl
H^+
$-H^+$
124
122
H
Cl
H
Cl
125
H
Cl
Cl
$(CH_2)_5$-Cl
123



In order to further evaluate the pathway for the formation of 127 and 126 ^{13}C-labeling experiments[110] were carried out, the results of which showed that the formation of 127 does not involve phenyl migration. The cleavage and rearrangement products, 123 and 124, are apparently derived from the same intermediate (122) (see Scheme 6).

Scheme 6

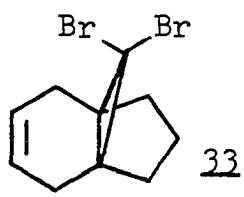


127 127

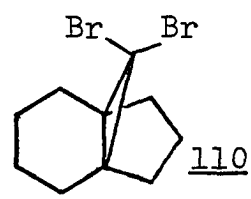
RESULTS AND DISCUSSION

Synthesis

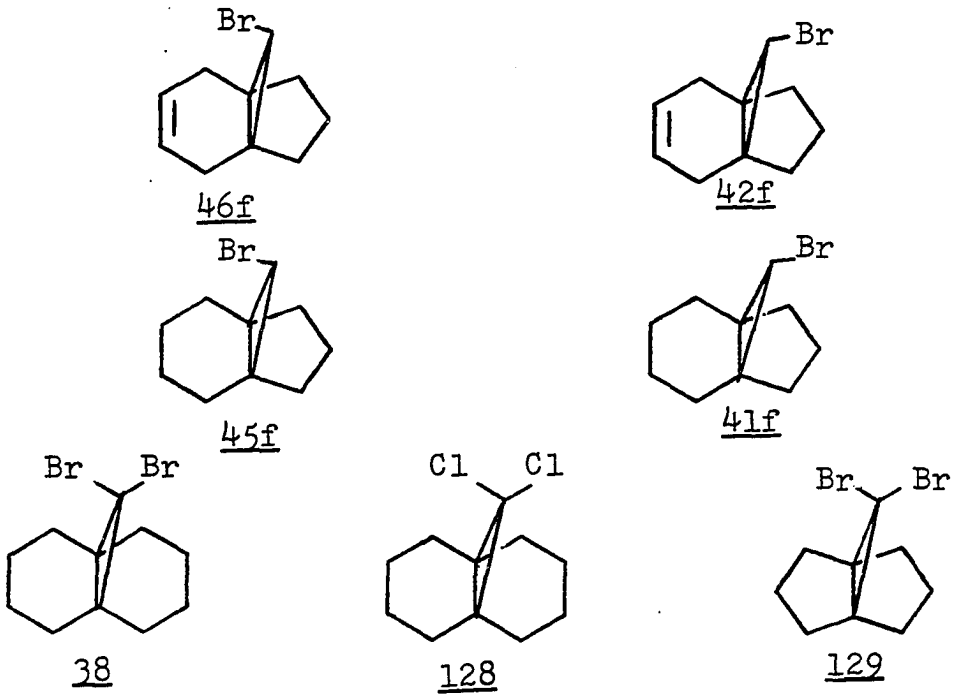
The compounds studies were either already known (33,[7] 110,[105] 93,[8] and 129[111]) or readily prepared via tri-n-butyltin hydride reduction[112] of dibromide derivative 33 for monobromides 46f, 42f, 45f and 41f). The latter two were generated by catalytic hydrogenation of 46f and 42f in ether. Separation of epimers 46f and 42f was accomplished by column chromatography. The stereochemistry or 46f and 42f was assigned on the basis of (i) similar pmr signals for the allylic protons of 33 and 46f which are distinctly different from those of 42f; (ii) lithiation of 46f with n-BuLi followed by retentive deuterolysis and catalytic hydrogenation to give [4.3.1]propellane, where the cyclopropyl protons are well separated in the pmr spectrum; (iii) lithiation of 46f with n-BuLi followed by carboxylation to give a single carboxylic acid which could be converted to the iodolactone, indicating overall stereoretention. ^{13}C-Enriched 128 was synthesized via a standard procedure using ^{13}C-enriched chloroform.



33

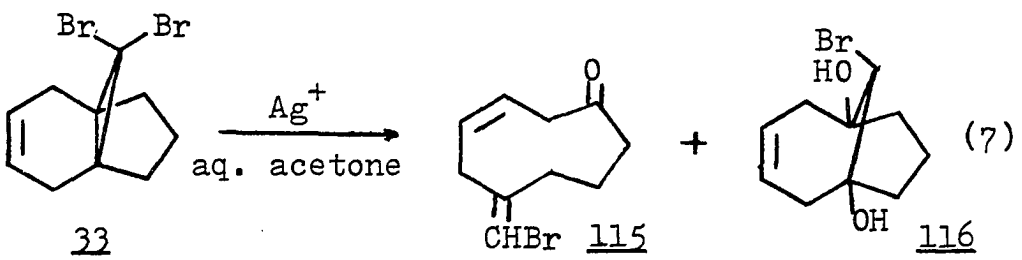


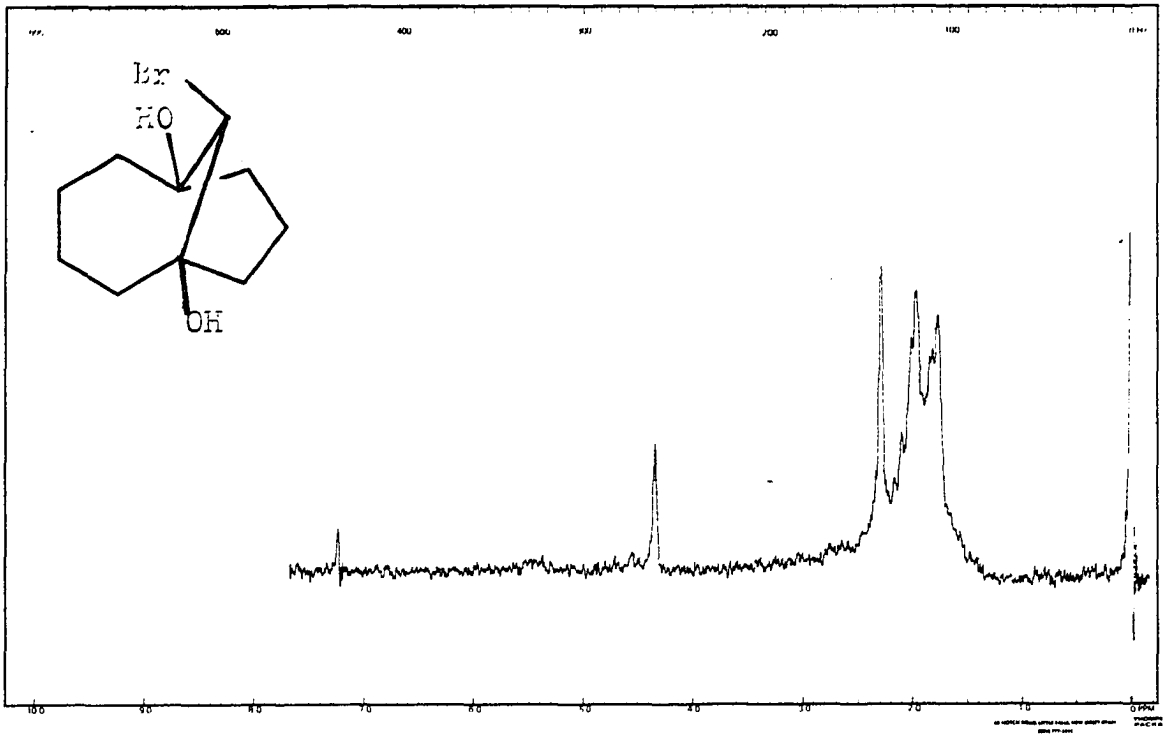
110



The [4.3.1]propellane System

Previous work[105,106] on the solvolyses of 33 and 110 in aqueous acetone utilized excess silver ion. Isolable products were identified as 115 and 116 (see Fig. 31) from 33, and as 111, 112 and 113 (see Fig. 32) from 110 (see Eq. 7 and 8). However, when 110 was solvolyzed with 1.1 equivalents of silver perchlorate in 90% aqueous acetone, two new compounds, 130 (11%) and 131 (0.2%), were isolated.





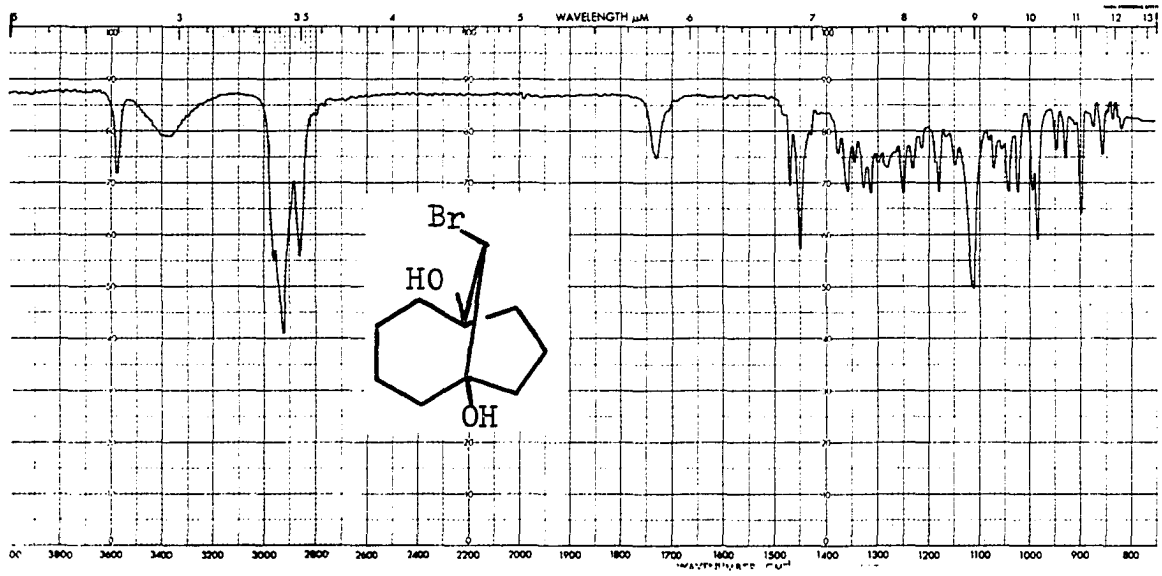


Figure 31. Pmr (Top) and Ir (Bottom) Spectra of 10α-Bromo-1,6-dihydroxybicyclo[4.3.1]decane (113).

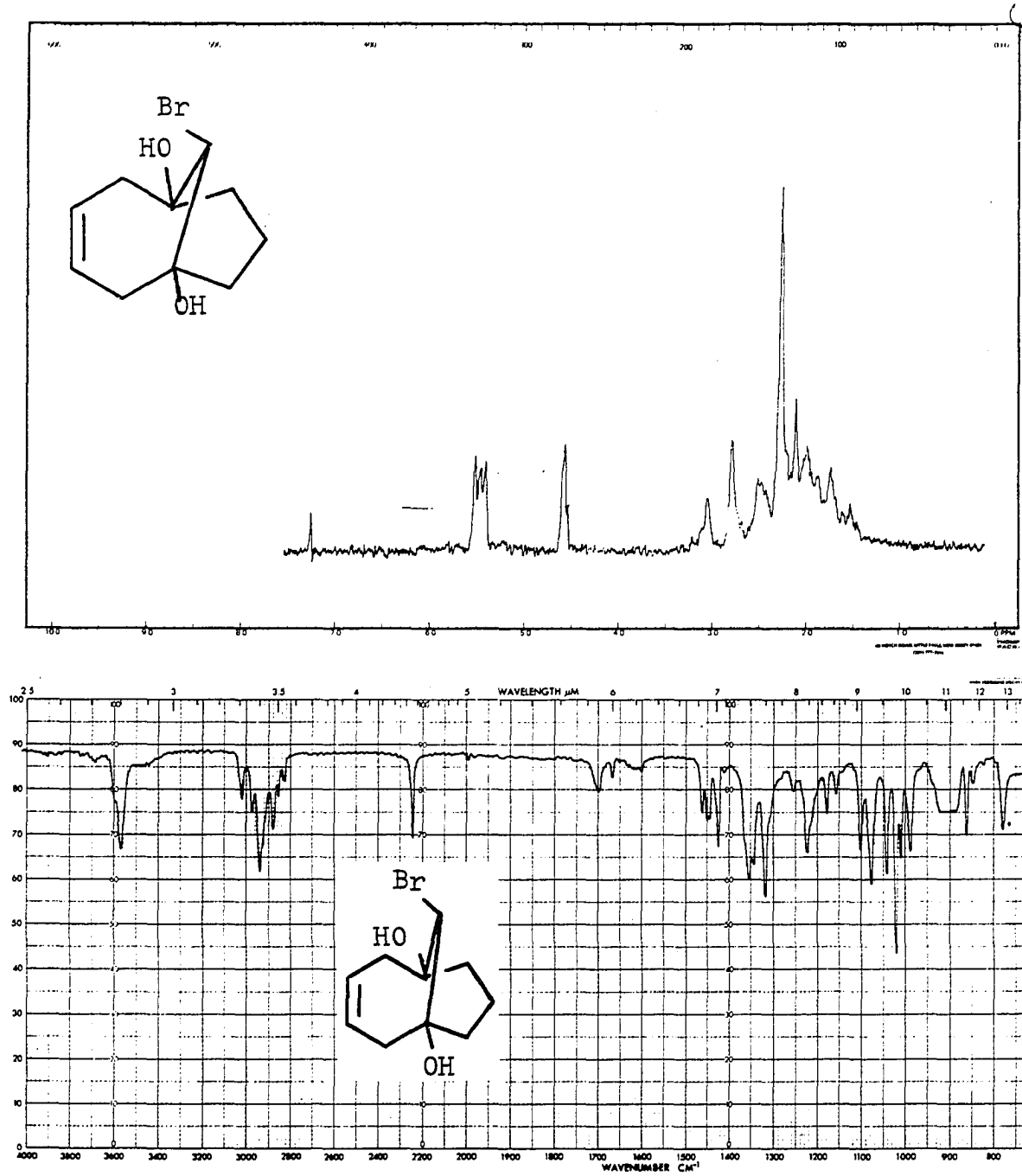


Figure 32. Pmr (Top) and Ir (Bottom) Spectra of 10α-Bromo-1,6-dihydroxybicyclo[4.3.1]dec-3-ene (116).

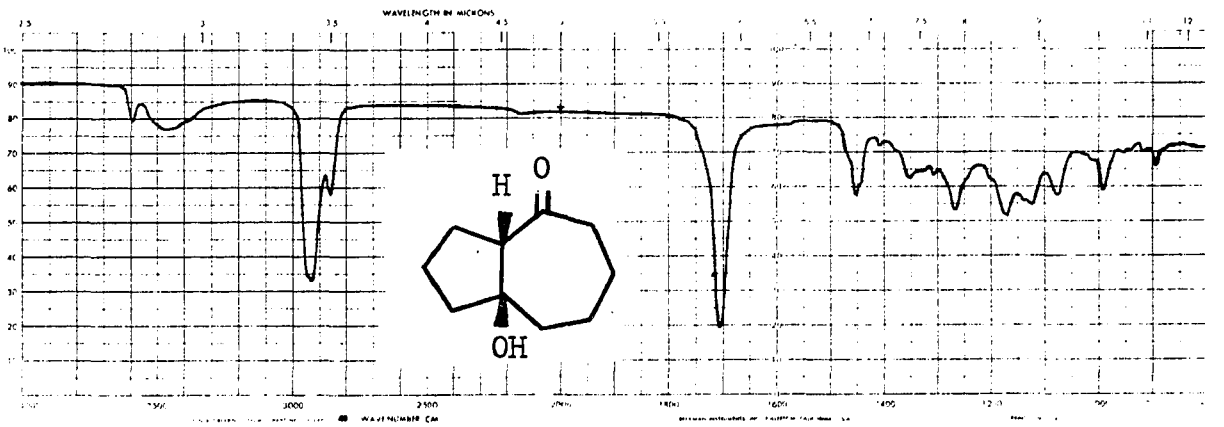
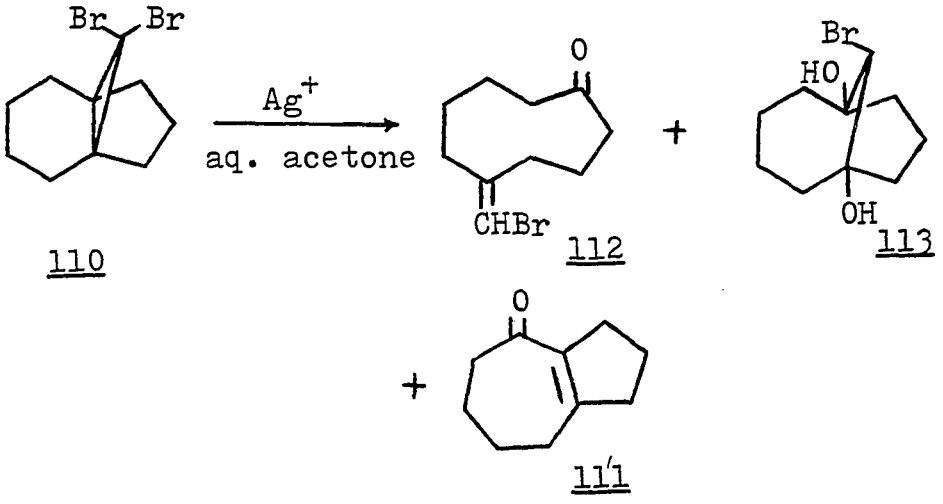
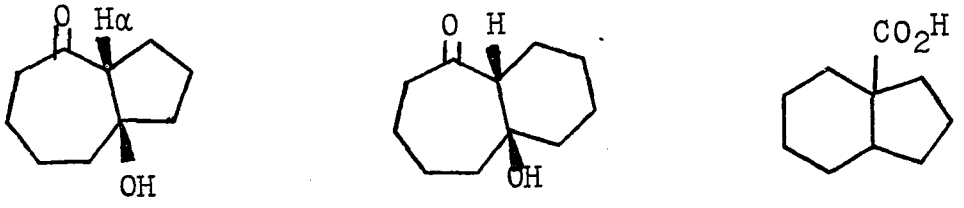


Figure 33. Ir Spectrum of 7-Hydroxybicyclo[5.3.0]decan-2-one (130).



110 112 113 111 (8)



130 137 131

β-Hydroxy ketone 130 solidified in the refrigerator mp, 94-95° (after recrystallization from hexane/ether). Infrared (see Fig. 33) peaks at 3600, 3450 and 1707 cm^{-1} served to indicate the presence of the two functional groups; elimination of water (70-72% perchloric acid) to give 111 established the skeleton of 130, as well as the position of the carbonyl group. The β positioning of the hydroxyl group was assumed by analogy with the corresponding bicycloundecanone 137 (vide infra). The cis stereochemistry of the ring fusion of 130 was established using

$Eu(fod)_3$; at a 1:1 mole ratio of shift reagent to 130, Hα showed an induced shift of -12.3 ppm, while no other carbon-bound proton had undergone a larger LIS (see experimental section). Carboxylic acid 131 had a typical ir spectrum (3600-2400, 1705 cm^{-1}) and mass spectrum [168 (P), 151 (P-OH), 123 (P-CO_2H). The stereochemistry of 131 was tentatively assigned as cis-fused by analogy with our results for the solvolysis of 11,11-dibromo[4.4.1]propellane (vide infra). No diol 113 was isolated in a reaction of 110 with 3.6 equivalent of silver ion in 90% aqueous acetone, but the yield of 111 increased to 16% at the expense of 130, and that of 112 grew slightly to 52%. It seems reasonable that Reese did not observe 113, since he utilized excess silver perchlorate. Reese's unidentified product (~5%) was probably a mixture of 130 and 131, which is consistent with the results obtained from the solvolysis of 110 with 3.6 equivalent of silver perchlorate (see Table 9). A control experiment for hydroxy ketone 130 under the solvolysis conditions showed that enone 111 was indeed an elimination product from 130.

Furthermore, when diol 113 was treated with excess silver perchlorate in aq. acetone, a 14:1 mixture (glc analysis) of hydroxyketone 130 and enone 111 was obtained. This observation further suggested that products 111 and 130

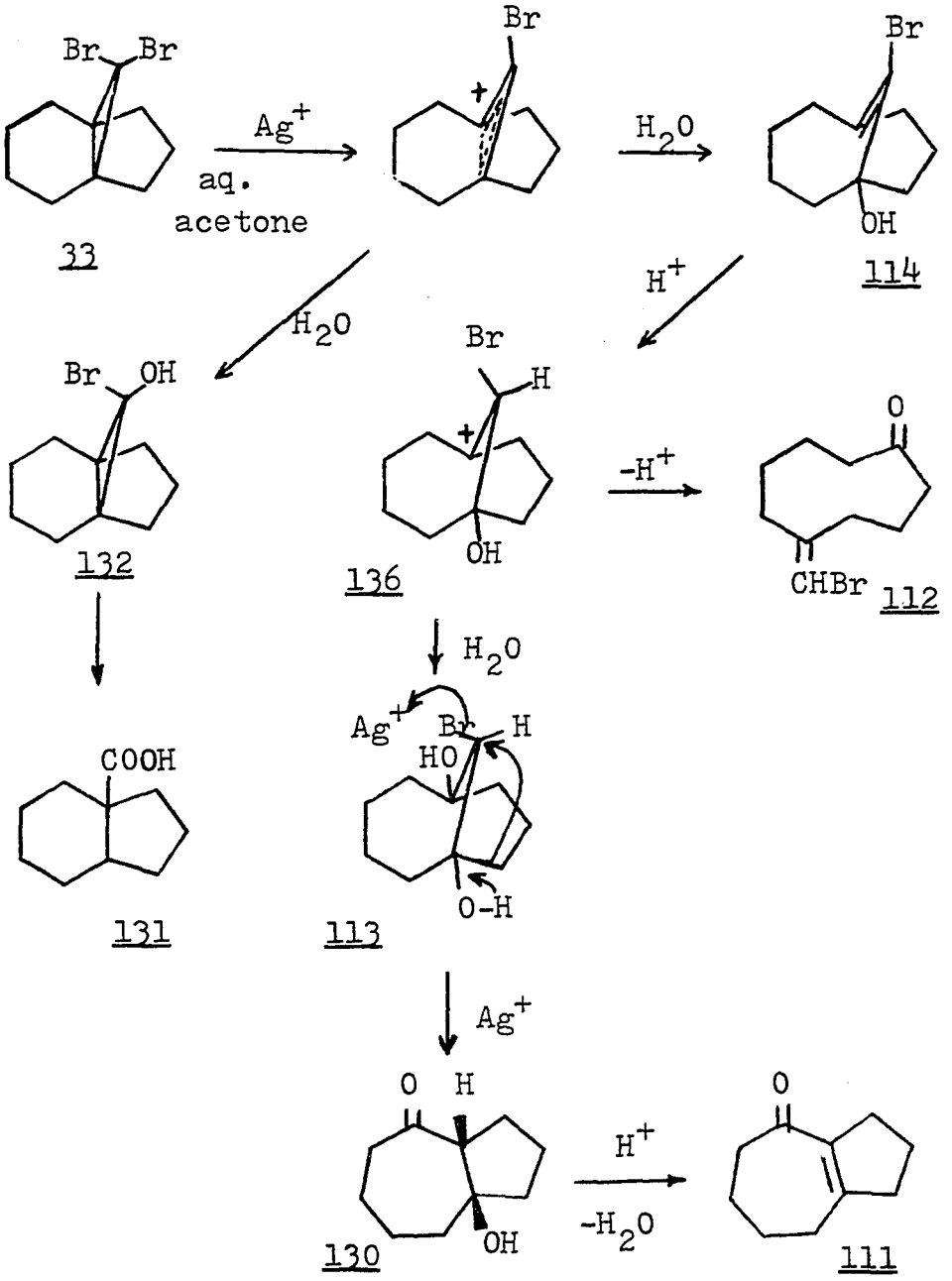
Table 9. Products of Ag^+ Assisted Solvolysis of 110 under Various Conditions.

$[Ag^+]$ / [49]	[110], M	Acetone/H_2O Vol. %	Time Min.	Yields of Products 112	111	113	130	131	Ref.
excess	?	95	10	50	15	-	ca. 5		105
1-2	0.02-0.06	90	20-30	43	13	15	-	-	106
1.1	0.32	90	15	42	3	10	11	0.2	this work
3.6	0.19	90	300	52	16	0	4.4	0.2	this work

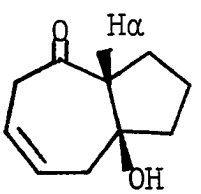
as well as 112, are derived from the same intermediate (i.e., 114). However, the minor product 131 must arise from a different intermediate, most likely 132 (ring opening of such an intermediate is precedented by the work of Groves and Ma[113]). That 110 does not directly yield 131 via acid-catalyzed addition of water was indicated by the finding that 110 can be recovered unchanged after being subjected to the acidic hydrolysis conditions (simulated by reacting one equivalent of ethyl bromide with a similar amount of silver perchlorate prior to adding 110 to the solution). Furthermore, [4.3.1]propellane was recovered unchanged after treatment with acidic silver perchlorate indicating

that carbon-halogen bond cleavage is necessary for further molecular transformations under these (aqueous acetone) hydrolysis conditions. Scheme 7 summarizes the pathway for the hydrolysis of 110.

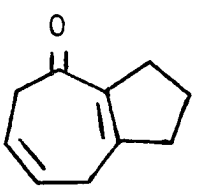
Scheme 7



In a parallel study, diol 116 gave hydroxy enone 133 (see Fig. 34) in 97% yield in the presence of excess $AgClO_4$ in 90% aq. acetone (20 hr.). The lanthanide shifted pmr spectrum of 133 at a 1:1 molar ratio of Eu $(fod)_3$ to 133 showed an LIS of -11.0 ppm for Hα; since Hα was again the most shifted carbon-bound proton, 133 was judged to have a cis ring fusion. Catalytic hydrogenation of 133 gave a quantitative yield of 111 Neither 133 nor 134 were mentioned in the early reports.[105,106] No further investigation of these compounds was pursued.

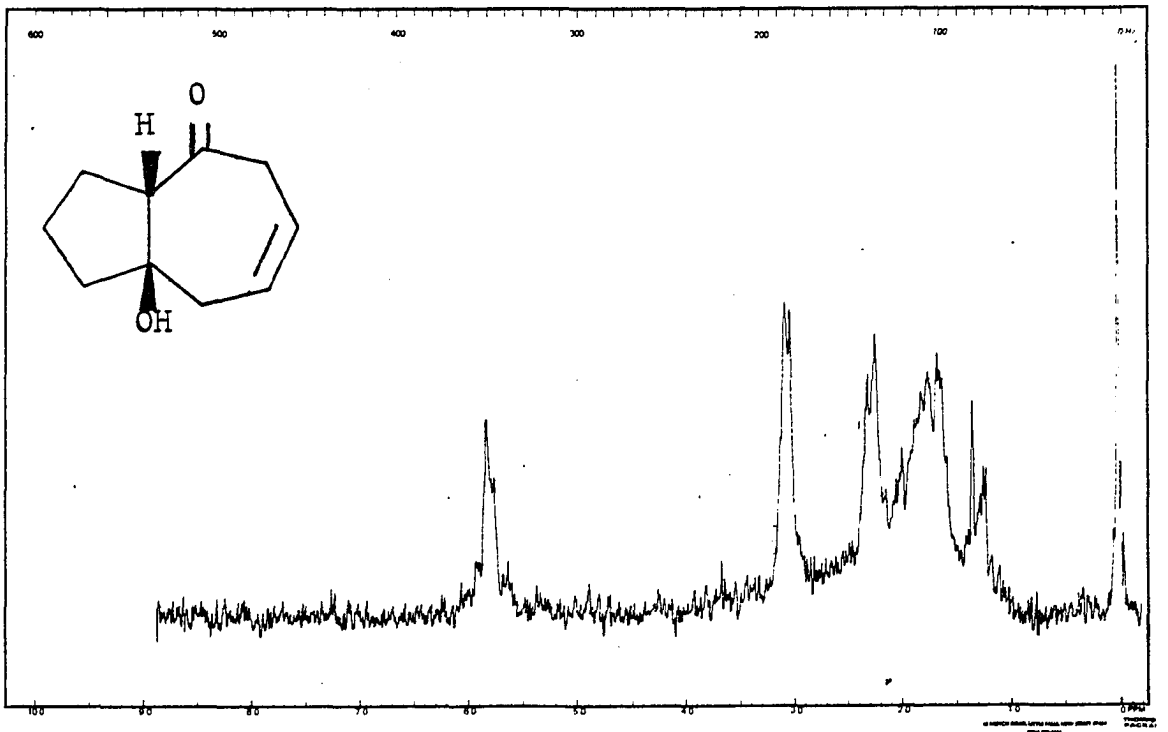


133



134

It was reported[105] that the formation of ketones 112 and 113 was stereospecific on the basis of the sharpness of the bromomethylene proton resonances in their respective pmr spectra. However, the detailed structure of 113 (and 112) was unknown (either 112a or 112b was correct). In order to determine the stereochemistry of 112, its 2,4-dinitrophenyl-hydrazone derivative (135) was synthesized (see Fig. 35). An X-ray study of this yellow crystalline substance



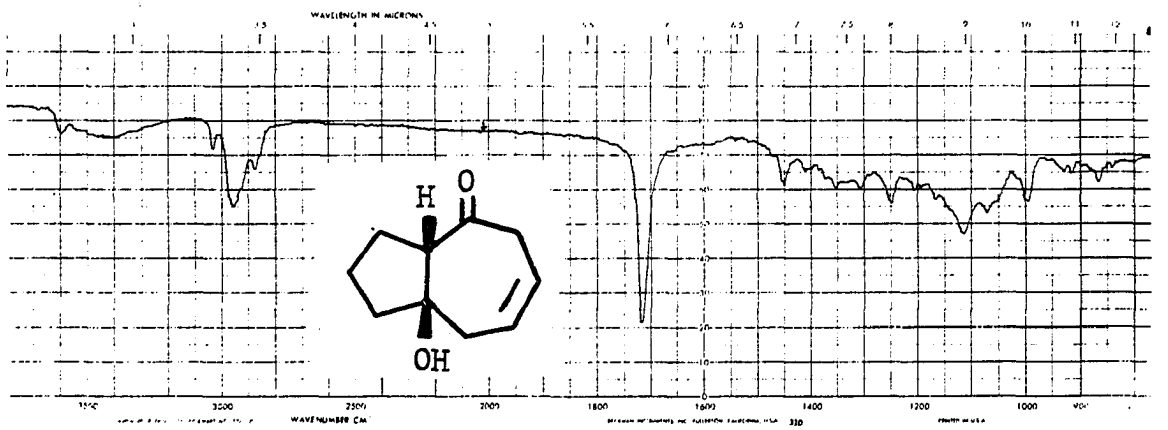


Figure 34. Pmr (Top) and Ir (Bottom) Spectra of 7-Hydroxybicyclo[5.3.0]dec-4-en-2-one (133).

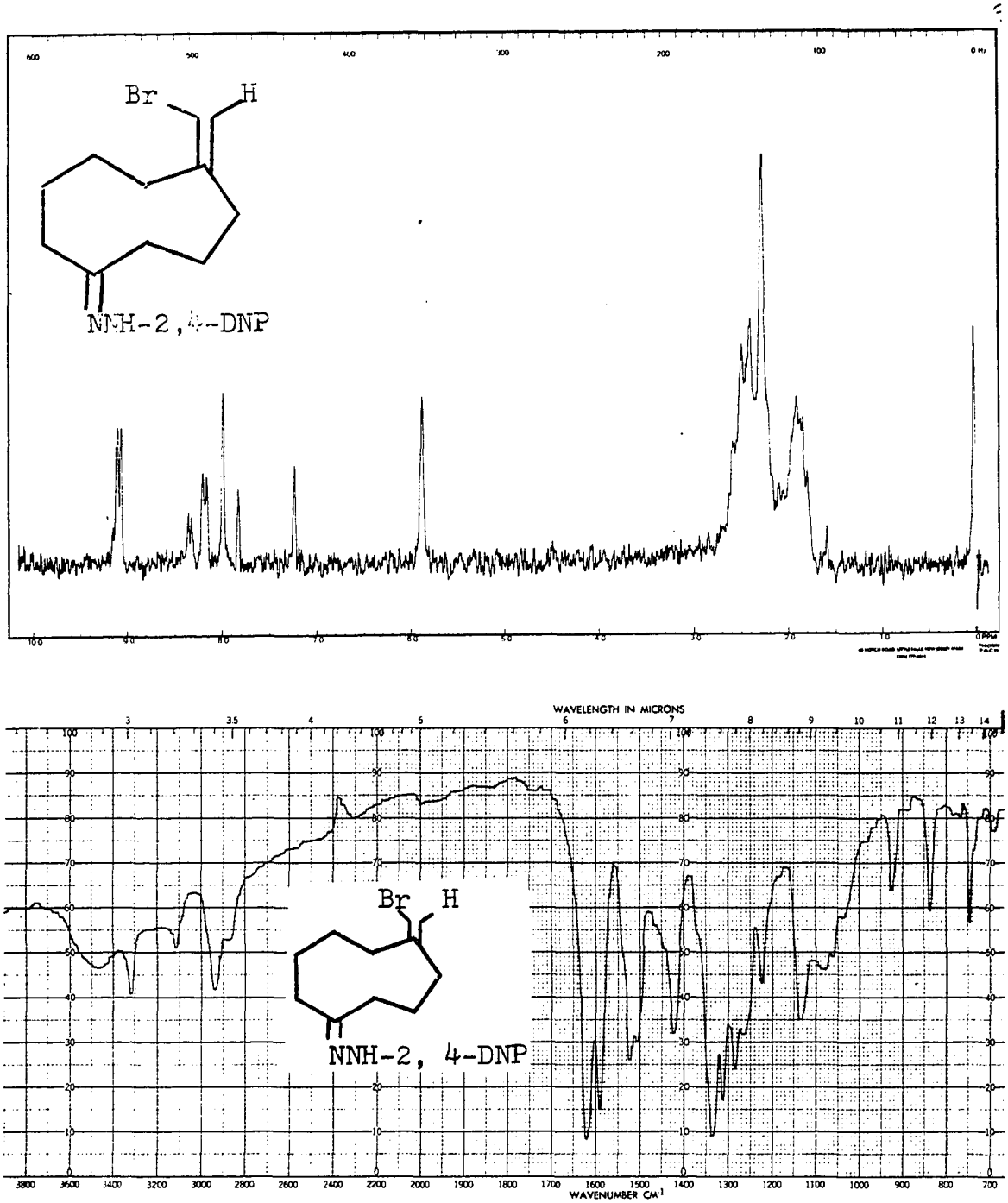
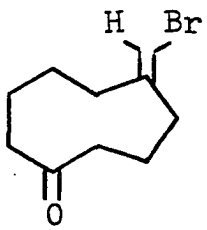
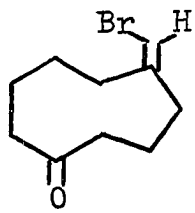


Figure 35. Pmr (Top) and Ir (Bottom) Spectra of 2,4-Dinitrophenylhydrazone Derivative of 112, (135).

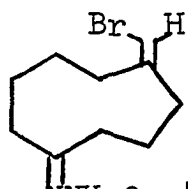
was undertaken. The space group was found to be $P\bar{1}$, with 2 molecules per unit cell of dimensions a = 11.048 (5) b = 11.997 (6), c = 7.514 (2) A, and α = 98.42 (3), β = 97.09 (3), γ = 116.70 (4)°. The structure was solved by heavy atom methods and fully refined (excluding H's) to a discrepancy index of R = 0.094 for 1920 uniquely measured structure factors ($F_o^2 > 3\sigma_1$).[114] The key feature of 135 (and thus 115) is the orientation of the bromine atom, which is as in 112b. Since Warner, et al.[106] demonstrated the stereochemistry of diol 113 (and thus 136), the fragmentation of 136 to 112 must occur with retention of configuration to give 112b only. The cmr spectrum of 112 (see experimental) confirmed that 112 is probably ≥ 99% epimerically pure, since only 10 peaks were observed even after 21,000 pulses. In a parallel study, Reese discovered that the pmr of 112 in the presence of shift reagents shows no evidence for the epimer of 112b.



112a

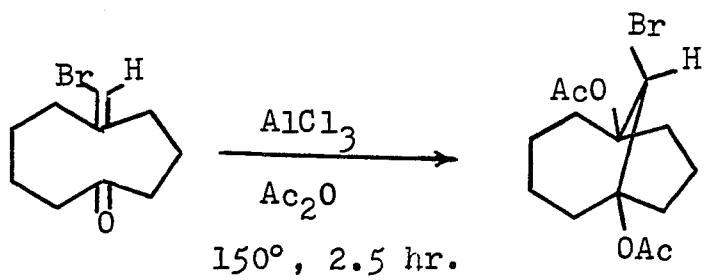


112b

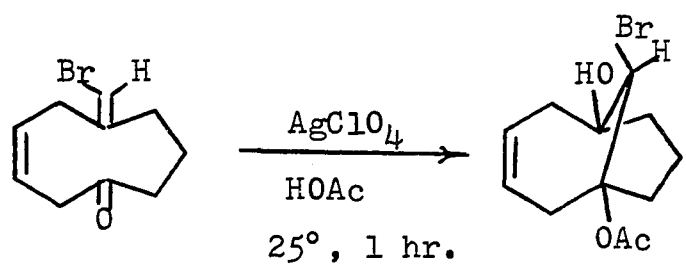


135

A noteworthy conformational feature of 135 is that the exocyclic carbon projects above the nine-membered ring ($r_{C_1-C_6}$ = 3.07A, $r_{C_1-C_{10}}$ = 3.44A), making transannular interaction in 112 seem attractive. Although 112 is stable under aqueous solvolytic conditions, it suffers conversion to the bicycle, 136, upon treatment with aluminum trichloride in acetic anhydride (52% yield) (see Eq. 9). Furthermore, Warner[43] observed a similar transannular cyclization of 115 which was converted to bicyclic derivative 137 during prolonged acetolysis of 33 at room temperature (see Eq.10).



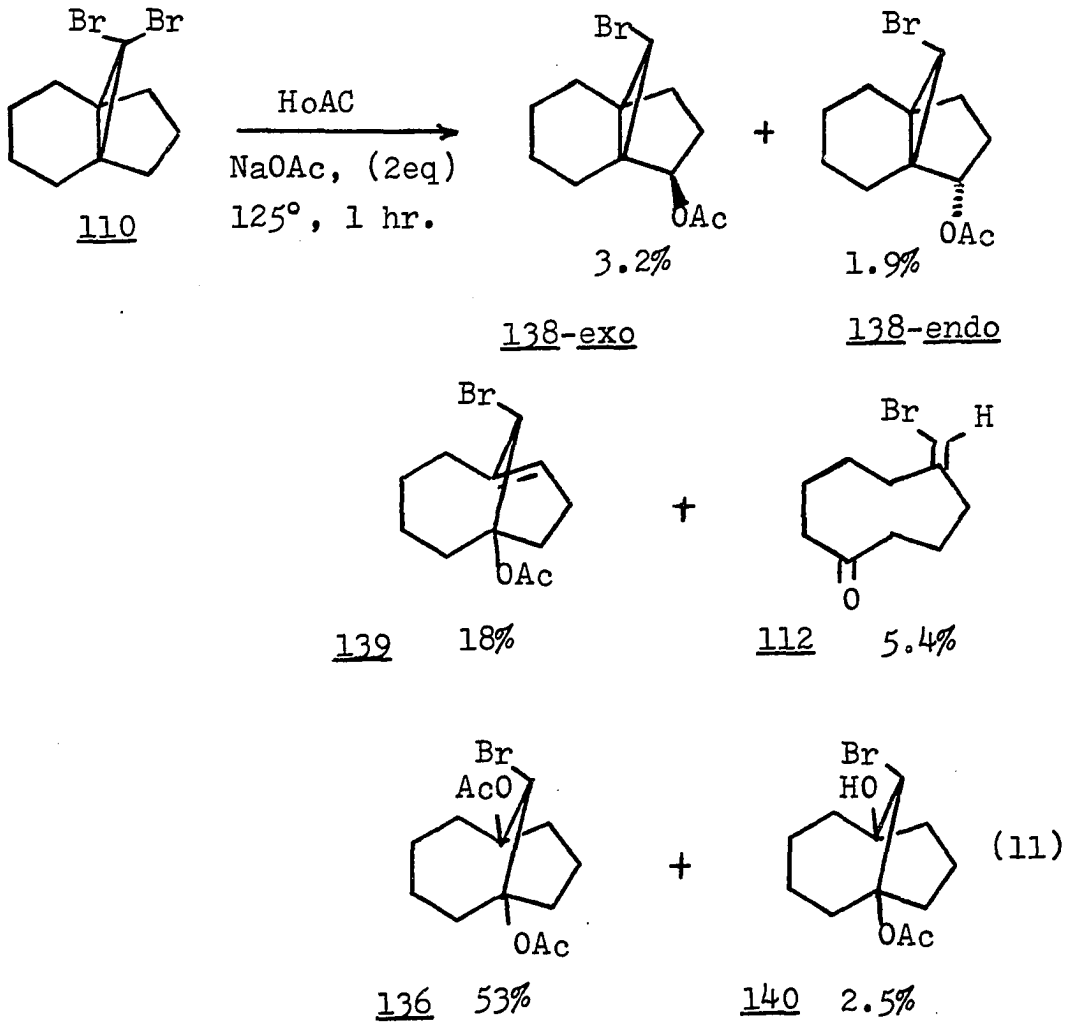
112 136 (9)



115 137 (10)

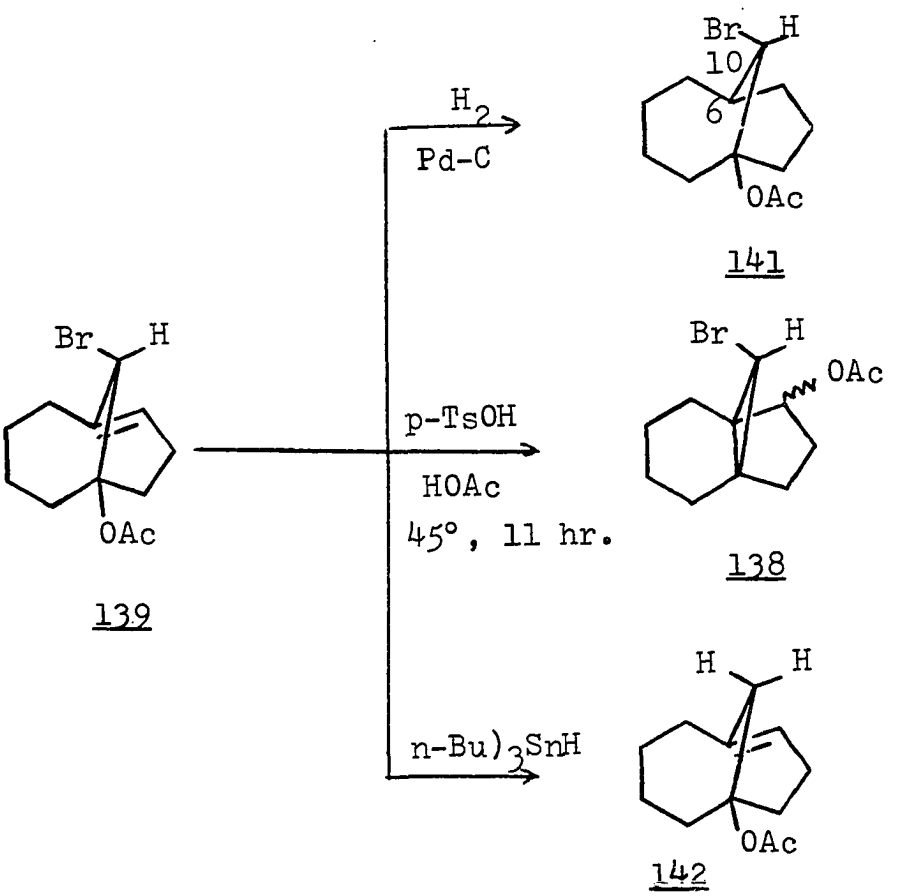
In order to study the unassisted solvolysis of 110, an acetic acid solution of 110, buffered with 2 equivalents of sodium acetate, was heated at 125° for one hr. The resulting products, summarized in Eq.11, also implicate a reaction pathway involving bridgehead olefins.[115]

Thus upon column chromatography, the products first eluted consisted of a mixture of epimeric cyclopropyl acetates, 138-exo and 138-endo. No further attempt to



(11)

separate the epimers was made. The structure of the epimers was confirmed when it was found that the same epimers are produced by catalytic hydrogenation of 153 (the analogous solvolysis products from 33), the structure of which was firmly established (vide infra). The exo/endo ratio was determined from the pmr integration of the cyclopropyl proton resonances (δ3.18 for 138-exo, δ2.80 for 138-endo). Compound 139, eluted next, proved to be a bridgehead olefin containing an acetate group at the other bridgehead position (see Fig. 36). The following chemistry supported the proposed structure:



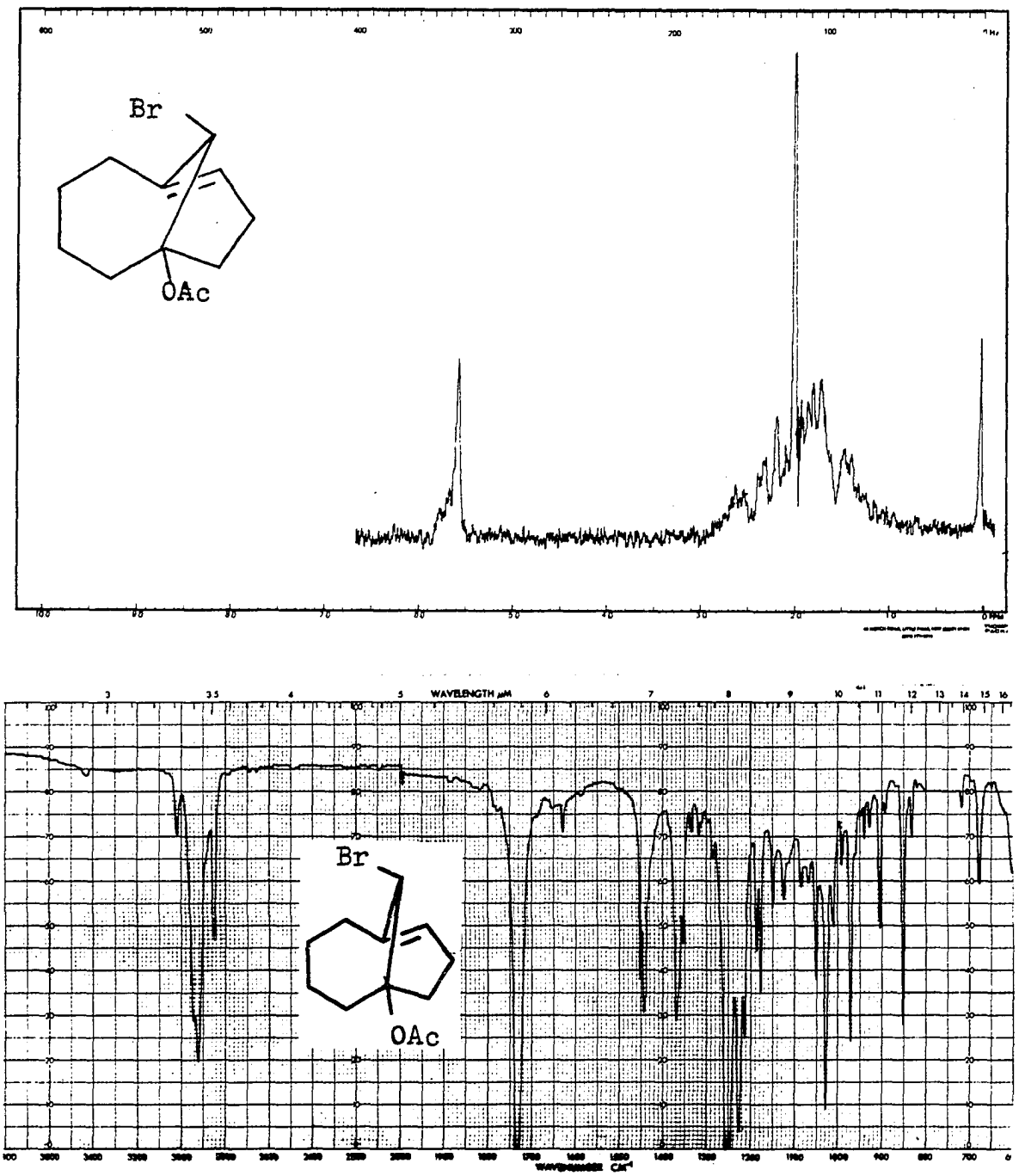
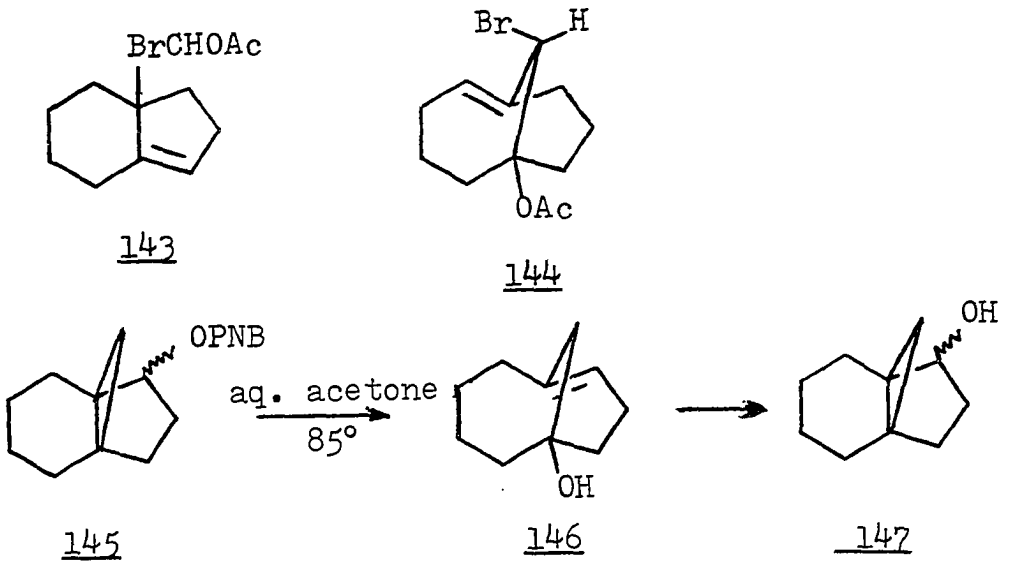


Figure 36. Pmr (Top) and Ir (Bottom) Spectra of 6-Acetoxy-10α-bromobicyclo[4.3.1]dec-1(9)-ene (139)



143 144 145 146 147

Thus catalytic hydrogenation of 139 afforded a single product (141) (see Fig. 37). A doublet at δ 4.95 (J = 5Hz) in 141 suggested H_{10} is coupled to H_6. The alternative structure, 143, could not lead to a reduction product in which the low field proton would be vicinally coupled. Acid-catalyzed isomerization of 139, which afforded the epimeric mixture 138, served to establish the positioning of the double bond (i.e. 144 was excluded vide infra for discussion of this regioselectivity). Diacetate 136 was also found as the minor product from the acid-catalyzed isomerization of 139. It should be noted that the rearrangement of 139 to 138 is precedented by the work of Gassman, et al.[116] 145→146→147. Tri-n-butyltin hydride reduction of 139 gave 142; its pmr spectrum reveals a broad triplet (J = 5.5Hz)

at δ 5.55 as the only low field absorption, which also mitigates against structure 143 (it would give two low field peaks upon reduction). Also, the very small change in chemical shift seen for the olefinic proton upon reduction (δ = 0.15 ppm) made structure 144 seem unlikely. Monocyclic ketone 112, eluted next, was a known compound.[105] The major product, diacetate 136 (see Fig. 38), was subsequently eluted and converted to the known[106] diol, 113, via basic hydrolysis in methanol. Finally, hydroxyacetate 140 was obtained (see Fig. 39). Since the analogous unsaturated hydroxyacetate 137 (see Fig. 49) had previously been observed from the acetolysis of 33[43] the finding of 140 was not unexpected. The structure of 140 was confirmed by its conversion to 136 with acetyl chloride in pyridine. Since in the earlier work[43] in glacial acetic acid Warner had noted that unsaturated diacetate 154 was slowly converted to unsaturated hydroxyacetate 137, it was suspected that some water was involved in the production of 140. Therefore, the acetolysis was repeated in the presence of 10% Ac_2O, whereby the products given in Eq. (12) were obtained.

$$\underline{110} \xrightarrow[\text{NaOAc(2eq)}]{\text{HOAc/Ac}_2\text{O}} \underset{21\%}{\underline{139}} + \underset{63\%}{\underline{136}} \qquad (12)$$

129°, 1 hr.

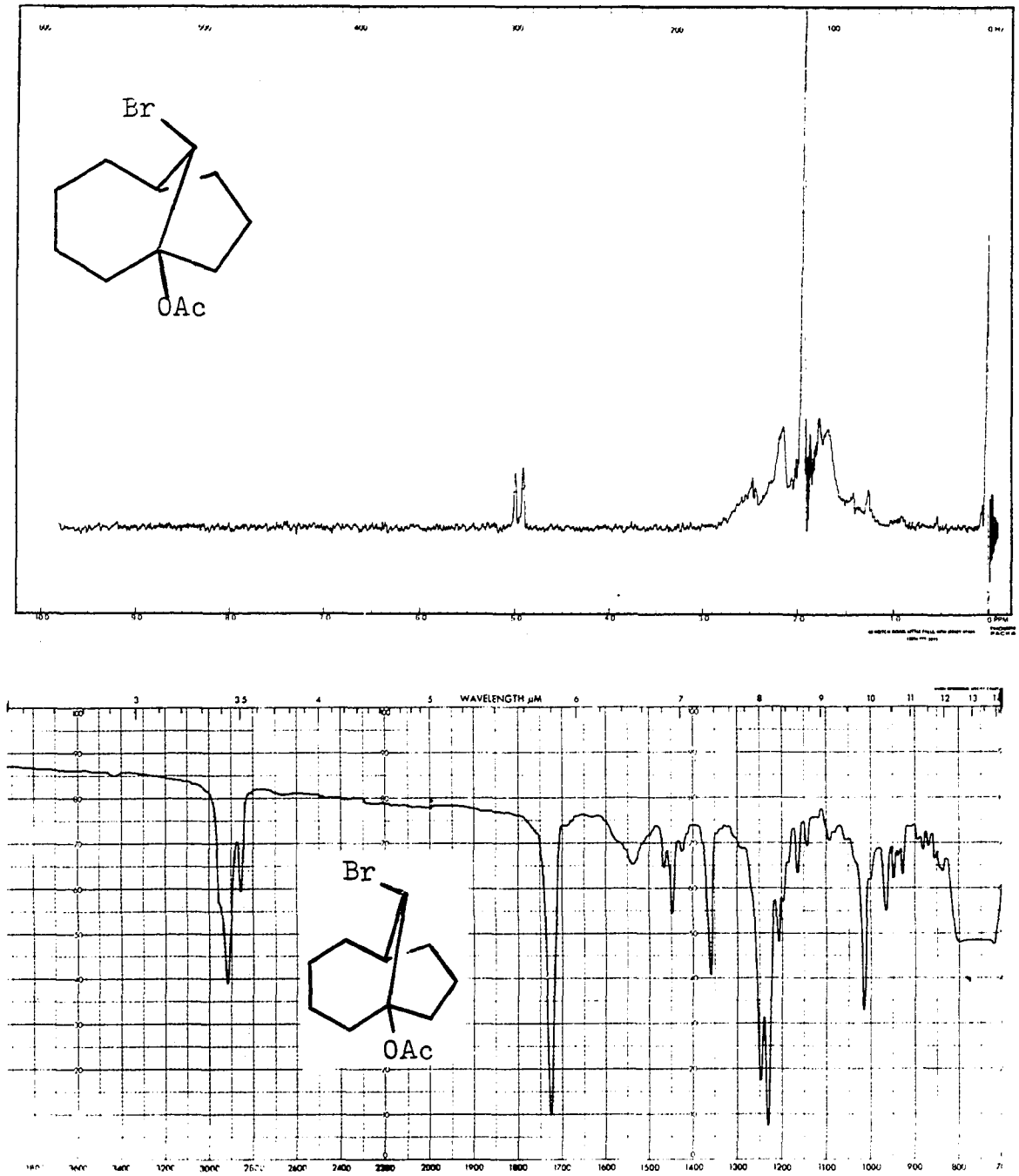


Figure 37. Pmr (Top) and Ir (Bottom) Spectra of 1-Acetoxy-10α-bromobicyclo[4.3.1]decane (141).

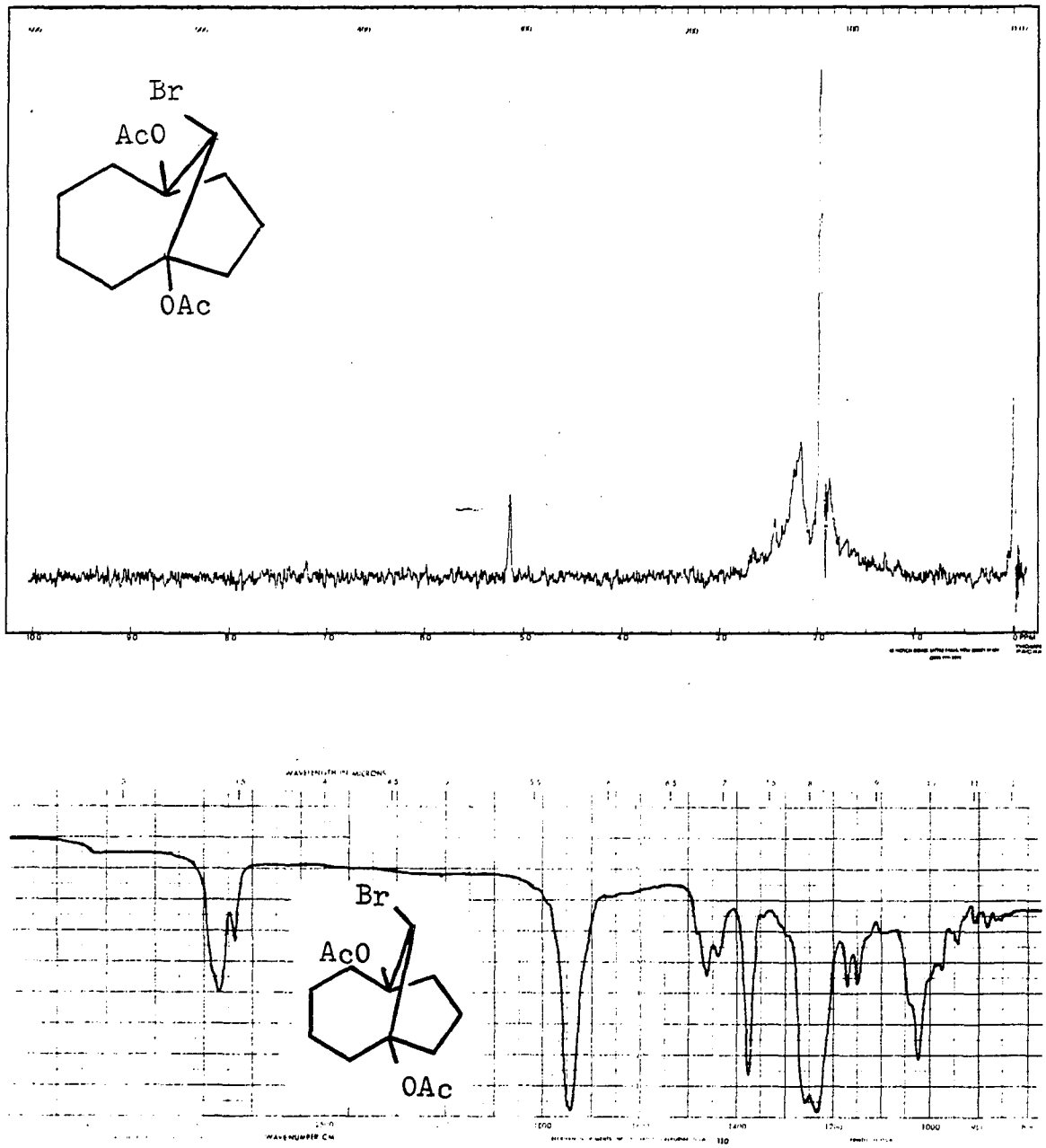


Figure 38. Pmr (Top) and Ir (Bottom) Spectra of 10α-Bromo-1,6-diacetoxybicyclo[4.3.1]decane (136).

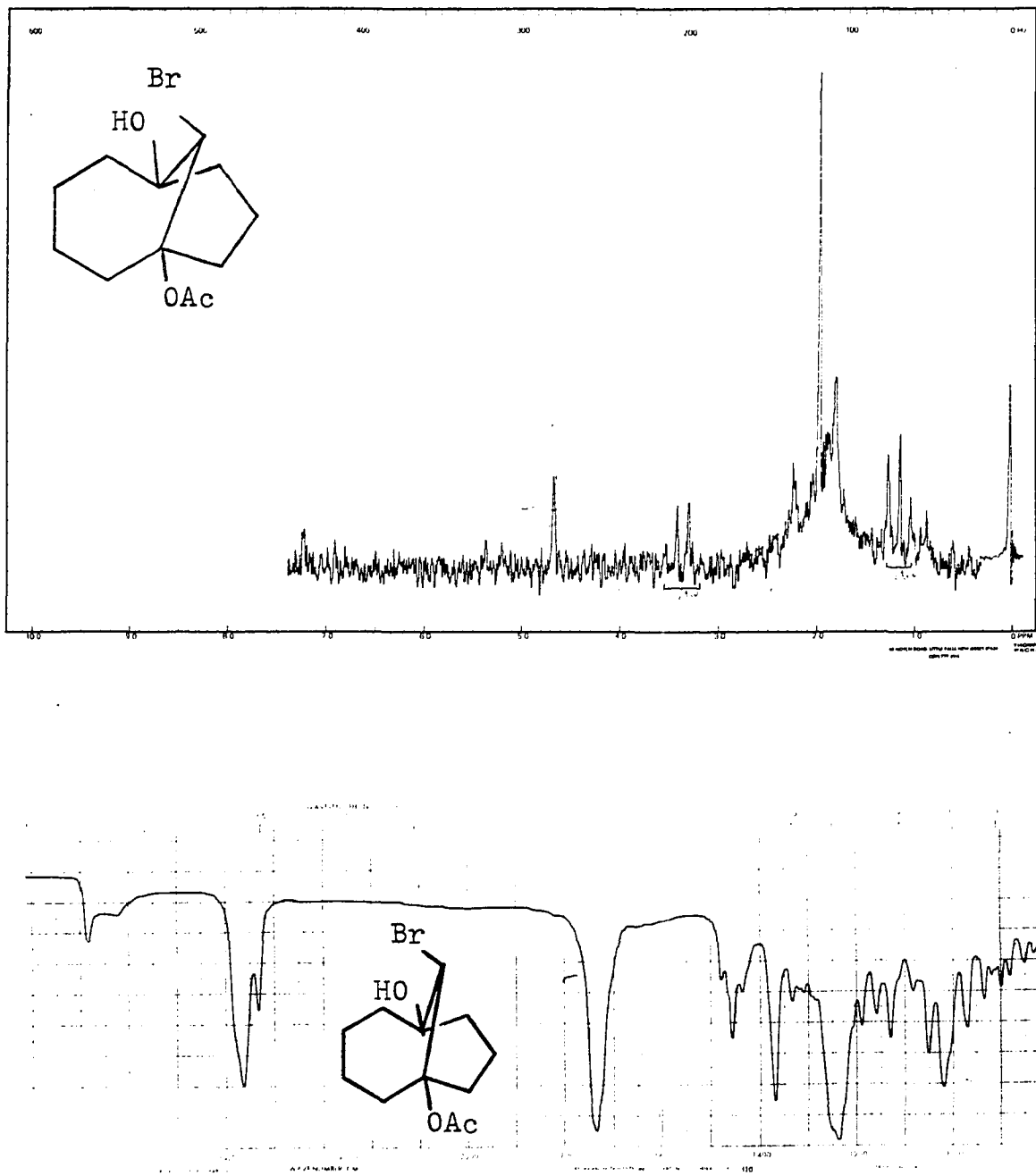
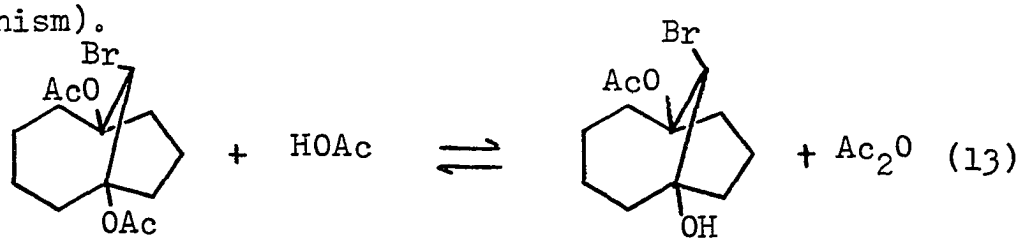


Figure 39. Pmr (Top) and Ir (Bottom) Spectra of 1-Acetoxy-10α-bromo-6-hydroxybicyclo[4.3.1]decane (140).

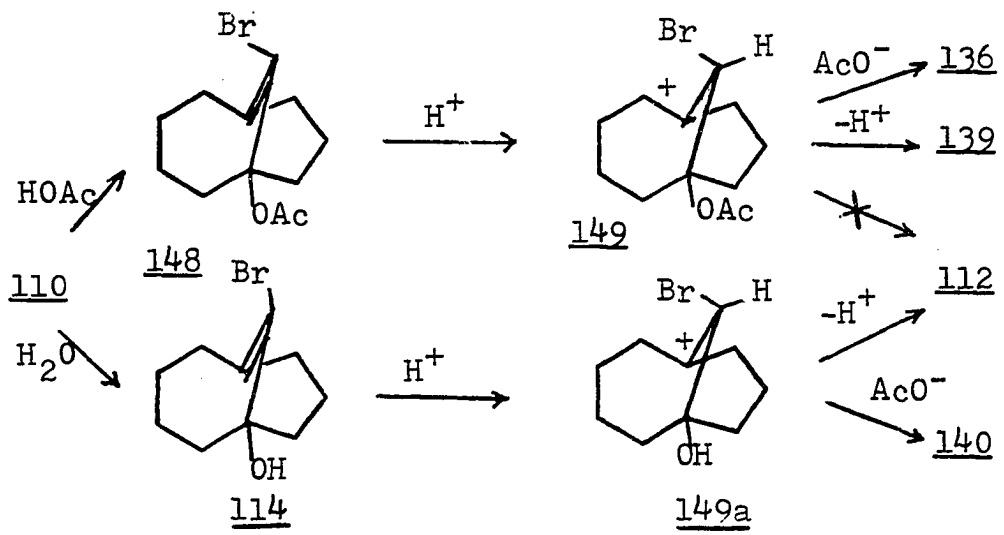
This seemed to verify that 140 arose via intervention of water. More importantly, the absence of monocyclic ketone 112 showed that ion 149 cannot fragment with loss of acylonium ion; this strongly supports the concept[105] of a concerted fragmentation of 149a to 112 with the added requirement of a good departing cation (in this case a proton) (see Scheme 8).

It should be noted that 140 did not give 112 under the reaction conditions, which made the alternative mechanism for the formation of 140 shown in Eq. 13 unlikely (or at least less important than the involvement of water mechanism).

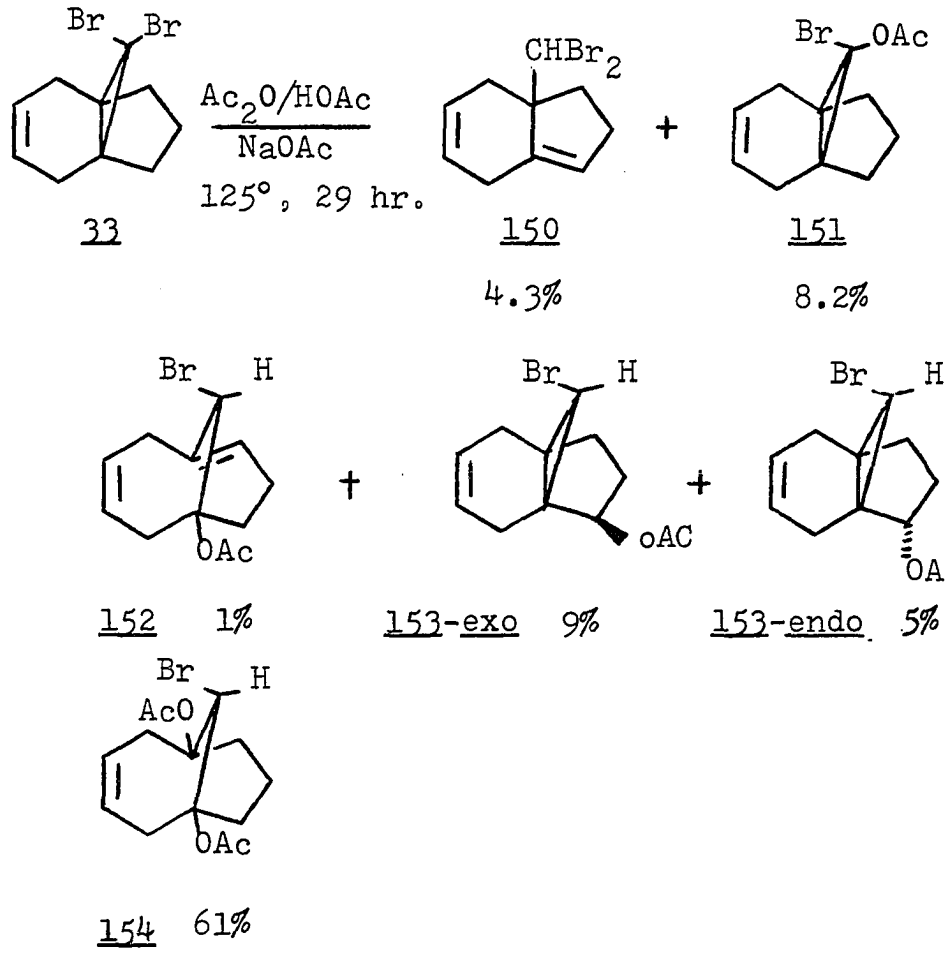


136 140

Scheme 8



The buffered acetolysis of 33 utilizing 10% Ac_2O, resulted in the products show in Eq. 14.



33 → 150 4.3% + 151 8.2% + 152 1% + 153-exo 9% + 153-endo 5% + 154 61% (14)

Thus products 152 (see Fig. 40), 153, 154 are the unsaturated analogs of 139, 138 and 136. The regioselective formation of 139 and 152, to the exclusion (or nearly so) of isomeric bridgehead olefins with the double bond in the four carbon bridge, can be due to several factors. First of all, the Δ 1, 2 isomers appear to be more strained than

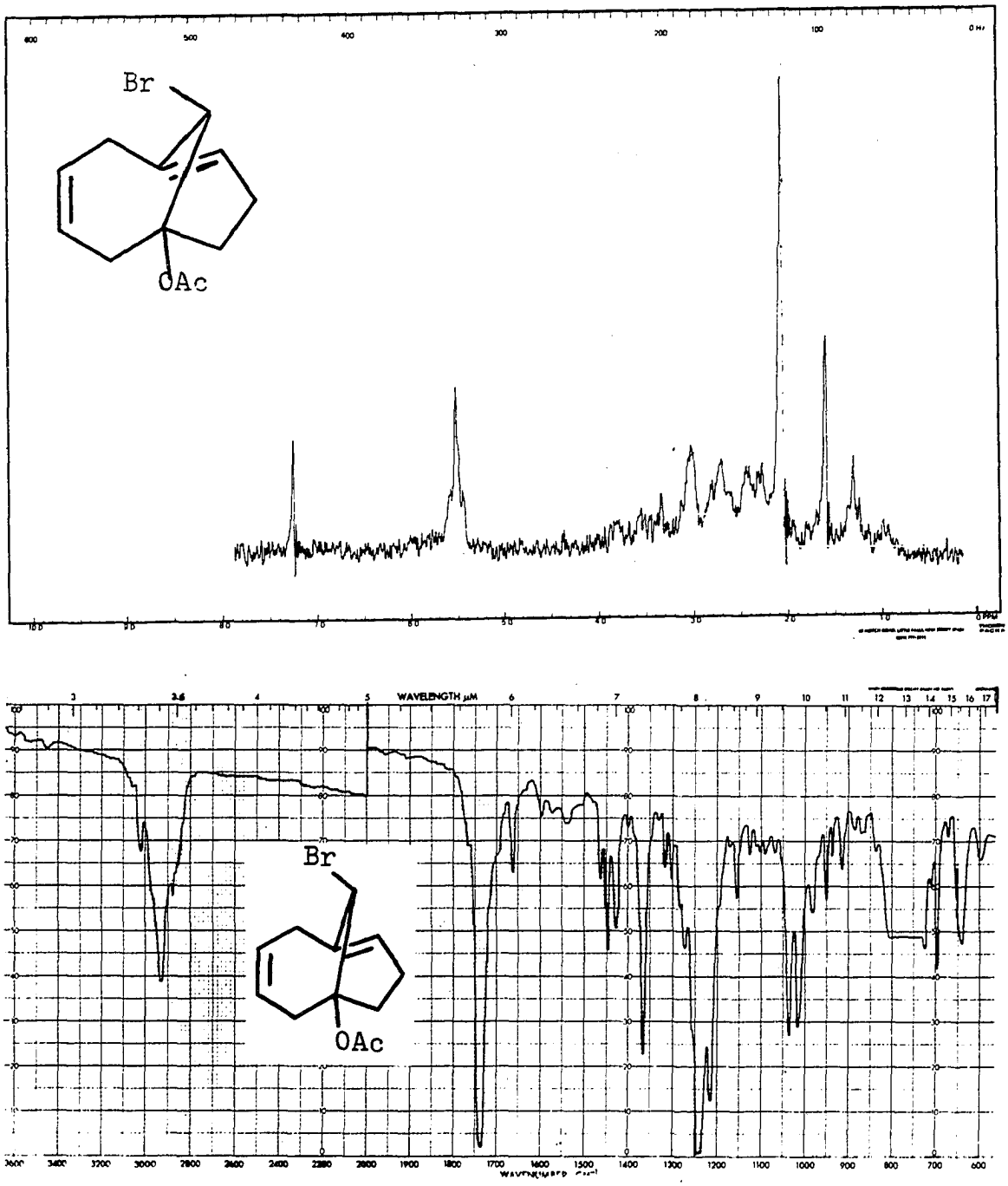


Figure 40. Pmr (Top) and Ir (Bottom) Spectra of 1-Acetoxy-10α-bromobicyclo[4.3.1]deca-3,6(7)-diene (152).

the ones observed (examination of Dreiding models). Alternatively, depending on the conformation of 149, $H_{7\text{-exo}}$ may be better aligned for elimination than H-5. More importantly, perhaps the stereochemistry of reaction of 148 (and 158), in which protonation from the right-hand side may leave an acetate ion closer to H-7, may portend the ultimate formation of 139 (and 152). It is doubtful that 148 (or 158) was directly transformed into 139 (or 152) via a 1,3[H] shift (thermally disallowed). Also an acetic acid-mediated concerted [H] shift would be disallowed (8 electrons).

Two of the products obtained from the acetolysis of 33 had no analogy in the products obtained from 110. The first one, 150 (see Fig. 41), was formed by a solvent protonation-deprotonation process, which became competitive with the slower solvolytic process of 33 (relative to 110). In fact, the unbuffered acetolysis of 33 gave primarily (ca. 40%) 150.[43] The regiolocation of the angular double bond of 150 was indicated by the absence of anything but end absorption in the UV spectrum. This sensitive probe, coupled with the fact that the cmr showed only 10 peaks (4 olefinic and 6 aliphatic) even after 11,264 scans, made it unlikely that 155 was present in the solvolysate. However, one could not be confident that 155 wasn't formed,

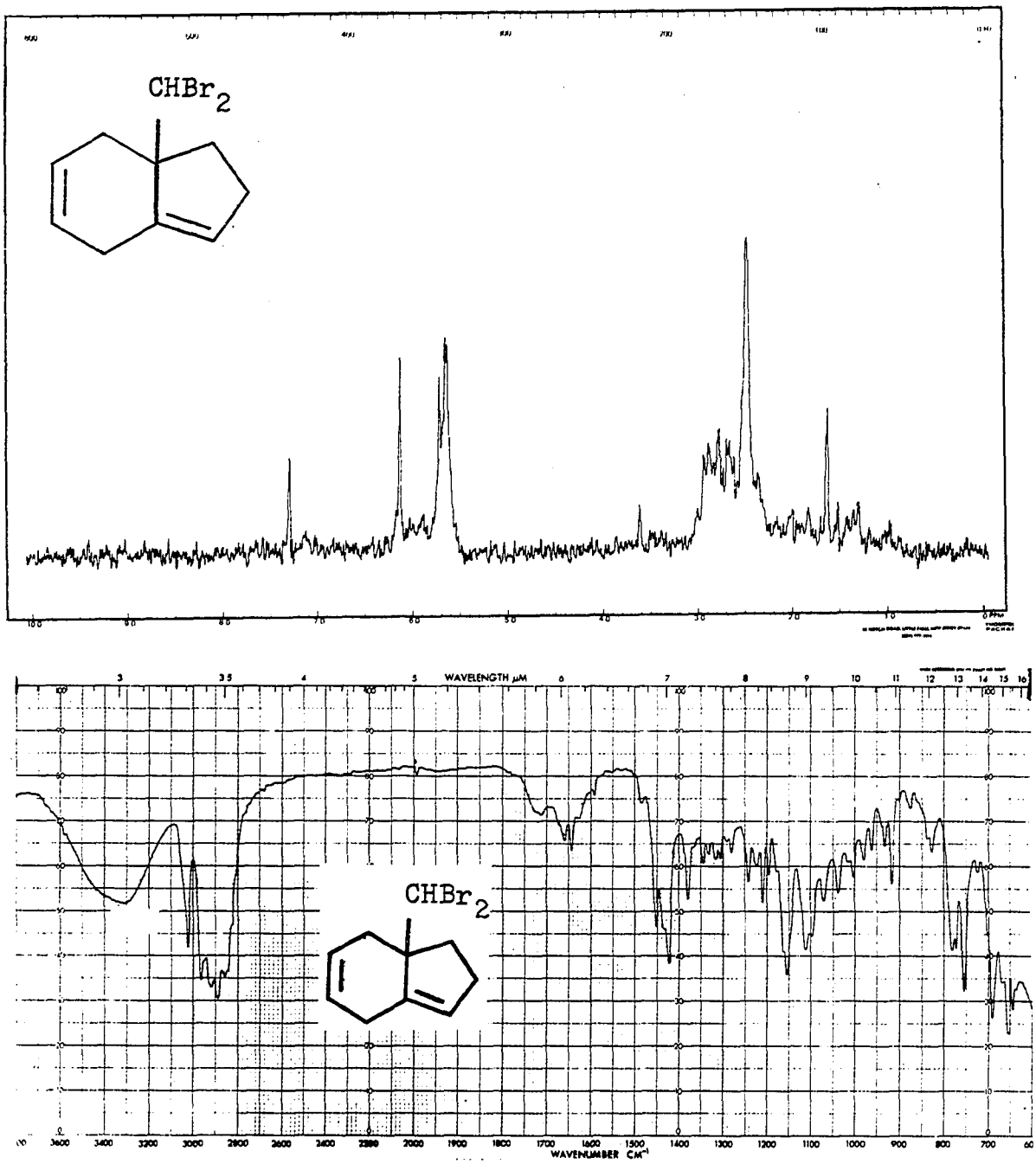
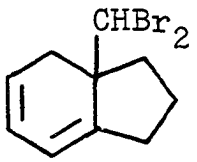
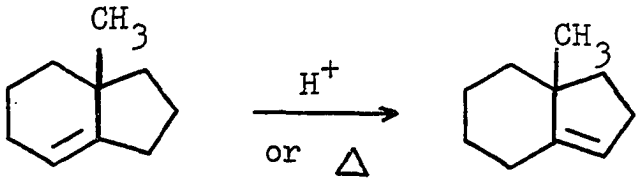


Figure 41. Pmr (Top) and Ir (Bottom) Spectra of 1-Dibromomethylbicyclo[4.3.0]deca-3,6(7)-diene (150).

since it had been shown[43] that 156 rearranged to 157 under acidic and thermolytic conditions. The isolation of 150 raised the possibility that 153 and 152 were formed via solvolysis and rearrangement of 150, rather than via solvolysis of 33 (see Scheme 9). Indeed, treatment of 150 under the solvolysis conditions[43] led to 25% rearrangement to 153 (predominantly 153-exo) and perhaps some 152 (but small relative to the amount of 153). Thus roughly 10% of the total amount of 152 and 153 formed arose via solvolysis of 150, whereas 90% came through 158. It is interesting that the rearrangement of 150 occurred stereospecifically (with respect to the bromine orientation).

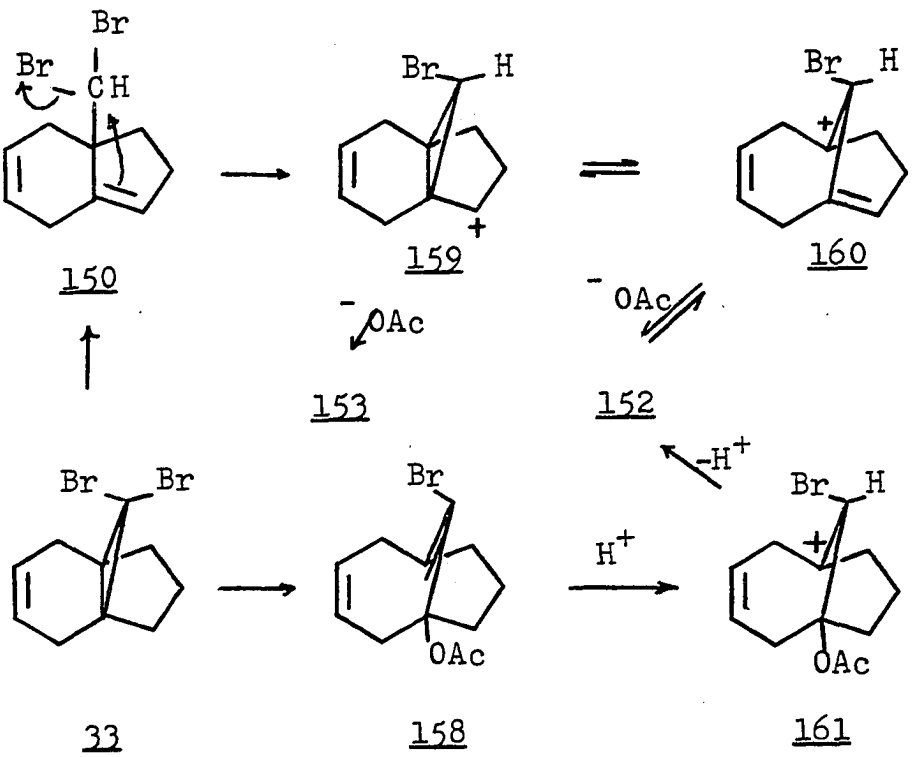


155



156 157

Scheme 9



The second novel compound isolated proved to be propellane 151 (earlier thought to be a bridgehead olefin dimer[106]) (see Fig. 42), formed via collapse of the initially formed ion at the cyclopropyl position. The stereochemistry of 151 was assigned by analogy with solvolysis product 162 (vide infra), but is unproven. Basic hydrolysis of 151 led to the expected, known carboxylic acid,[117] 163. A second product, assigned structure 164 on the basis of an ir absorption at 1825 cm^{-1}, was also isolated from the hydrolysis mixture.

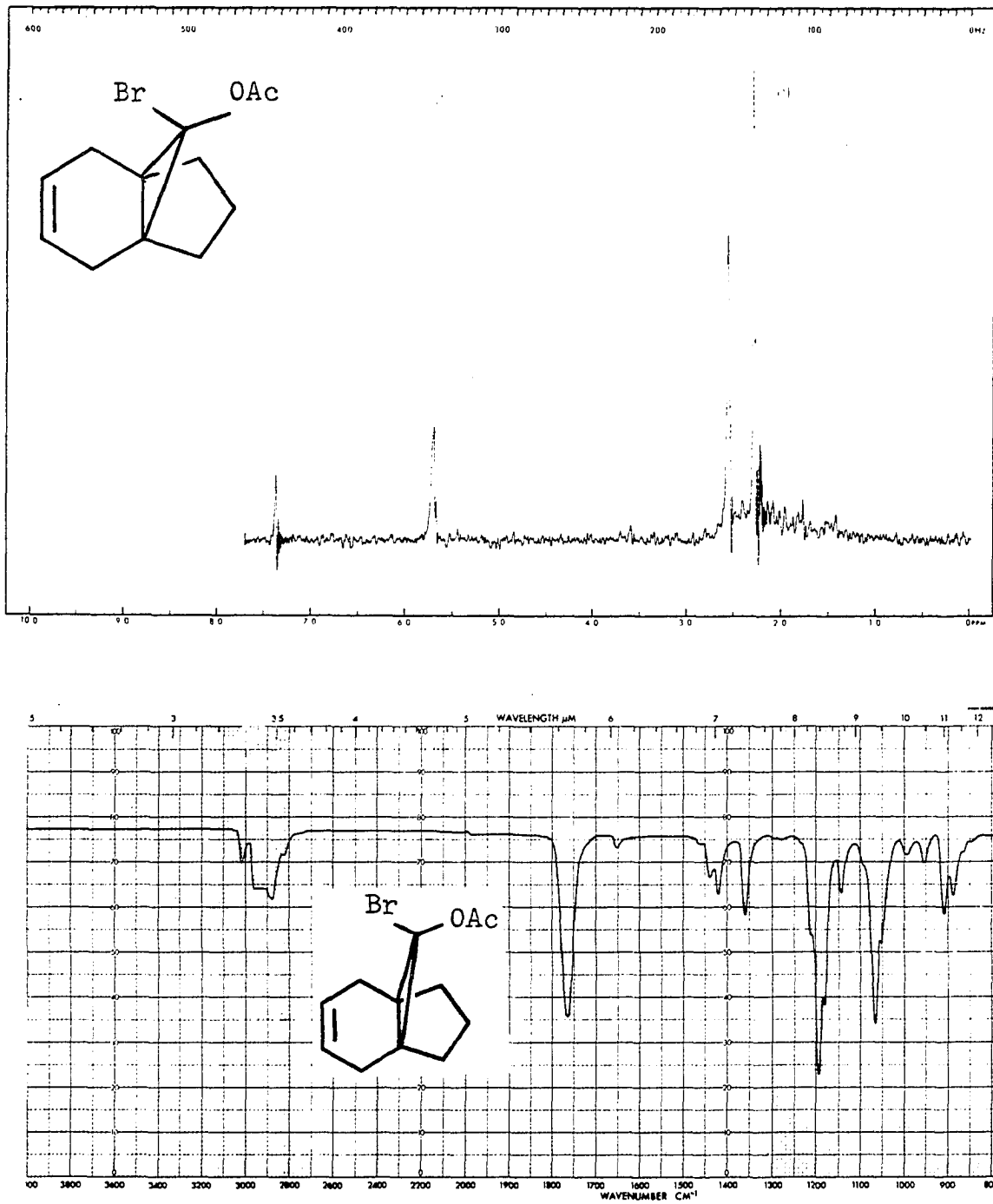
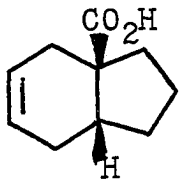
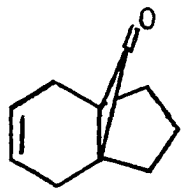


Figure 42. Pmr (Top) and Ir (Bottom) Spectra of 10β-Acetoxy-10α-bromotricyclo[4.3.1.$0^{1,6}$]dec-3-ene (151).

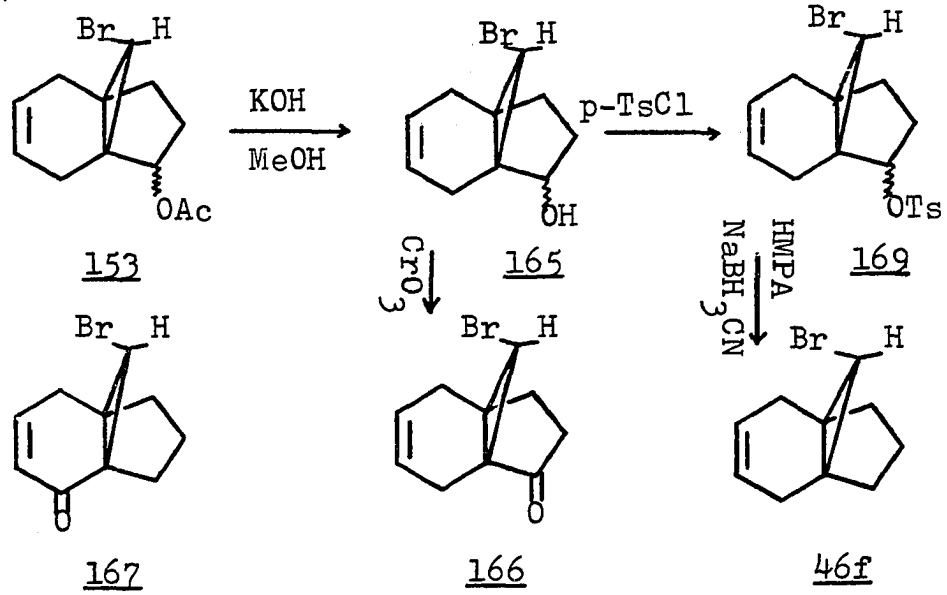


163



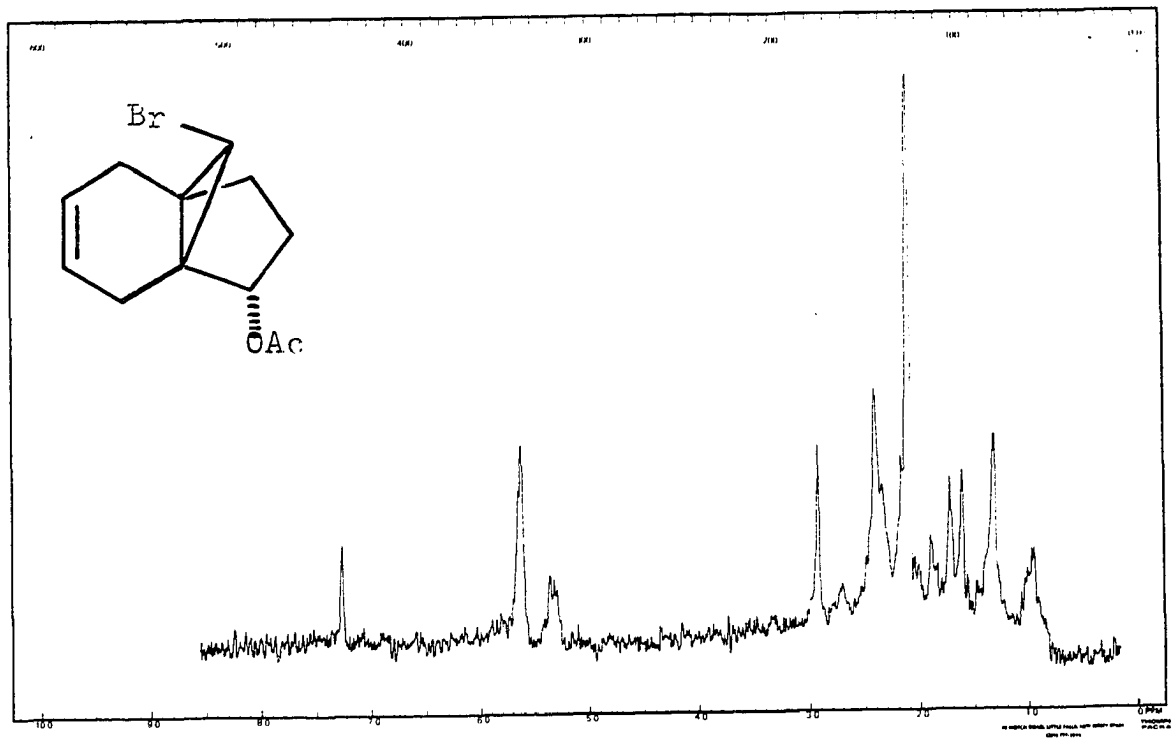
164

The epimeric mixture of 153-endo and 153-exo was separated by careful column chromatography (see Fig. 43 and 44). The position of the acetate group was ascertained by separate hydrolysis and oxidation of the epimers to the same ketone (166, see Fig. 45, which also served to prove the epimeric nature of the isomers). This ketone showed an ir absorption at 1735 cm^{-1}, entirely appropriate for a 5-membered ring ketone conjugated to a cyclopropane, but clearly inconsistent with a conjugated cyclohexenone (e.g. 167).



153 165 169

167 166 46f



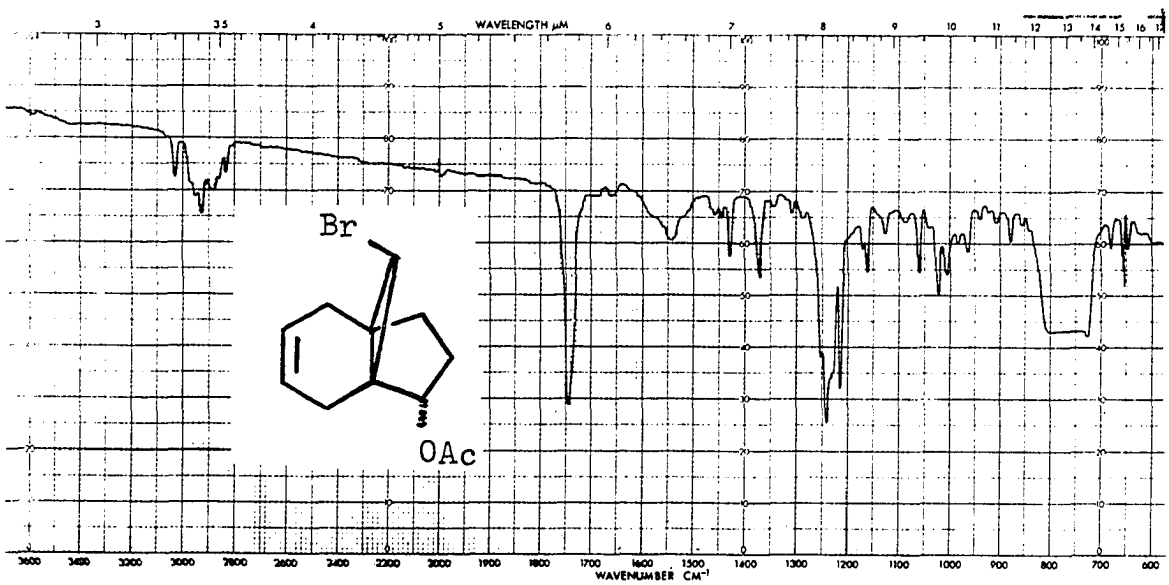


Figure 43. Pmr (Top) and Ir (Bottom) Spectra of 7<u>endo</u>-Acetoxy-10α-bromotricyclo[4.3.1.$0^{1,6}$]dec-3-ene (<u>153</u>-<u>endo</u>).

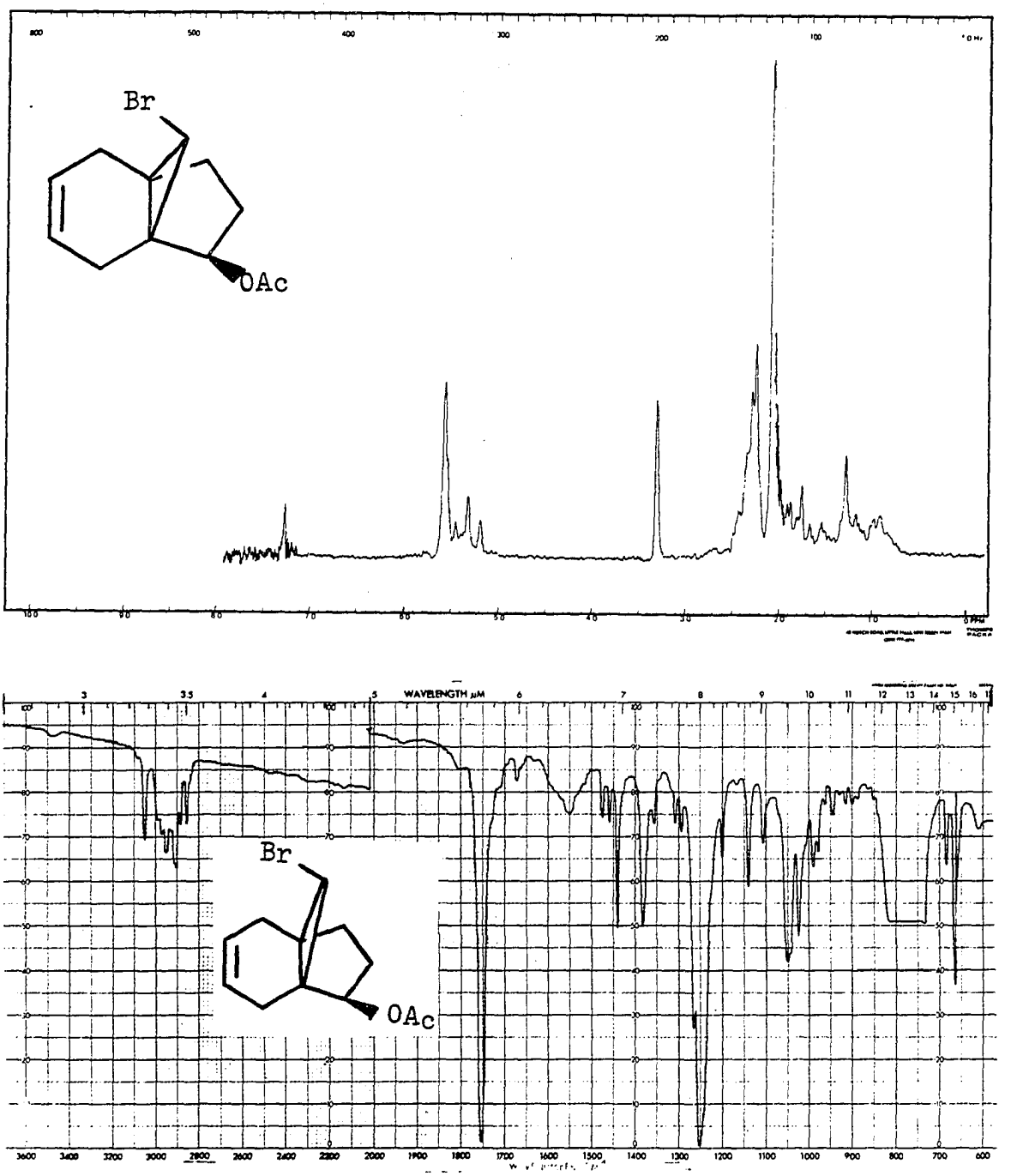
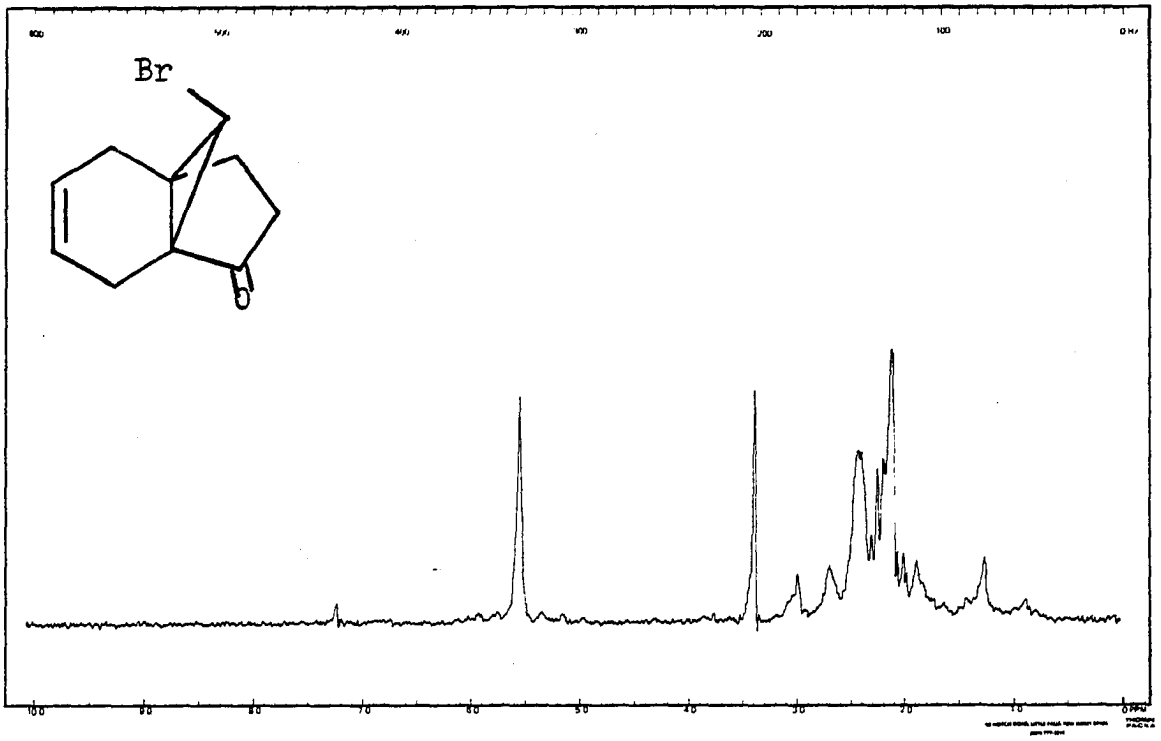


Figure 44. Pmr (Top) and Ir (Bottom) Spectra of 7$_{\underline{exo}}$-Acetoxy-10α-bromotricyclo[4.3.1.0^{1,6}]dec-3-ene (153-exo).



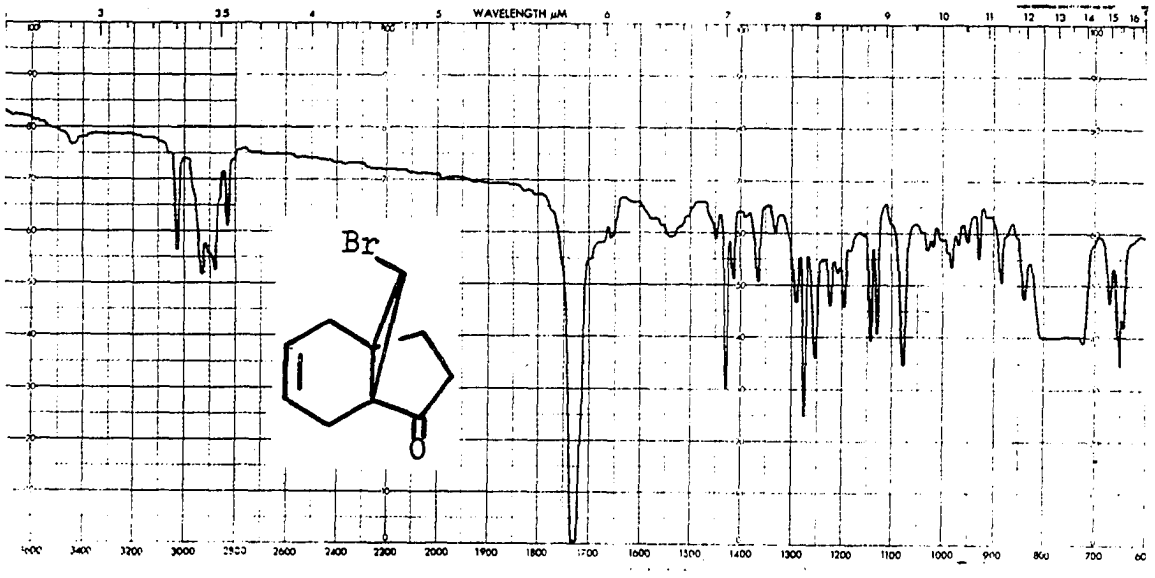
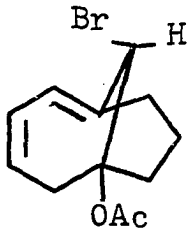
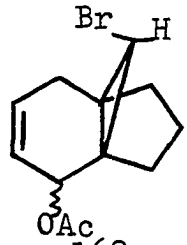


Figure 45. Pmr (Top) and Ir (Bottom) Spectra of 10α-Bromo-7-exotricyclo[4.3.1.$0^{1,6}$]dec-3-ene (166).



170



168

Thus 168 and/or the bridgehead olefin 170 were not solvolysis products. The orientation of the bromine atom on the cyclopropane ring was proven via hydrolysis of the epimeric acetates, 153 to the epimeric alcohols, 165 (see Fig 46 and 47), followed by tosylation and sodium cyanoborohydride reduction of the tosylates, 169, to the known (vide supra) bromide, 46f It should be noted that the reduction of the tosylate had to be carried out *in situ* (with addition of HMPA), since attempts to isolate the tosylates failed. Also, sodium cyanoborohydride reduction of the tosylhydrazone derivative of 166 did not lead to any identifiable products, as did not similar reduction with catechol borane.

The structural differentiation between 153-*exo* and 153-*endo* was made on the basis of the coupling pattern observed for the methine proton at C_7 (carbon bearing acetate). Thus it was concluded, from an examination of models and use of the Karplus equation, that H_{7}-*endo* (of 153-*exo*) should be coupled to both neighboring protons almost equally, with J = 7.5-8.5 Hz (observed: triplet,

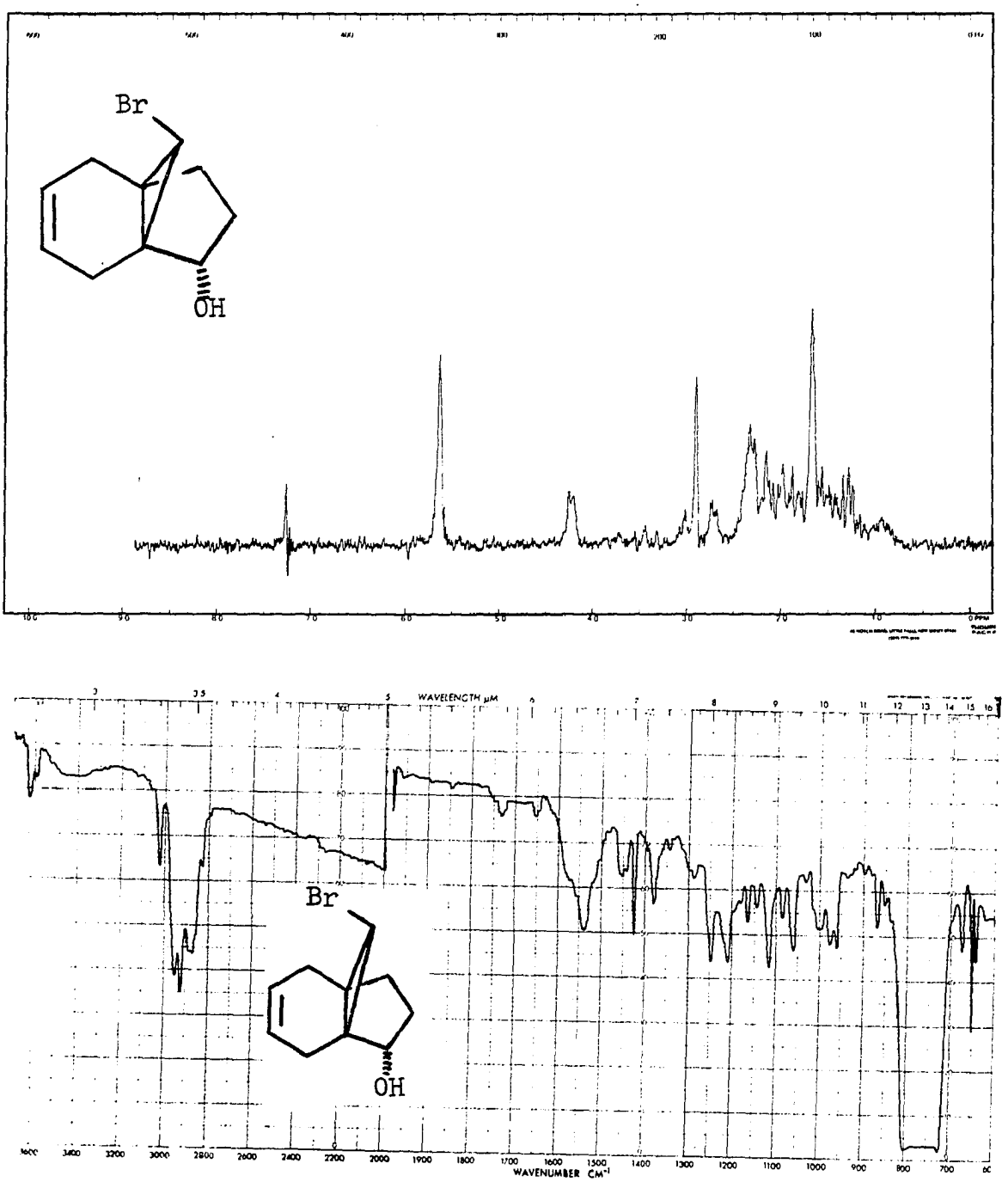
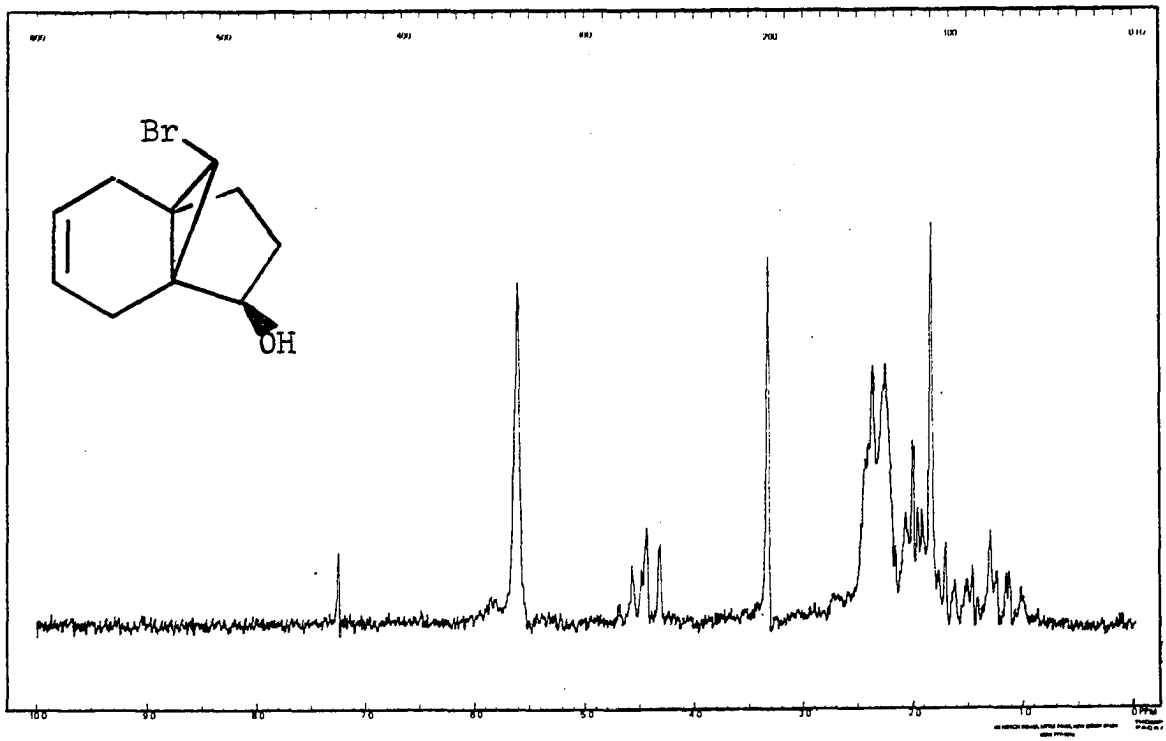


Figure 46. Pmr (Top) and Ir (Bottom) Spectra of 10α-Bromo-7$_{\underline{endo}}$-hydroxytricyclo[4.3.1.0^{1,6}]dec-3-ene (<u>165-endo</u>).



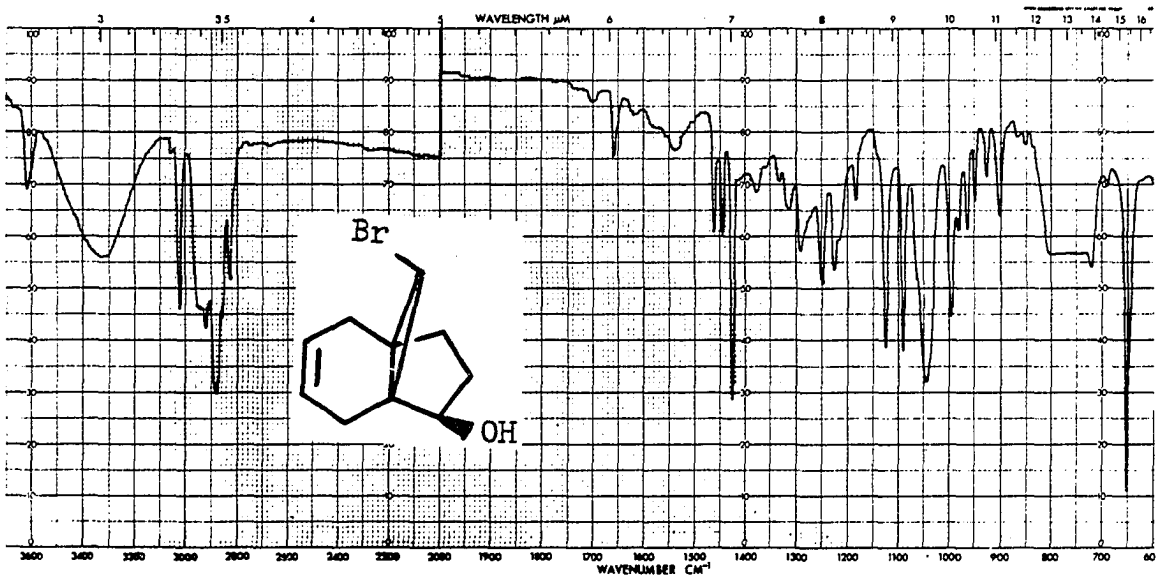


Figure 47. Pmr (Top) and Ir (Bottom) Spectra of 10α-Bromo-7$_{\underline{exo}}$-hydroxytricyclo[4.3.1.0^{1,6}]dec-3-ene (<u>165</u>-<u>exo</u>).

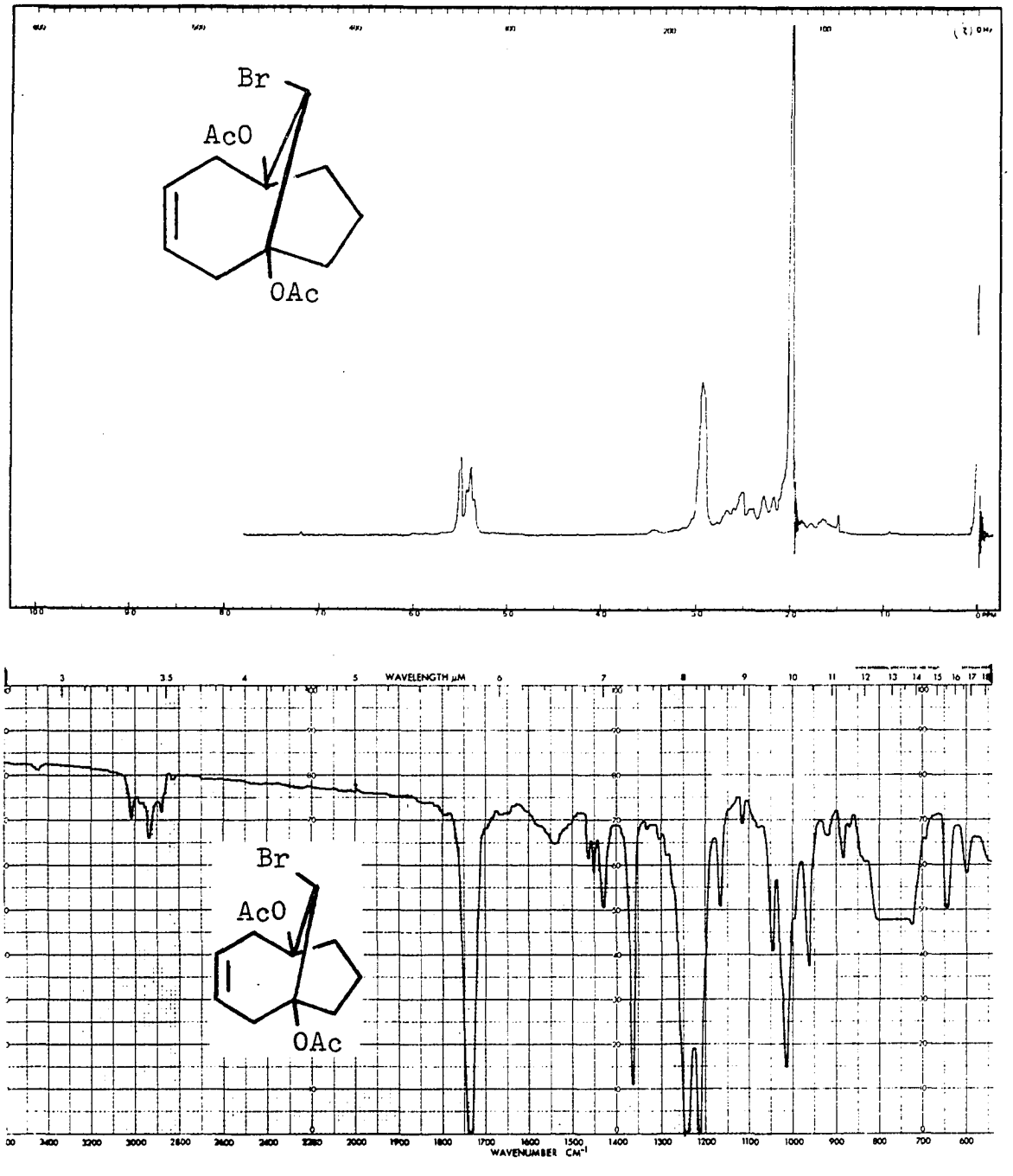


Figure 48. Pmr (Top) and Ir (Bottom) Spectra of 10α-Bromo-1,6-diacetoxybicyclo[4.3.1]dec-3-ene (154).

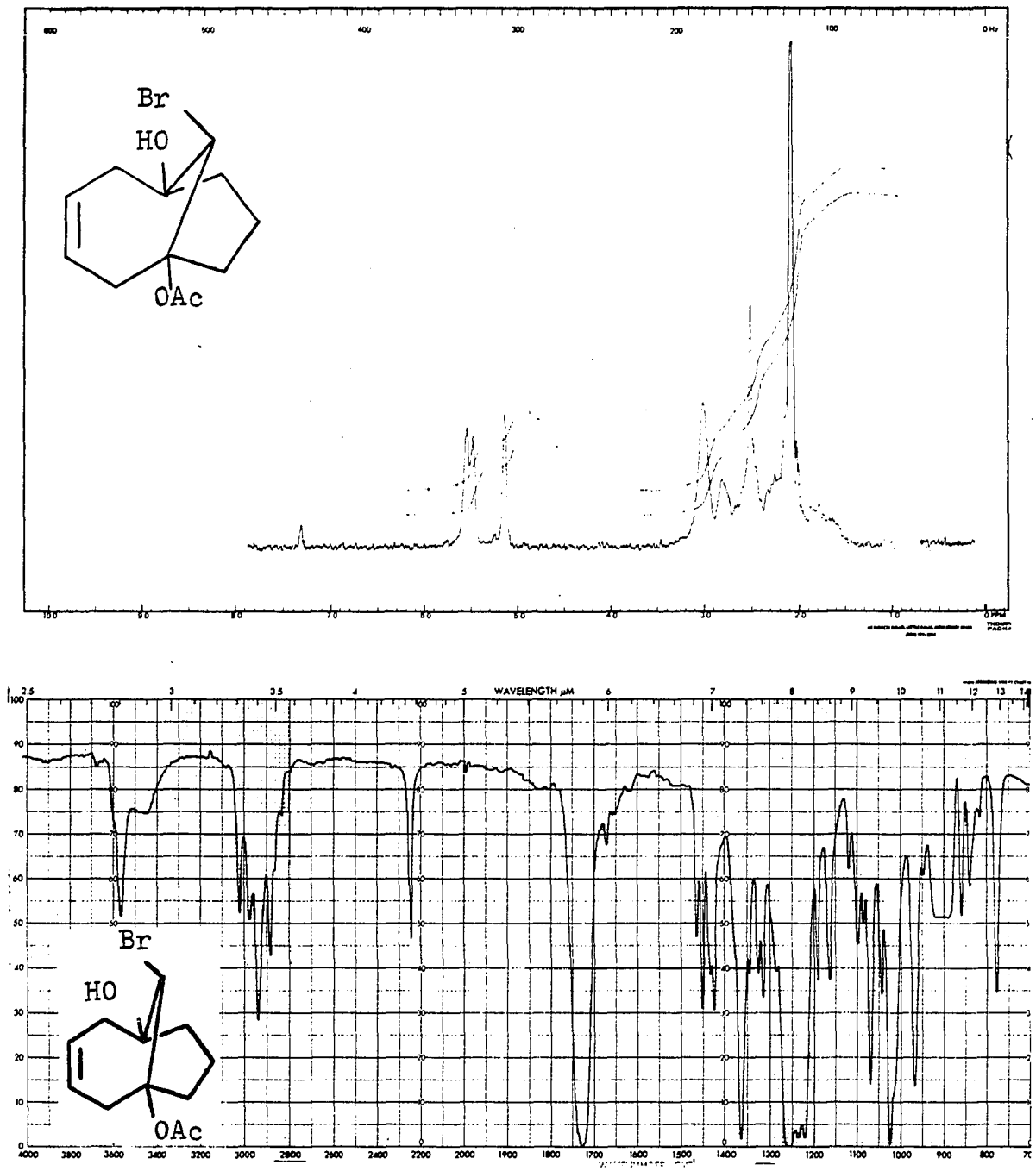
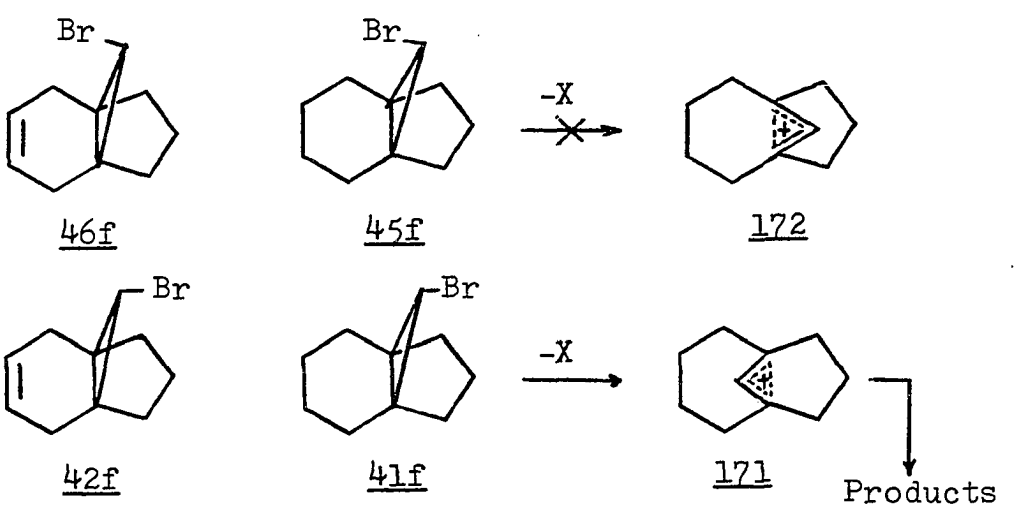


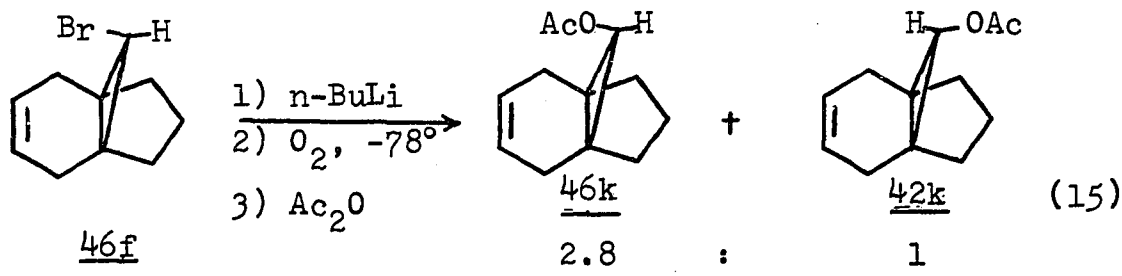
Figure 49. Pmr (Top) and Ir (Bottom) Spectra of 1-Acetoxy-10α-bromo-6-hydroxybicyclo[4.3.1]dec-3-ene (137)

J = 8Hz). On the other hand, $H_{7\text{-}\underline{exo}}$ (of 153-endo) should be coupled to $H_{8\text{-}\underline{exo}}$ (J = 5Hz), but not to $H_{8\text{-}\underline{endo}}$ (observed: doublet, J = 3.5Hz). Corroborative evidence for these assignments came from the cyclopropyl hydrogen chemical shifts. These were δ 3.30 for 153-exo and δ 2.92 for 153-endo (compare δ 2.85 for the corresponding proton of 46f), wherefrom the expected deshielding effect of the exo acetoxy group was clearly seen. The above spectral features were also seen in the corresponding alcohols, 165.

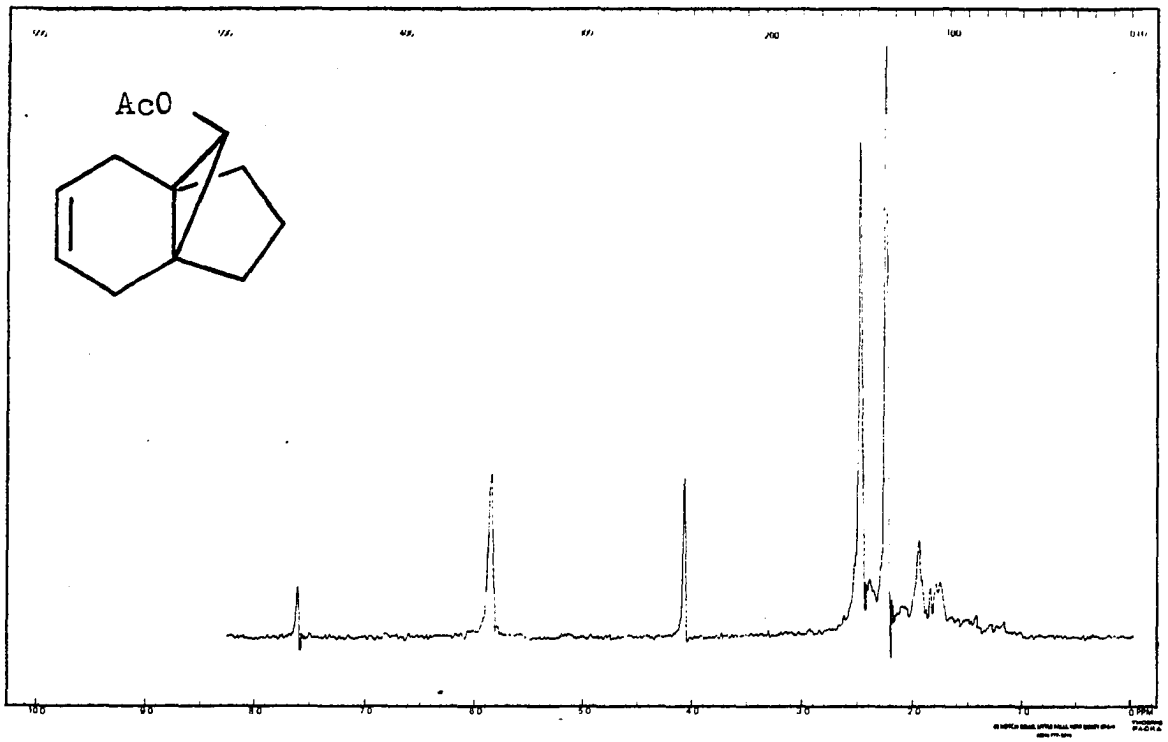
The solvolysis of 46f, 45f, 42f, 41f was undertaken, in part, to demonstrate that the bromine atom syn to the five-membered ring was the more reactive one, and also to further investigate the role of the "partially-opened" cyclopropyl ion, first suggested by Schöllkopf, et al.[71] where we hoped to look at both kinetics and products, with the thought that the three membered ring might be retained in the products.



As could be predicted on the basis of the trans-cyclohexenoid character that would result in the ions derived from 46f and 45f (see 172), neither 46f nor 45f underwent any solvolysis in buffered acetic acid at 125°. While solvent addition eventually intervened for 45f, 46f could be recovered unchanged after 42 days.[43] On the other hand, 42f and 41f which lead to ions with trans-cycloheptenoid character (see 171), both solvolyzed smoothly under buffered conditions to give one product each (in approximately 90% yield, as judged by internally standardized pmr, and in ca. 75% isolated yield[117]). Since spectral data were inconclusive, cyclopropyl acetates 42k and 46k were independently, synthesized (38% overall yield) via lithiation, oxygenation and acetylation of 46f (see Eq. 15). The minor acetate (162) proved to be identical to the solvolysis product from 42f (see Fig. 50 and 51). Similarly, by catalytic hydrogenation of the mixture of 42k and 46k, it was shown that 41k was the solvolysis product from 41f. Similarly, a mixture of 41k and 45k with 1 to 1 ratio was obtained via lithiation, oxygenation and acetylation of 45f (see Fig. 52).



46f → 46k : 42k = 2.8 : 1 (15)



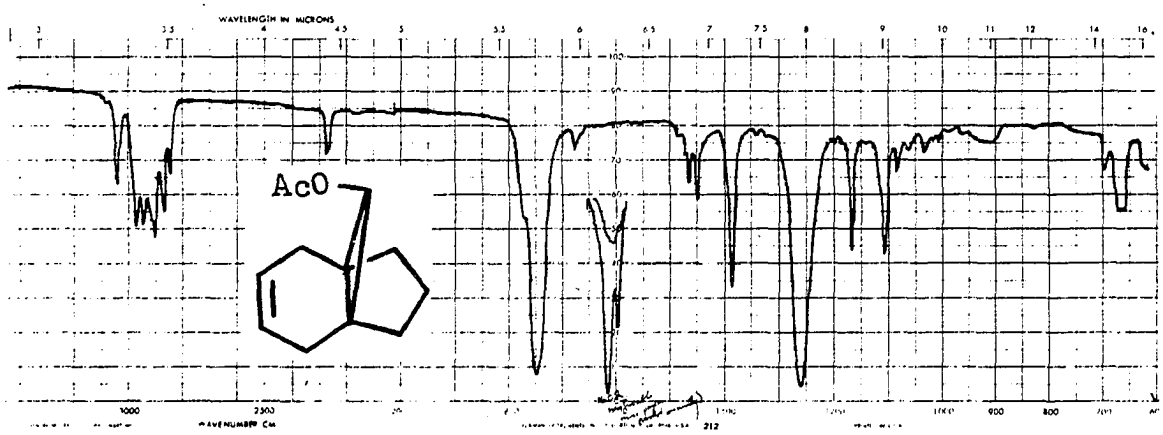
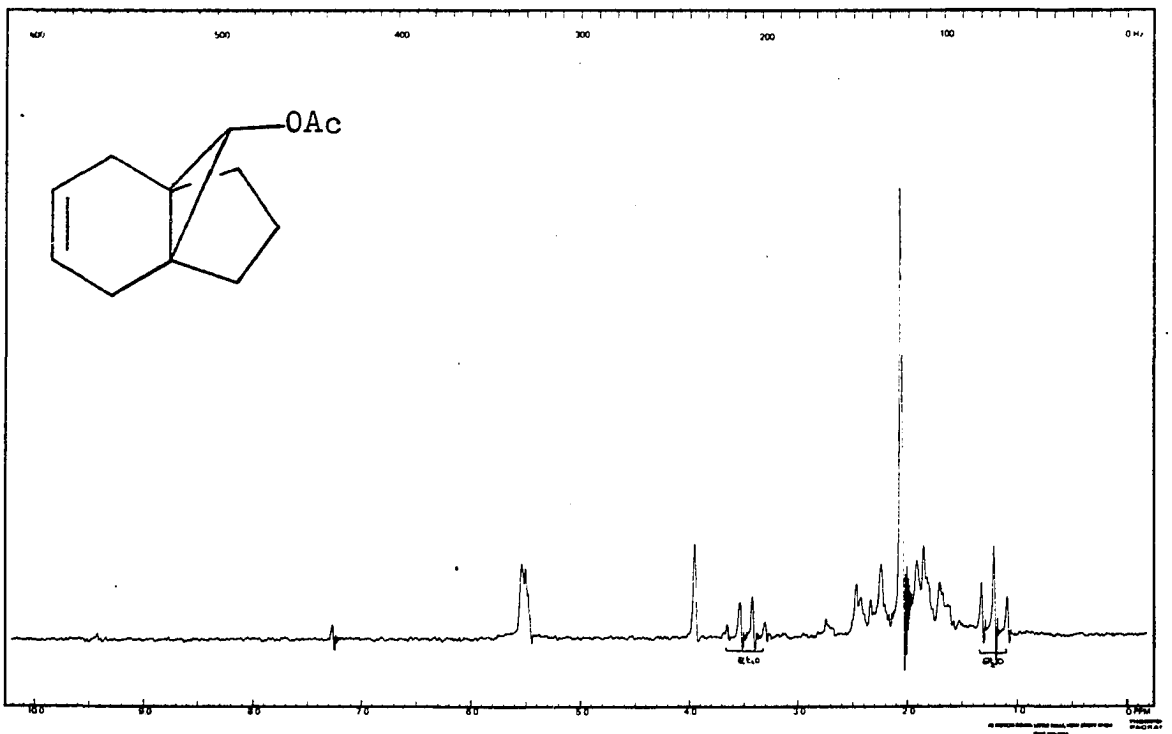


Figure 50. Pmr (Top) and Ir (Bottom) Spectra of 10α-Acetoxytricyclo[4.3.1.$0^{1,6}$]dec-3-ene (<u>46k</u>)



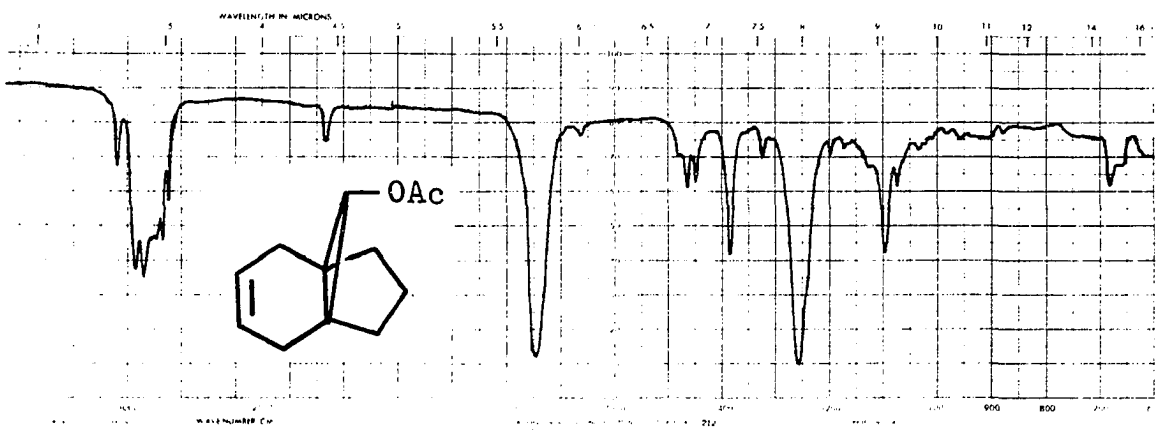


Figure 51. Pmr (Top) and Ir (Bottom) Spectra of 10β-Acetoxytricyclo[4.3.1.$0^{1,6}$]dec-3-ene (42k).

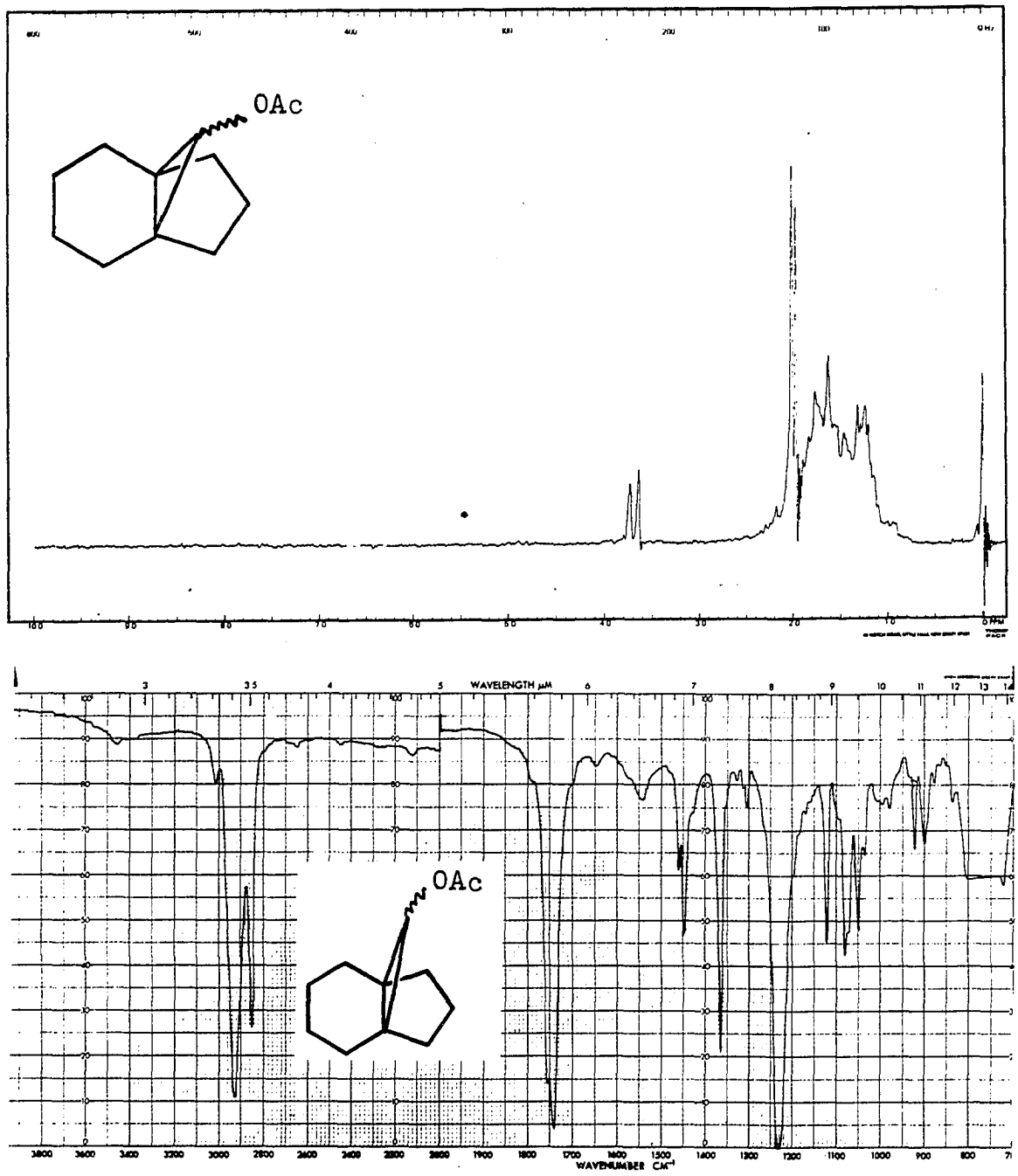
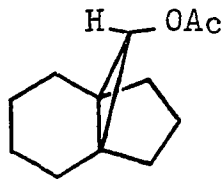
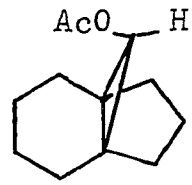


Figure 52. Pmr (Top) and Ir (Bottom) Spectra of Epimeric Mixture of 10-Acetoxytricyclo[4.3.1.$0^{1,6}$] decane (41k and 45k).



41k

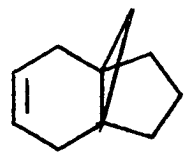


45k

The crucial stereochemical distinction between 42k and 46k was made in two ways. First of all, the pmr pattern of the four allytic H's of 46k is the same as that of 33 and 46f, but differs greatly from 42k and 42f. Secondly, acetates 42k and 46k were separately hydrolyzed back to their alcohols (42k-OH and 46k-OH). Whereas 42k showed normal free (3600 cm^{-1}, m, sh.) and intermolecularly hydrogen-bound (3430 cm^{-1}, m, br.) hydroxyl absorptions in the ir ($CDCl_3$), 46k-OH showed an important intramolecularly hydrogen-bound (3540 cm^{-1}, m, sh.) hydroxyl peak, as well as diminished free (3590 cm^{-1}, w, sh.) and intermolecularly hydrogen-bound (3440 cm^{-1}, w, br.) hydroxyls, thereby confirming the stereochemical assignments.

Warner, et al.[106] had shown that the solvolysis of 33 in the presence of excess silver ion involved a complicated process including silver ion complexation, from which it was not feasible to draw conclusions regarding "partially-opened" cyclopropyl cations. In fact, when the [4.3.1]propellene 42g was treated with excess silver nitrate in acetonitrile, the broad singlet due to the cyclopropyl

protons was split into an AB quartet centered at δ 0.38 (J = 5Hz), which indicated the formation of a silver-olefin complex. Thus Ledlie's reported[99-101] silver assisted solvolysis rates for some [4.4.1]propellanes were deemed to be of limited value.

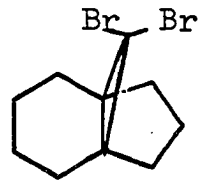
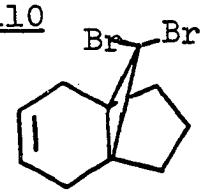
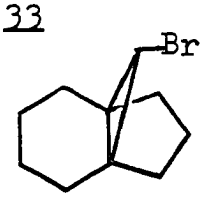
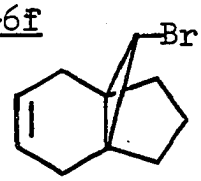
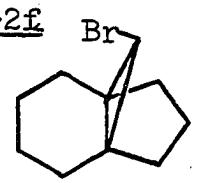
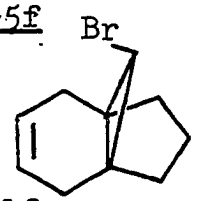


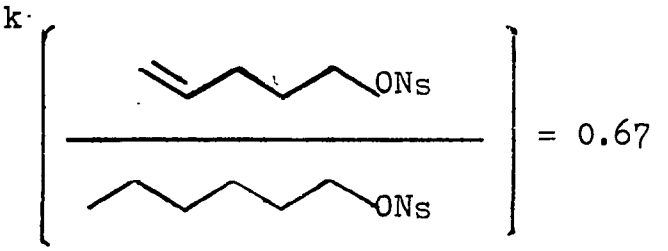
42g

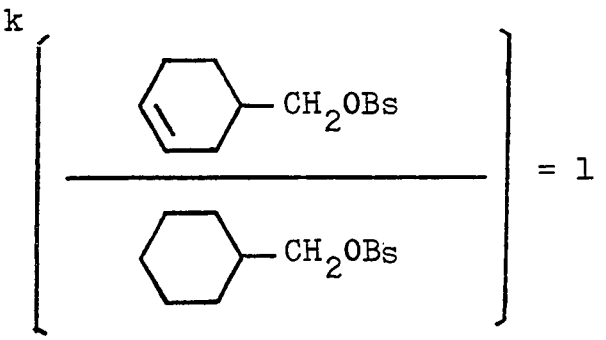
Consequently, the solvolysis rates of 33, 110, 42f, and 46f were measured in buffered acetic acid. The observed first order rate constants (summarized in Table 10) show that the double bond of 33 produces essentially the same decelerative effect as that of 42f. If the developing charge were to be localized at the cyclopropyl bridge position, C_{10}, in the transition state for the ionization of 33 and 42f, then the double bond in each case should exert a normal δ inductive effect. Some known[118-120] values for δ inductive effects for acetolysis reveal only very modest rate retardations, even for a nearly limiting case (176-178).

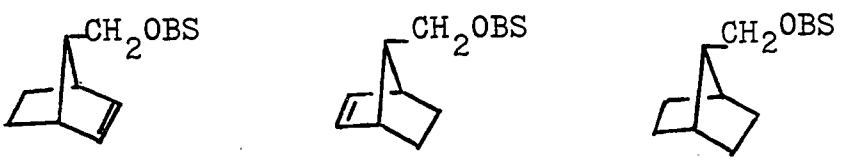
Additionally, no serious decelerative field effect was observed (compare 176 and 178). Interestingly, in 33 and 42f through-space involvement of the double bond should have led to an accelerative interaction (of the bishomo-$C_5H_5^+$ type,[121] 179). Recently, Creary[122] has shown that an

Table 10. Buffered Acetolysis Data for Some Cyclopropyl Halides.

Compound	Temp, °C	k_1, sec^{-1}	krel, 125°	ΔH, kcal/mol	ΔS, eu
 110	125	$(1.80\pm0.18)\times10^{-3}$	307	17.7	-28.0
	100	$(3.44\pm0.28)\times10^{-4}$			
 33	125	$(6.94\pm0.59)\times10^{-5}$	11.8	20.7	-26.6
	100	$(1.01\pm0.02)\times10^{-5}$			
 46f	125	$(1.18\pm0.93)\times10^{-4}$	20.1		
 42f	125	$(5.86\pm0.26)\times10^{-6}$	1.0		
 45f	125	no solvolysis	-		
 41f	125	no solvolysis (42 days)	-		

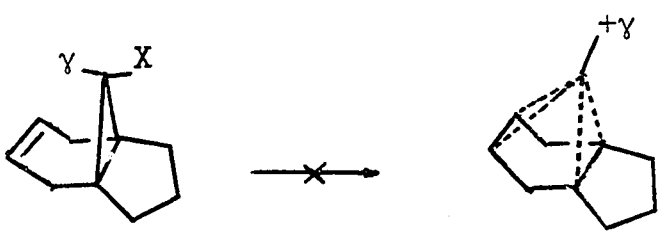




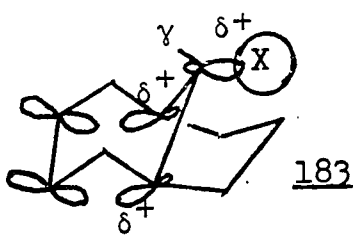


krel 1.50 1.08 2.64

176 177 178

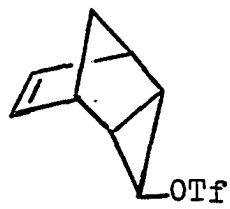


179

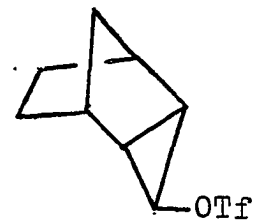


183

appropriately constrained double bond accelerates the solvolysis of a cyclopropyl derivative by at least a factor of 81 (see 181, 182). Clearly, then, our kinetic results cannot be understood in terms of a δ inductive effect.

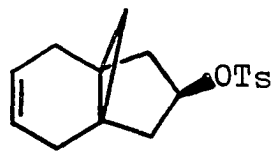


181

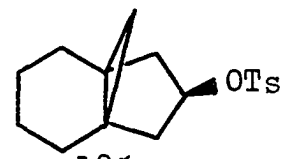


182

krel 81 1



184



185

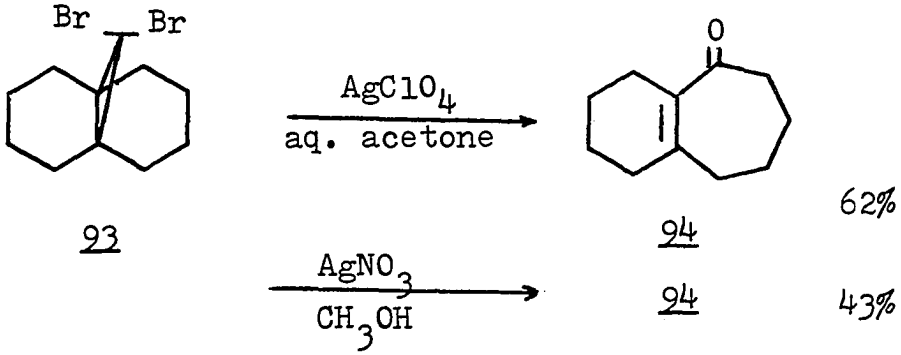
krel 1 5.5

If considerable ring opening did occur (to a partially-opened cyclopropyl cation) at the transition state, then the double bond could be in a γ position. The expected inductive rate retardation is a factor of 5-9, based on what was observed[123] for the cyclopent-3-enyl system. Also, the double bond in 42g retarded the addition of acetic acid to the cyclopropane ring (where charge developed at C_1) by roughly 5 fold.[43] Lastly, the decelerative effect

of the double bond in 184 (relative to 185) was 5.50.[124] This system is particularly valuable as a model since it is a limiting one and charge is known to be delocalized to the two cyclopropyl bridgehead positions (γ double bond). Therefore the observed "inductive" effects for 33 and 42f may be too large to explain without invoking an antibis-homoaromatic conjugative effect (see 183); however, this point requires further investigation. Whatever factors were responsible for the slower solvolysis rate of 33 (relative to 110) also caused the formation of 151 (as 10% of the observed products). Thus less charge was delocalized to the bridgehead positions in the ion derived from 33 then in that from 110. Nevertheless, considerable charge delocalization to the bridgehead positions must be invoked for 33 and 110 (where the products were those of ring opening) and 42f and 41f (where no ring opened products were formed). Certainly 41f achieved as much stabilization in its ionization to a partially-opened ion as did endo-7-norcaryl bromide (180) in its ionization to a cycloheptenyl ion. Thus our combined kinetic and product data should lay to rest any lingering doubts about the validity of the partially-opened cyclopropyl cation concept. The retentive stereochemistry observed in the products from 42f and 41f, which can be explained on the basis of a nonplanar ion, needs to be studied further.

The [4.4.1]Propellane System

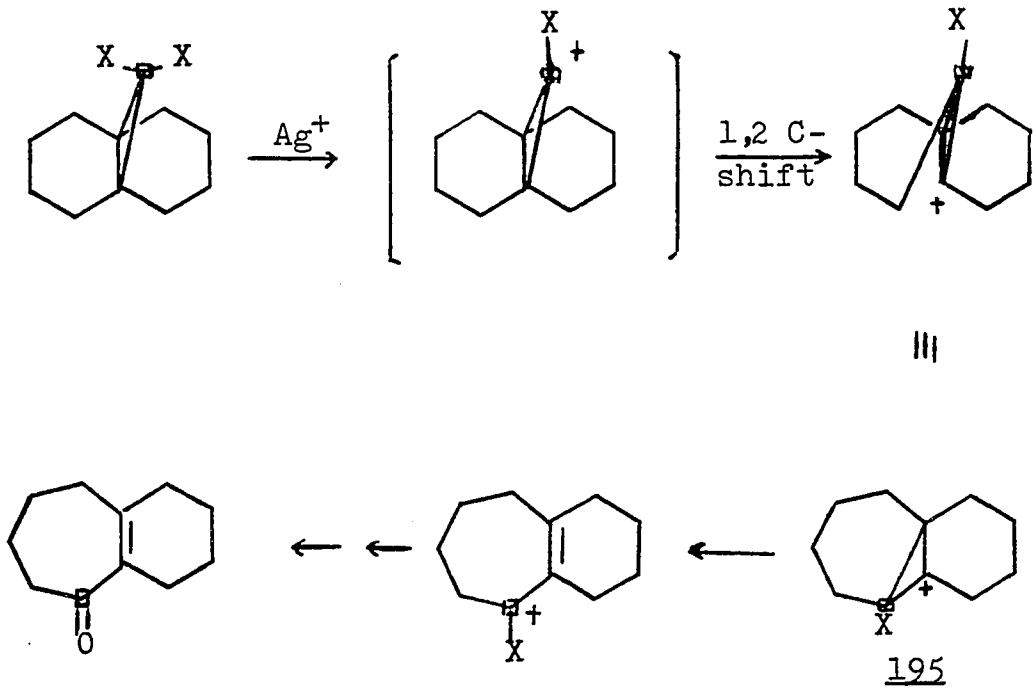
Reese and Stable[104] and Ledlie[99] have independently studied the silver-assisted solvolysis of 93 in aqueous acetone and methanol, respectively, and isolated one major product, which was identified as 94.



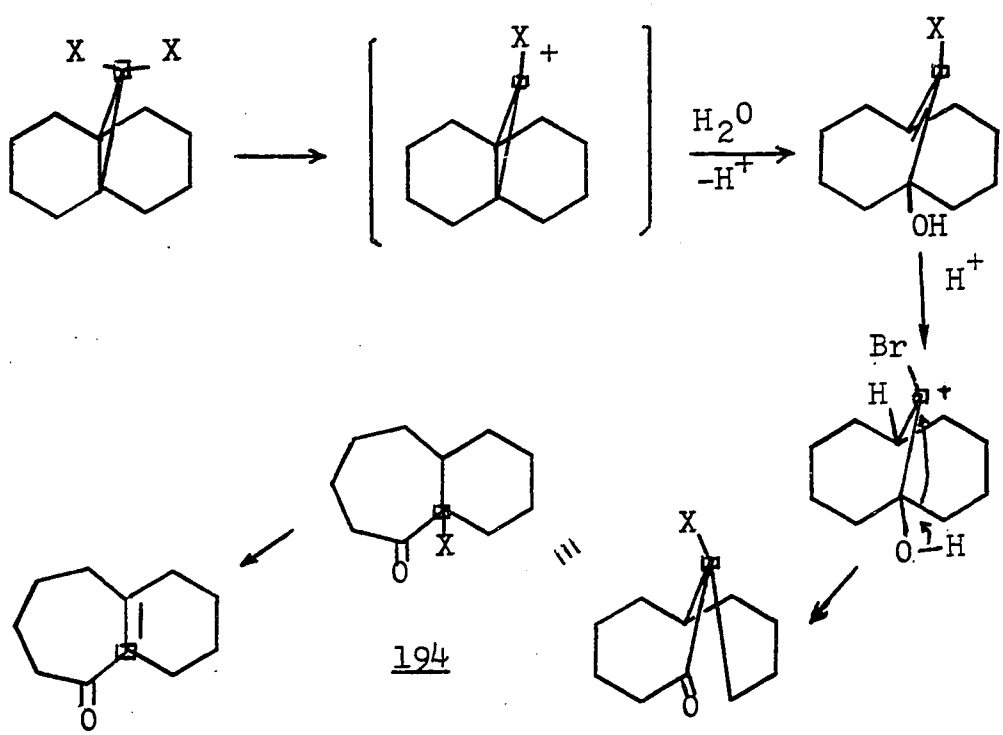
These authors rationalized 94 as arising via a mechanism involving a 1,2-alkyl shift in a cyclopropyl cation(Scheme 10). This work was reinvestigated, originally due to a desire to compare the acetolysis rate of 93 with that of 110. Our initial step was to investigate the acetolysis products. These were found to be 94 (36%), 187 (19%), 188 (21%) and two unidentified acetates (ca. 18%).[125]

The structure of compound 187 was established from spectroscopic (including exact mass) measurements, and by analogy of these spectra to those of 112. The UV and pmr spectra of 188 were as reported.[126] Compound 187 clearly arises from an intermediate containing a bridgehead double bond (see Fig. 53,54). Therefore, the

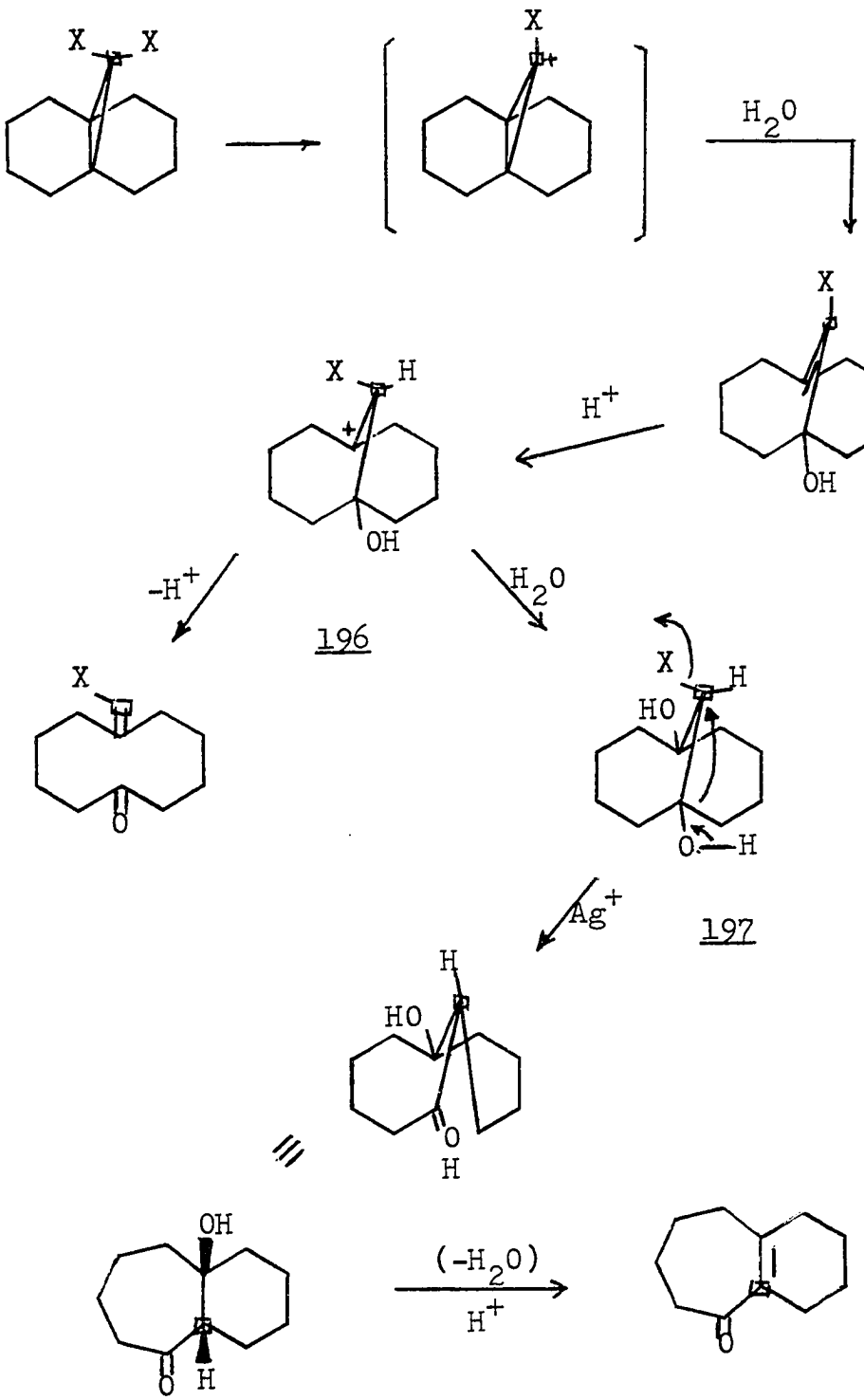
Scheme 10



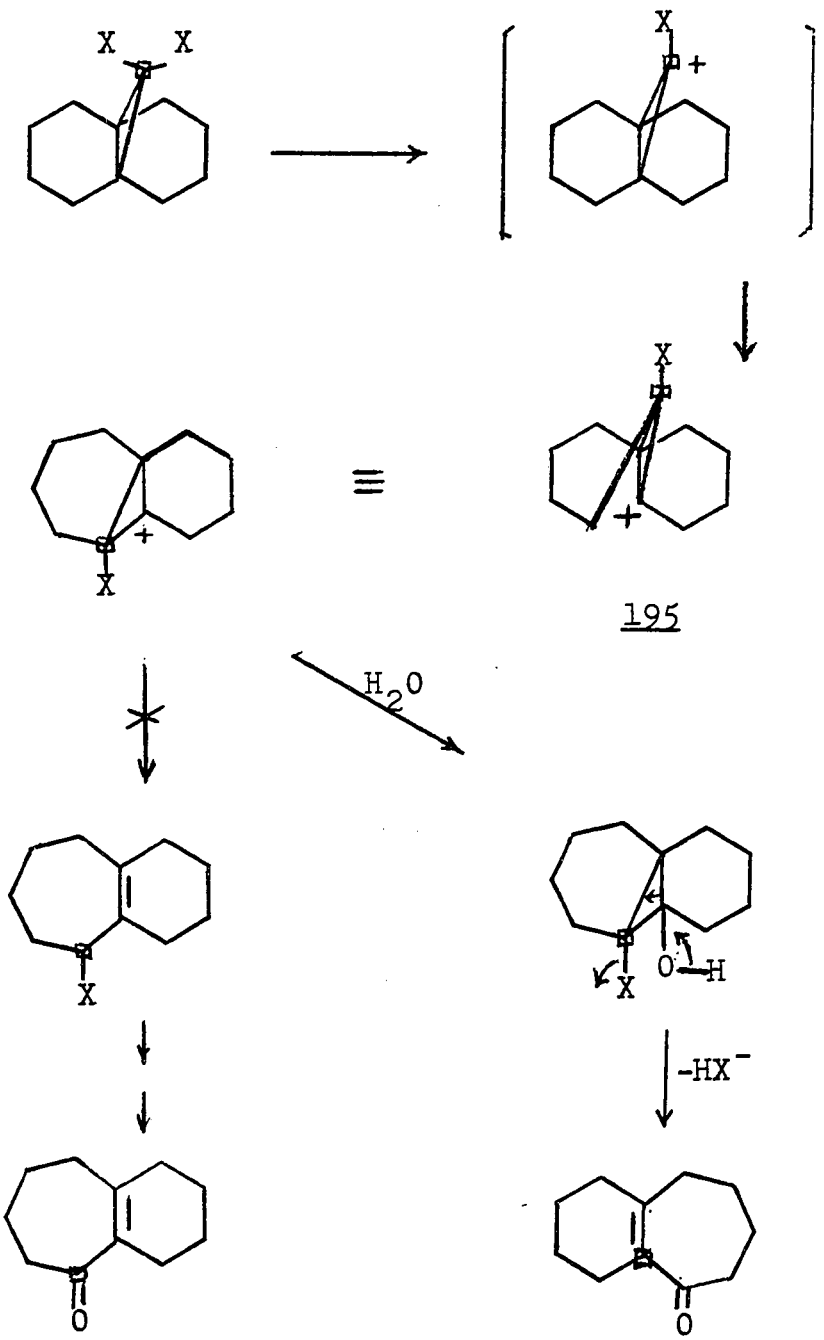
Scheme 11



Scheme 12



Scheme 13



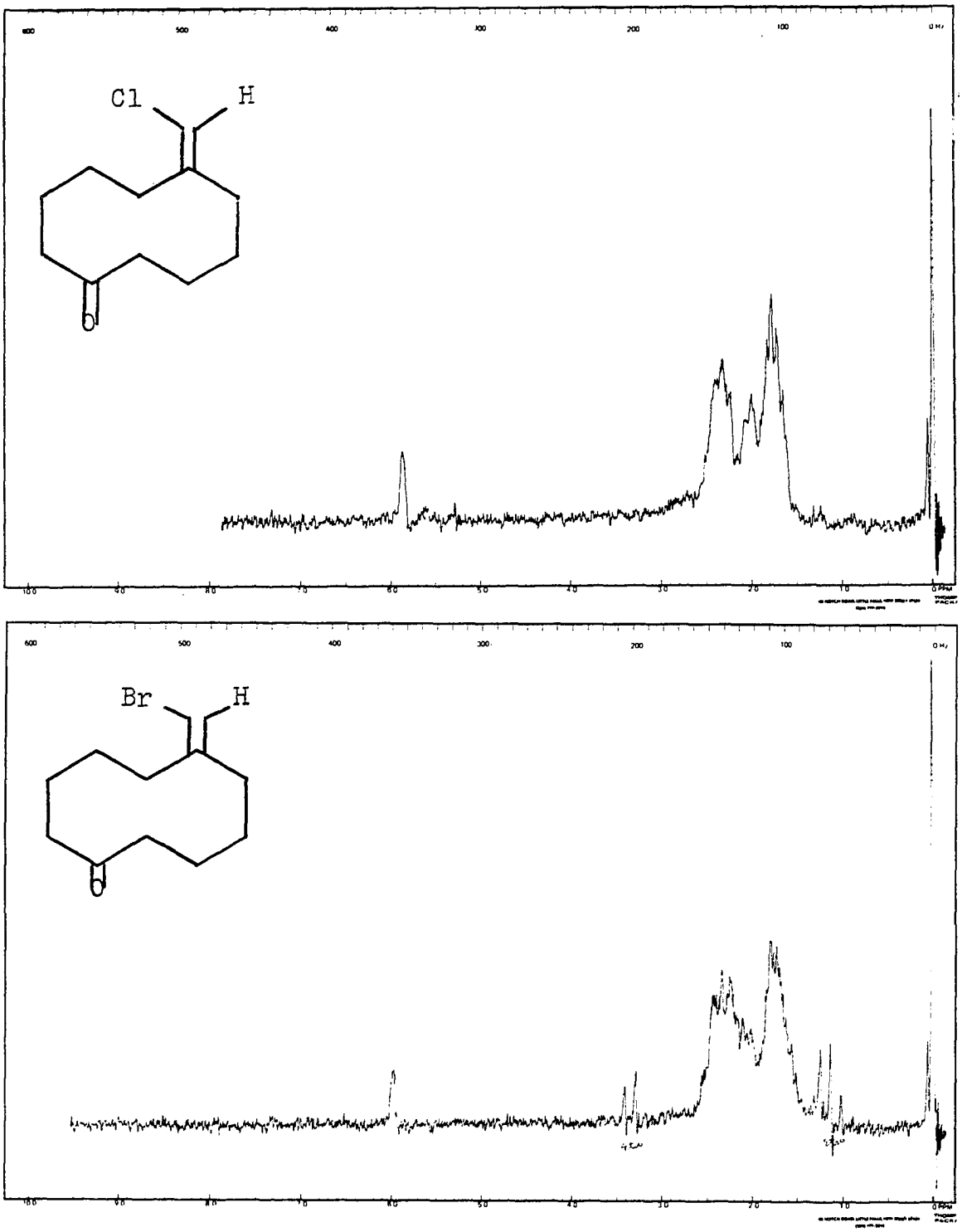


Figure 53. Pmr Spectra of 6-Chloromethylenecyclodecanone (189, Top) and 6-Bromomethylenecyclodecanone (187, Bottom).

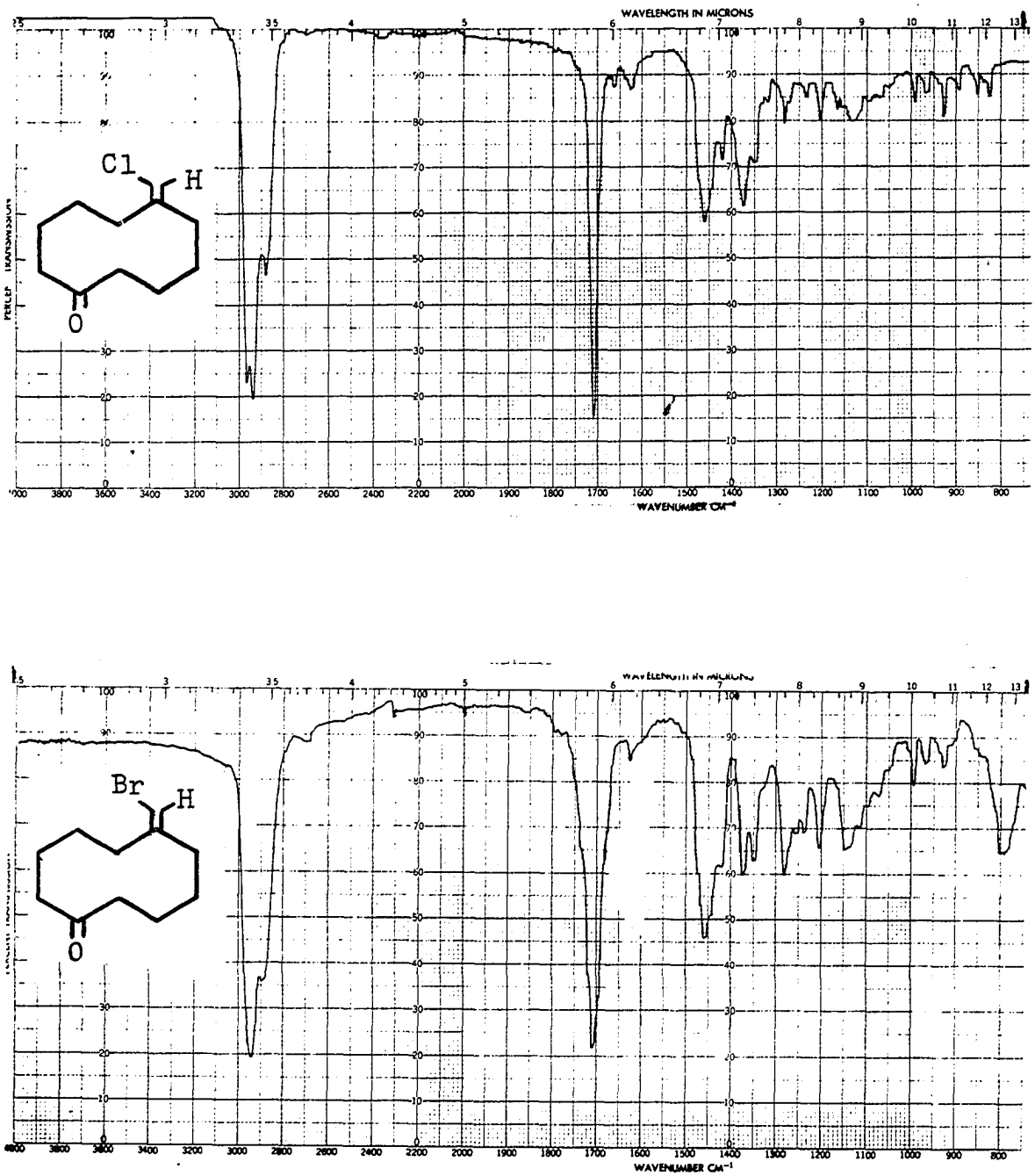
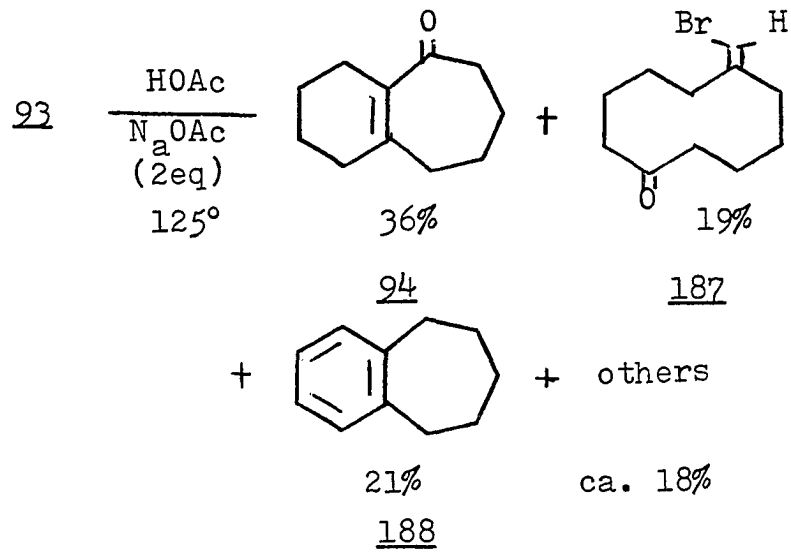


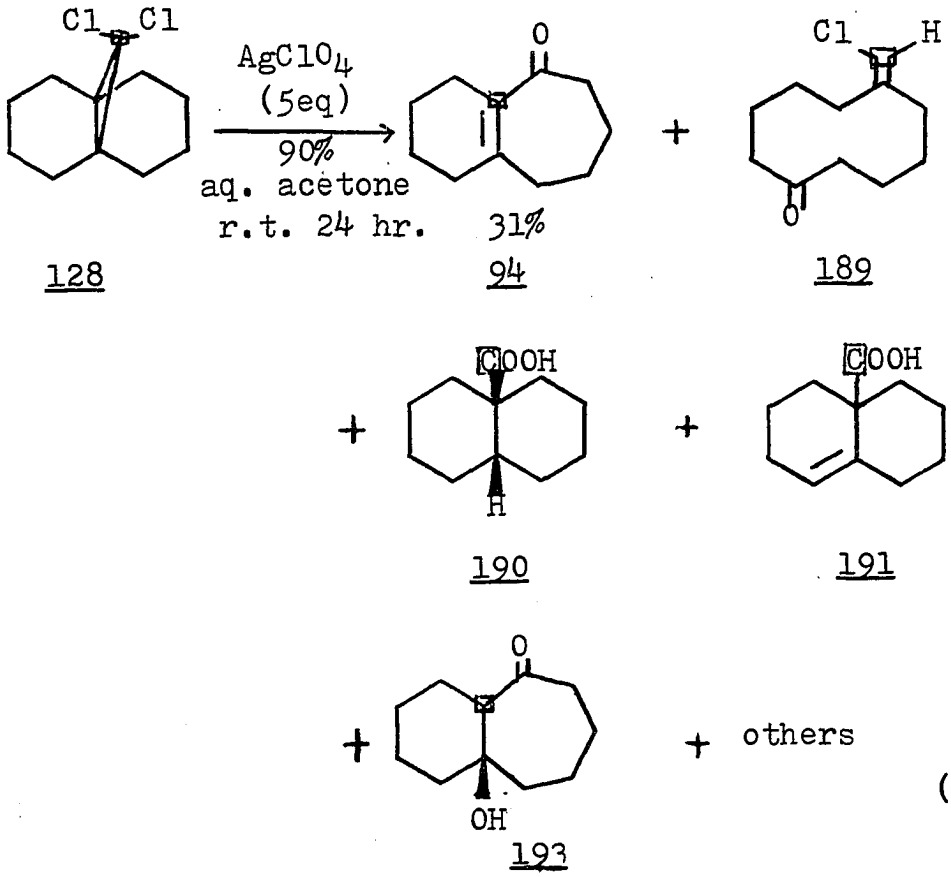
Figure 54. Ir Spectra of 6-Chloromethylenecyclodecanone (189, Top) and 6-Bromomethylenecyclodecanone (187, Bottom).



Ag^+-assisted solvolysis of 93 in 90% aq. acetone was repeated, and 187 was found to be a minor product (spotted first by ir: $\nu_{C=O}$ = 1710 cm^{-1}; pmr: δ 5.95 for vinyl proton, and positively identified by glc-mass spectrometry as being formed in ca. 0.4% yield), while 94 was indeed the predominant one. It thus occurred to us that alternate pathways for formation of 94. involving the intermediacy of a bridgehead olefin, were possible (Schemes 11 and 12.) An important distinction between the bridgehead olefin mechanisms (Schemes 11 and 12) and the originally advanced mechanism (Scheme 10) was that a label placed at C_{11} would end up at the α position of the enone 94 if 94 were formed via a bridgehead olefin, but at the carbonyl carbon if the alkyl shift process occurred. With this in mind, a ^{13}C labeling experiment, utilizing dichloro[4.4.1]propellane,

128, enriched at C_{11} such that C_{11} was 5.8% ^{13}C (synthesized by standard methods, using ^{13}C-enriched chloroform purchased from Merck), was undertaken.[69]

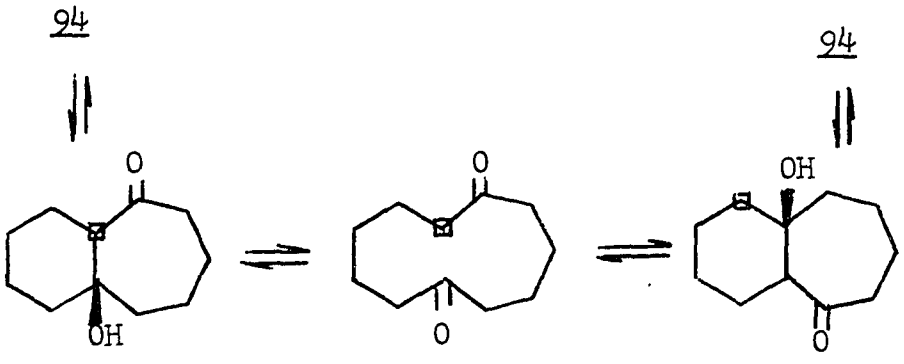
When 128 was allowed to react with 5 equivalents of $AgClO_4$ in 90% aq. acetone at room temperature, at least seven products were formed after 24 hr. (note the roughly 20-fold rate deceleration compared to 93). The isolable products were as shown in Eq. 16.



(16)

The carbons marked with a square indicate the position of the ^{13}C label, as determined by cmr spectroscopy (see experimental). The lower yield of carboxylic acids 190

and 191 is, in part, due to a mechanical loss during work-up. However, when the reaction was repeated, an 18% yield of carboxylic acids was obtained. From high resolution mass spectral data, it was calculated, assuming all of the excess ^{13}C remained at one carbon, that the enriched carbon position of 94 contained a total of 5.3% ^{13}C. In the cmr spectrum of 94, the carbonyl, C_α and C_β carbons exhibit resonances at δ 205.4, 153.2 and 135.3, respectively. Table11 shows the integrated intensity of these three peaks after data collection at 20-sec pulse intervals, both for enriched and unenriched samples of 94. If C_β was taken as a standard, then it appeared that, within experimental error, all of the label wound up at C_α. From the integration, the ^{13}C content at C_α was calculated to be 5.6%, in good agreement with the high resolution mass spectral data. However, a possible worry involved scrambling of the label, as follows:



193 193

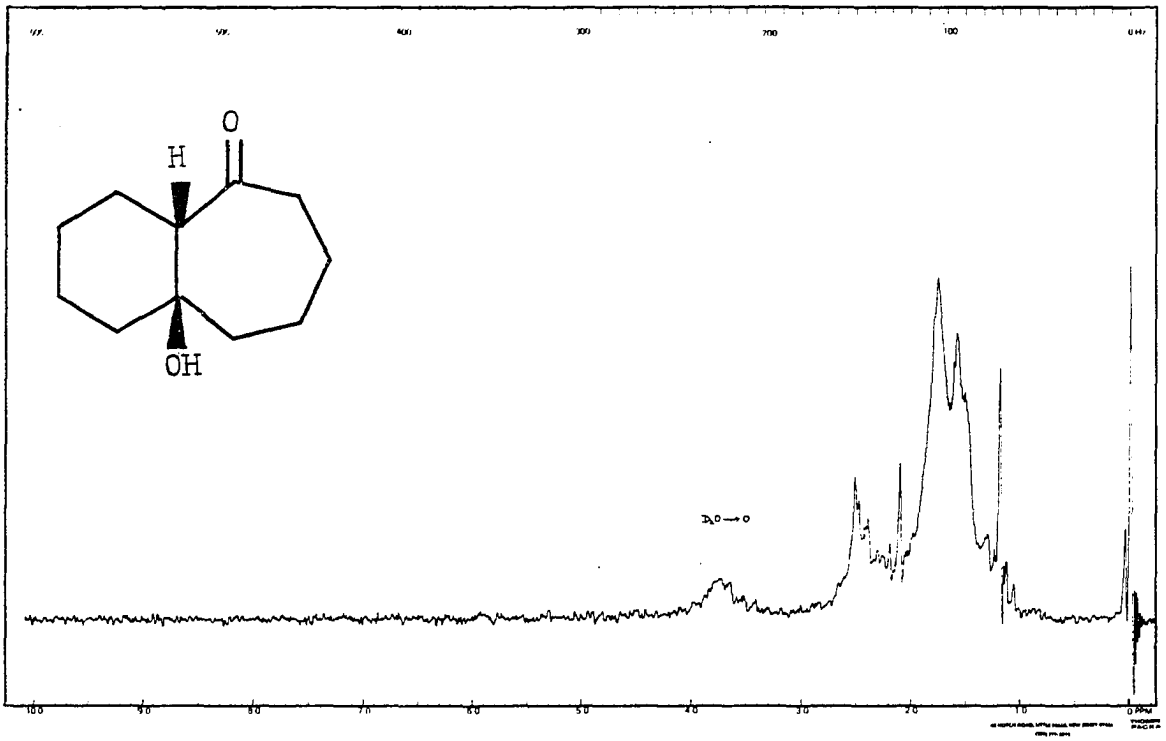
However, a control experiment showed that no change in the cmr intensities for 94 occurred after treating 94 under the reaction conditions for 48 hr; also, no buildup of 193 was noticed under these conditions, implying 94 is not readily hydratable. Thus the pathway shown in Scheme 10 proved to be incorrect.

Table 11. FT-CMR Data for Enone 94.

Compound	relative area carbonyl	C_α	C_β	no. of pulses (20-sec intervals)
unenriched 94	1.02	0.62	1.00	2000
^{13}C-enriched 94	0.84	5.06	1.00	1710

Obviously the isolation of hydroxyketone 193 was a key finding, for it mitigated strongly against the mechanism shown in Scheme 11. The structure of 193 was indicated by the finding that it yielded 94 upon brief treatment with conc. HCl at room temperature, or upon exposure to the acidic solvolysis conditions. The *cis* ring fusion has been assumed by analogy to the structure of its homolog, 130 (see Fig. 55 and 33).

However, the intervention of haloketone 194 still had to be considered, but as a source of carboxylic acid 190. The literature revealed two relevant cases[127] (see Eq. 17 and 18) Both tertiary α-bromoketones give Favorskii-type rearrangement products, but no α,β-unsaturated enone. If



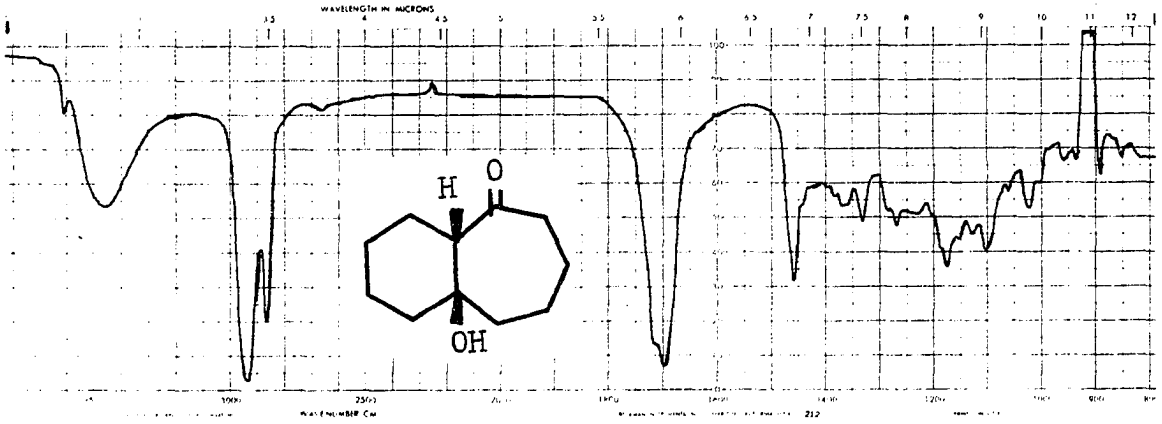
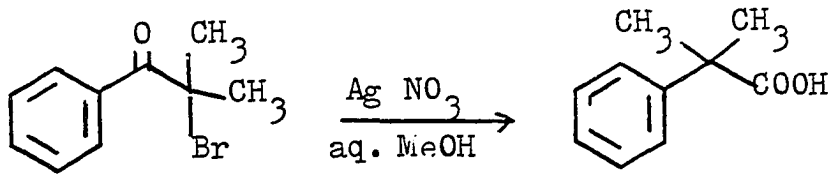


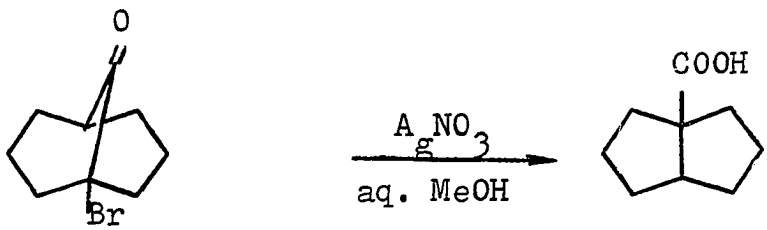
Figure 55. Pmr (Top) and Ir (Bottom) Spectra of 7-Hydroxybicyclo[5.4.0]undecan-2-one (193)

190 were to have arisen via 194, the ^{13}C label would have to have ended up at the carbon α to the carboxylic acid moiety (see Eq. 19). However, the finding of the ^{13}C label at the carboxylic acid carbon excluded the above pathway.

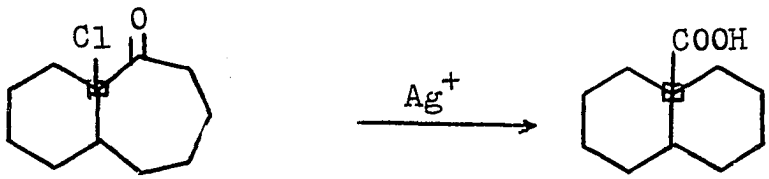


(17)

40%



(18)



(19)

195 190

The alkyl shift mechanism shown in Scheme 10, wherein the rearranged cyclopropyl cation 195 must be trapped with water prior to any ring opening (this unlikely requirement was made necessary by the failure to observe any scrambling of the ^{13}C label, which would occur otherwise), still

presented itself as a possibility, although it could not have been the sole route for the formation of 94 (the finding of 193 indicated that). It was noted that, in Scheme 12 ion 196 faced two fates: (1) fragmentation to ketone 189 or (2) collapse with water to diol 197 (and eventually 94). Contrariwise, 195 (Scheme 10) reacted with water only once, and led only to 94. Thus a simple test was evident. If the mechanism shown in Scheme 10 were dominant, then a decrease in the concentration of water should not dramatically affect the ratio of 94 to 189. Contrariwise, if the mechanism shown in Scheme 9 predominated (or were solely involved), the ratio should alter drastically. The results of treating 93 with 5 eq. of $AgClO_4$ in various concentrations of aqueous acetone are given in Table 12. The data are consistent only with Scheme 12.

It is interesting to note that the percentage of carboxylic acids (190-192) formed remained fairly constant (at ca. 35%), even when the amount of water was decreased to 1%. From the work of Groves,[113] one might have expected an increase in the percent of acids with decreasing amounts of water (as the solvent becomes less able to stabilize charge and tight ion pairing becomes more significant).

It was found that upon hydrolysis of 93 in 90% aq. acetone, the ratio of the resulting carboxylic acids (190:

191: 192), which were isolated by base extraction, was,

Table 12. Product Ratios for Various Aqueous Acetone Mixture (GLC Analyses of Duplicate Runs).

% water (by volunm)	% product composition			ratio
	94	193	187	(94+193)/187
1	93.5	1.5[a]	5.0	19
	96.3	- [b]	3.7	26
2	94.2	2.9[a]	2.9	34
	97.3	- [b]	2.7	36
5	90.3	7.4[a]	2.3	43
	98.5	- [b]	1.5	64
10	98.5	1.1[a]	0.4	246
	99.4	- [b]	0.6	170

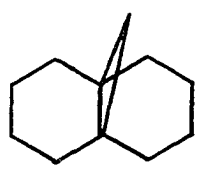
[a] Dil. sodium bicarbonate solution was utilized in the work-up.

[b] 5% Sodium hydroxide solution was employed in the work-up, thus only a trace of 193 was obtained (see experimental).

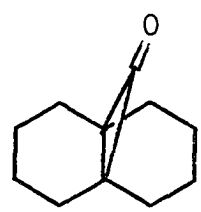
by glc analysis via their methyl esters, 3.6:1.0:1.2. An alternate determination (pmr integration of the methyl peaks of the corresponding methyl esters) gave a 3.0:1.0:1.6 ratio. The structure of 190 was indicated

by a comparison of its ir spectrum with the published one[128](a mixture of 190 and 191 were hydrogenated to give a sample of 190 contaminated with the known trans-9-decalin carboxylic acid). Acid 191, which was noticed from its pmr olefinic absorptions, was the minor acid. Hydroxyacid 192 which was isolated thanks to its insolubility, was assigned the trans fusion on the basis of the broadly split pmr absorptions for the aliphatic hydrogens, indicative of a rigid trans-decalin system[129] (see Fig. 56). Of the possible routes for formation of the acids, direct electrophilic attack by either H^+ or Ag^+ had to be condidered(see Scheme 14).

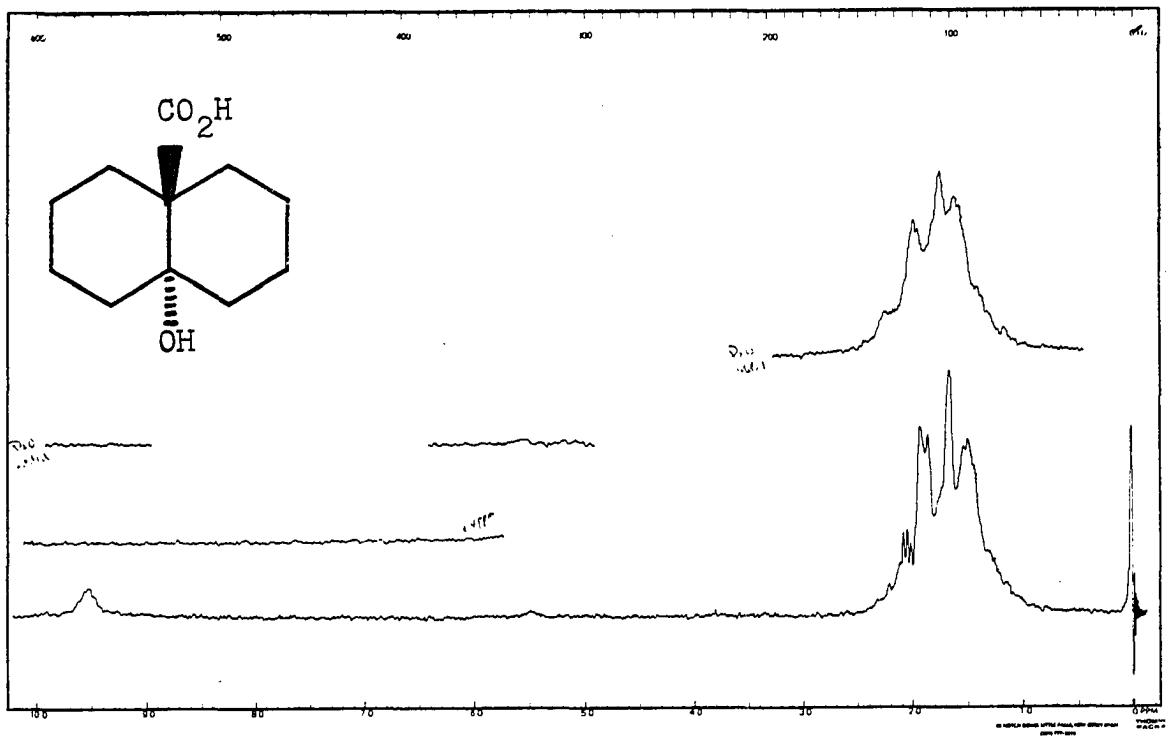
Protonic cleavage of 93 was ruled out by the finding that 93 could be reccvered unchanged after treatment under the acidic solvolysis conditions (simulated by reacting one equivalent of EtBr with an equivalent of $AgClO_4$, prior to adding 93 to the reaction mixture). Silver catalyzed cleavage was made doubtful by the finding that [4.4.1]propellane (198) was recovered unchanged after treatment under the acidic solvolysis conditions (simulated by reacting one equivalent of ethyl bromide with 2 equivalents of $AgClO_4$ and one equivalent of 198).



198



201



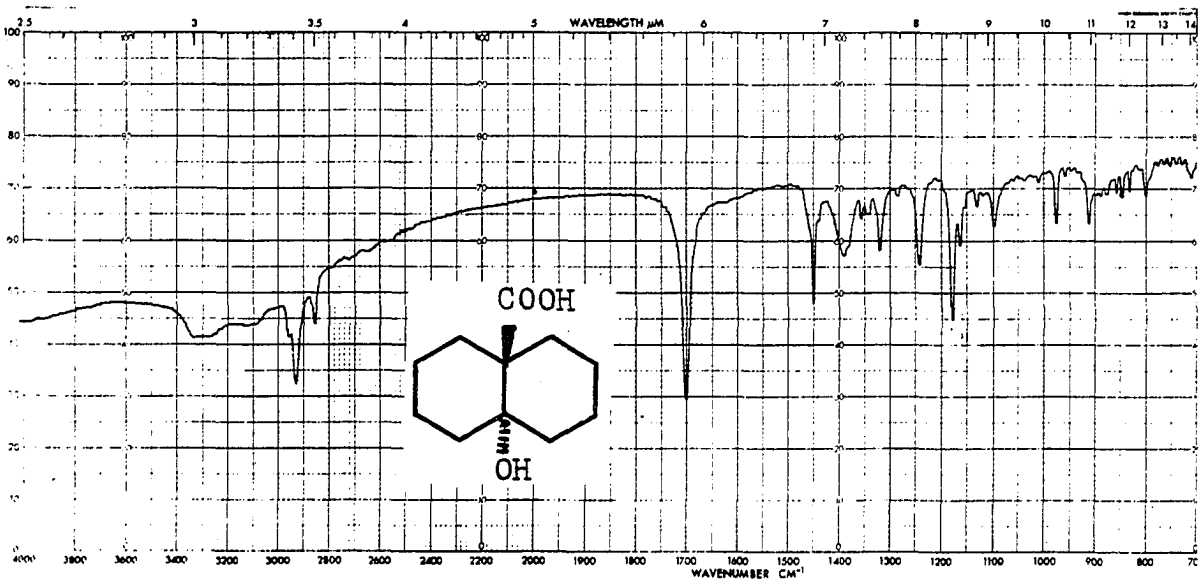
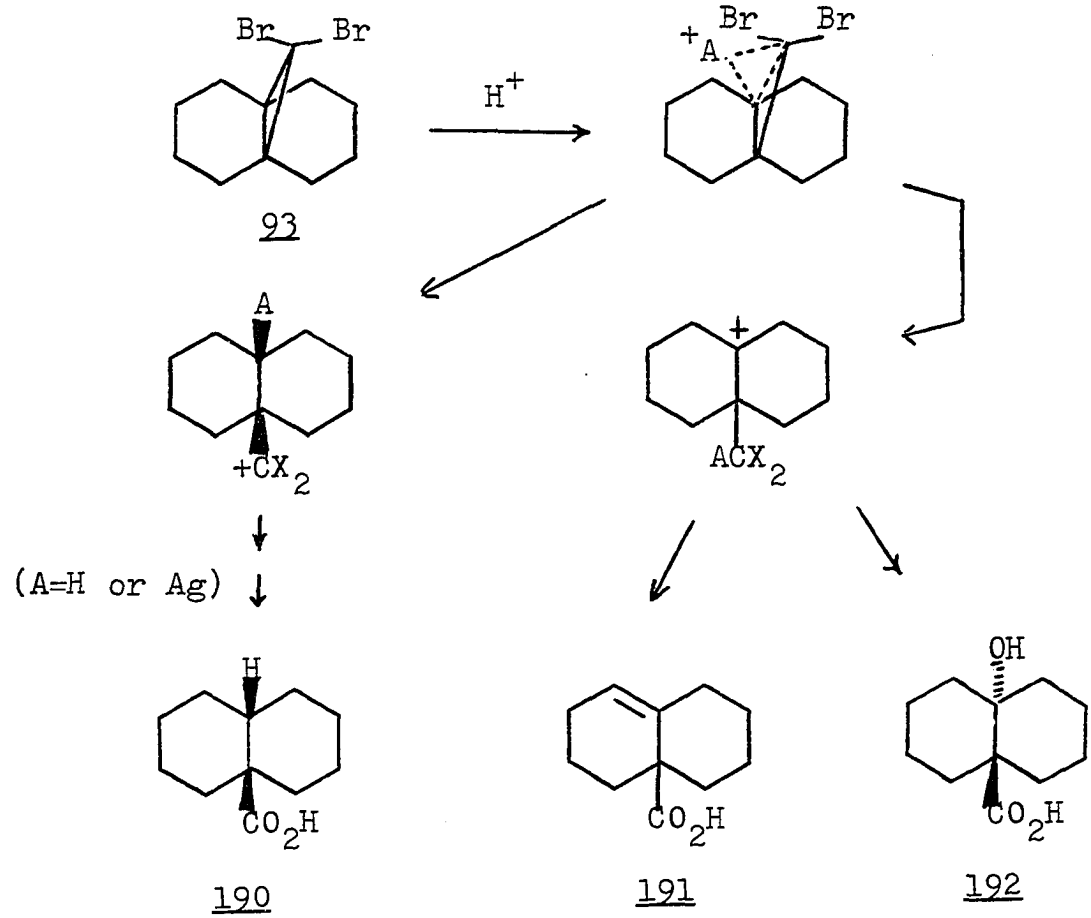


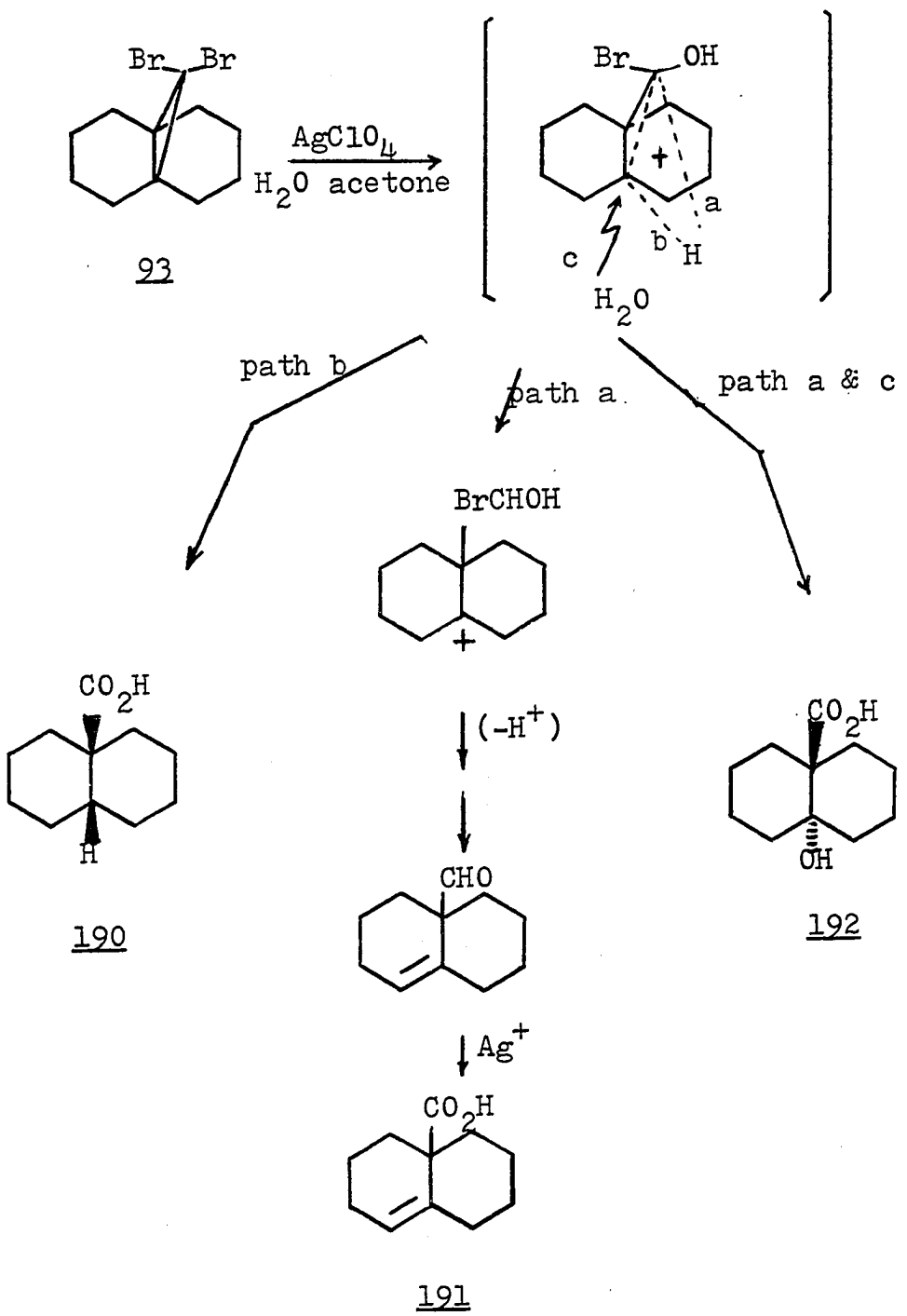
Figure 56. Pmr (Top) and Ir (Bottom) Spectra of trans-10-Hydroxydecalin-9-carboxylic Acid (192).

Scheme 14

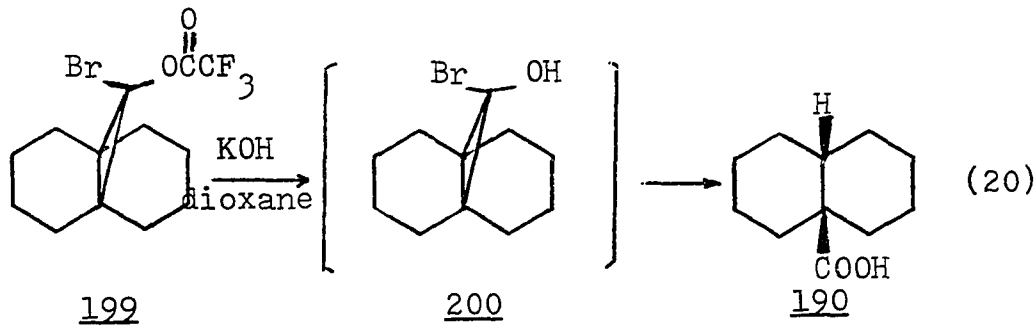


The above findings left, as an alternative, the sort of pathway precedented by the finding[113] that 199 gave 190 quantitatively, presumably via 200 (see Eq. 20). The complete pathway needed to account for 190-192 is summarized in Scheme 15. It should be noted that α-bromohydrin 200 is written as the intermediate for convenience; we certainly have no evidence for or against the intermediacy of a cyclopropanone (201, but see results for the [3.3.1]propellone system).

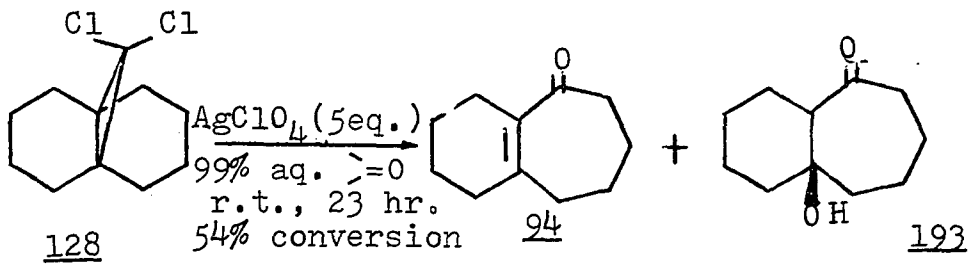
Scheme 15


Br Br
AgClO4
H2O acetone
93
Br OH
+
a
b H
c
H2O
path b
path a
path a & c
BrCHOH
+
CO2H
H
190
(-H+)
CHO
CO2H
OH
192
Ag+
CO2H
191

The increased amounts of 187 formed upon decreasing the percent of water in the aqueous acetone solvent led us to repeat the hydrolysis of 128 in 99% aqueous acetone. The product distribution after 54% reaction, highlighted by a 42% yield of 189, is summarized in Eq. 21.

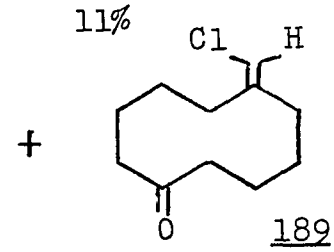


199 200 190 (20)



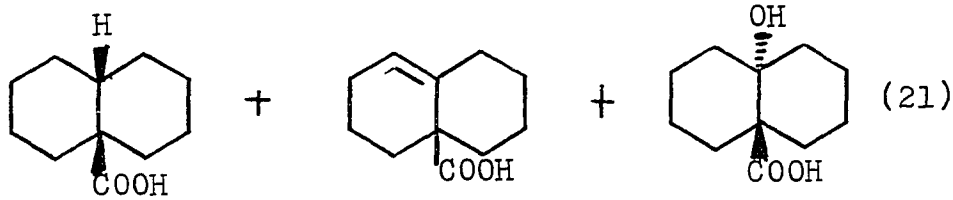
128 94 193

11% 12%



189

42%

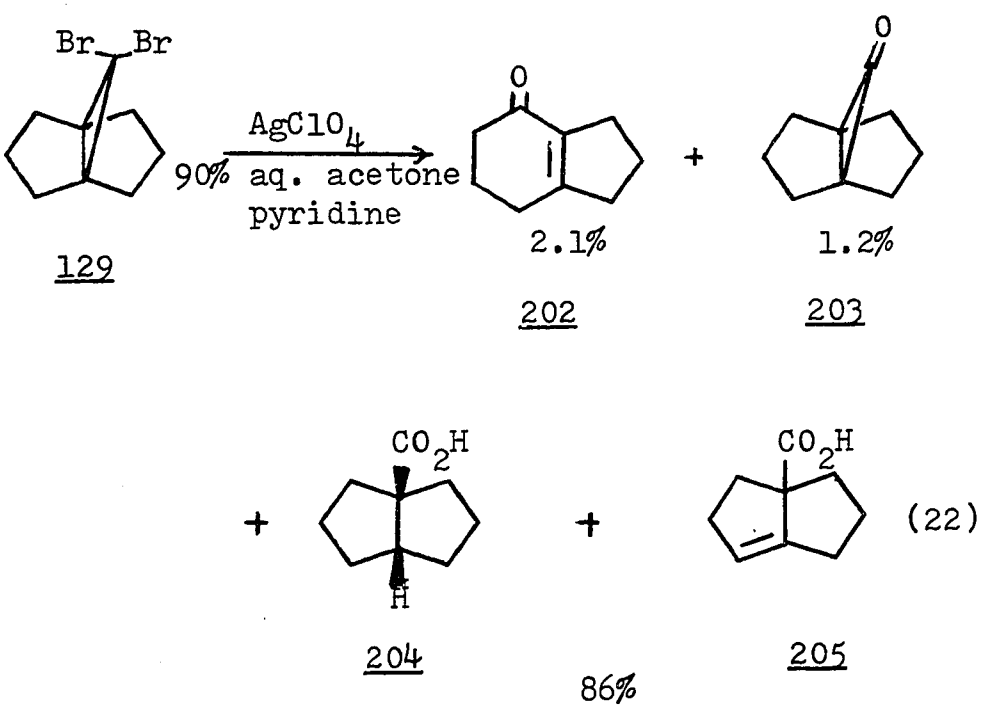


190 191 192 (21)

20%

The [3.3.1]Propellane System

Since the previous work discussed herein had established the relative ease of generating a bridgehead double bond transoid in a 7-membered ring, it became of interest to see whether it would be possible to force generation of a bridgehead olefin transoid in a 6-membered ring. The obvious precursor for such an endeavor was 9,9-dibromo[3.3.1]propellane (129). When 129 was subjected to silver perchlorate assisted hydrolysis in pyridine-buffered 90% aq. acetone, the products shown in Eq. 22 were isolated.



129 → 202 (2.1%) + 203 (1.2%) + 204 + 205 (86%) (22)

Thus enone 202, clearly the product of a bridgehead olefin (if 202 had been formed via an alkyl shift mechanism, there would be no explanation for its greatly diminished yield) intermediate, was as expected, a rather minor product (2.1%). Again, as expected, carboxylic acids 204 and 205 were the major products (86%). Hydrogenation of the mixture of acids gave pure cis acid 204, a known compound.[127] The ratio of 204 to 205 (5.3:1) was established from (a) pmr integration of the methyl peaks of the corresponding methyl esters and (b) comparison of the integrated pmr intensities of the vinyl proton of 205 and the carboxyl protons of 204 + 205 (whereby 205 was seen to be the minor acid).

The isolation of cyclopropanone 203 was a surprise, and, indeed, treatment of 203 under non-buffered hydrolysis conditions led to its isomerization to (mainly) 204, as did treatment of 203 with aqueous base (wherefore, efforts to isolate 203 required a neutral workup, where complete removal of 204 and 205 with aq. carbonate could not be performed). The carbonyl absorption of 203 at 1824 cm^{-1} was quite distinctive (see Fig. 57) (compare 1822 cm^{-1} for 1,1-di-t-butylcyclopropanone[130] and 1825 cm^{-1} for trans-1,2-di-t-butylcyclopropanone[131]). The mass spectrum showed a peak for the loss of carbon monoxide, and an almost equally intense peak for the loss of ethylene from the parent ion. The cmr showed only 4 peaks, with the carbonyl

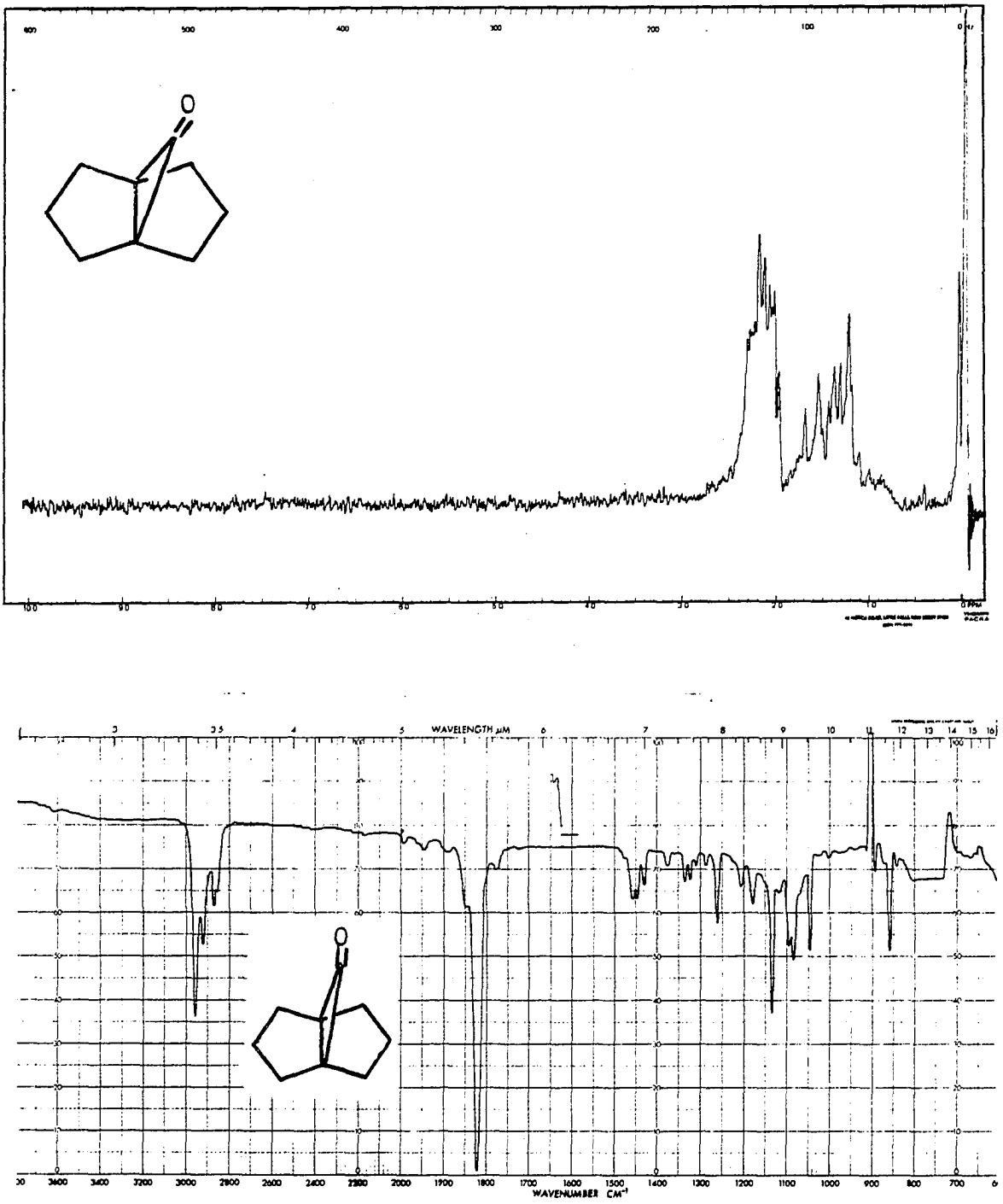
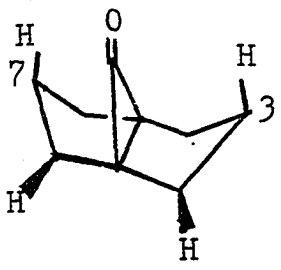
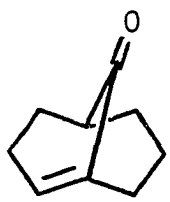


Figure 57. Pmr (Top) and Ir (Bottom) Spectra of Tricyclo-[3.3.1.$0^{1,5}$]nonan-9-one (203).

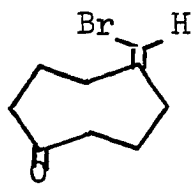
carbon appearing at δ 174. Attempts to generate the ketal of 203 failed, but heating in methanol caused rearrangement to a new compound, tentatively identified as 206 (on the basis of pmr: δ 5.35 (m) and ir: 1700 (C=o) and 1640 (C=C) cm^{-1}). It is interesting to consider the reasons for the stability of 203, in light of the instability of tetramethylcyclopropanone.[132] Models of 203, wherein the preferred boat conformation of the bicyclohexane rings is taken into account, indicate that severe torsional interactions with a hydrogen on 2 sides would develop upon attack at a bridgehead position, while the pseudoaxial protons at C_3 and C_7 protect the carbonyl group from attack (see 203a).



203a



206



207

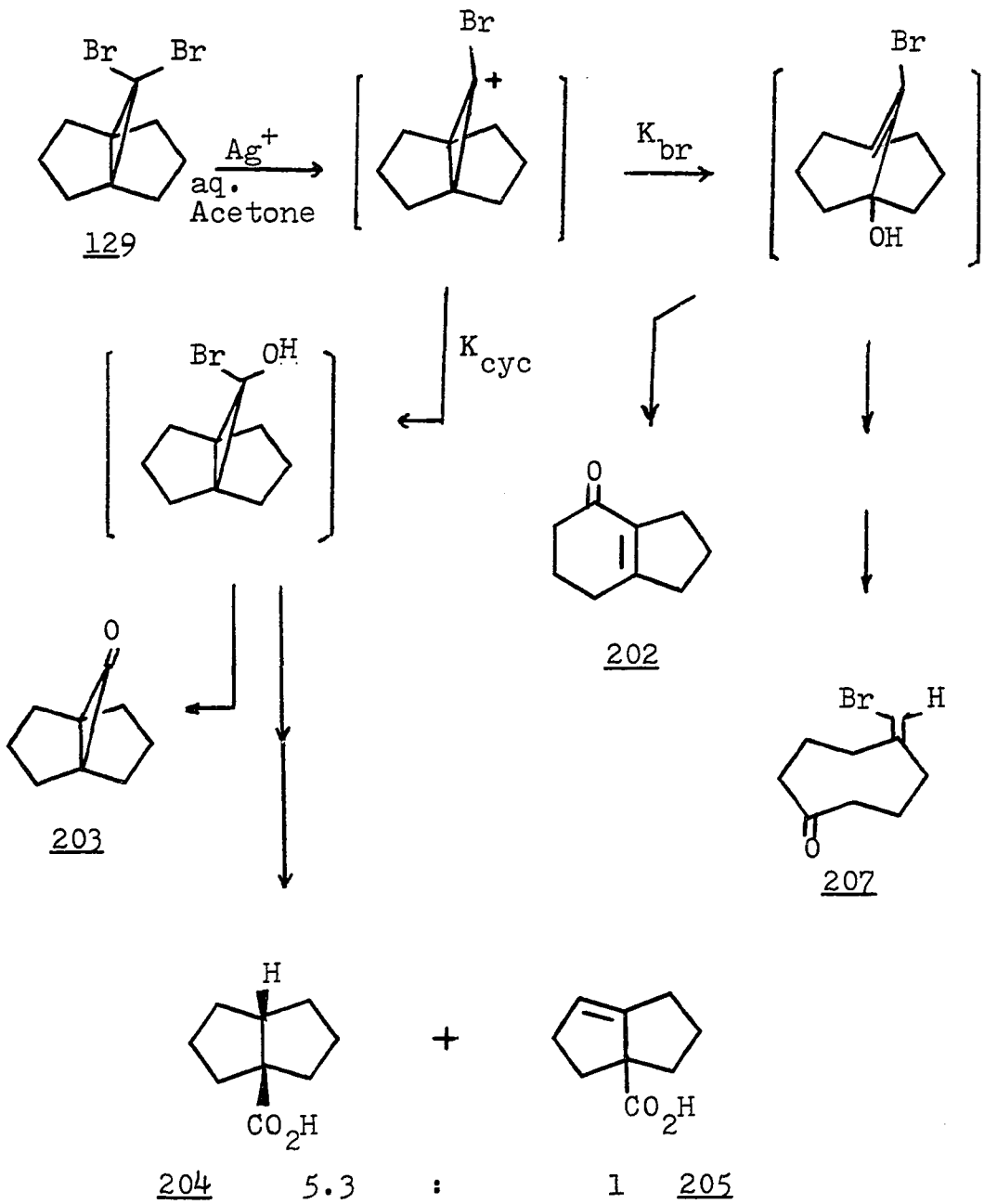
The absence of products, other than 202, attributable to a bridgehead olefin intermediate, led us to investigate the solvolysis of 129 in 99% aq. acetone. Aside from the

products previously obtained, evidence for the production of 207 was amassed [ir absorption at 1690 cm^{-1}, pmr singlet at δ 5.80, molecular ion at m/e 216.0156 (calc'd for $C_9H_{13}OBr$: m/e 216.0150)]. The most reasonable pathway for the formation of the observed products is presented in Scheme 16. The possibility that 204 and/or 205 were produced by direct electrophilic cleavage of the cyclopropane ring of 129 was again investigated (see discussions for similar studies on [4.3.1] and [4.4.1] propellane systems), and found not to occur. Whether or not formation of 204 and/or 205 funnels through 203 could not be established, but is a possibility.

It is interesting to note that 129 hydrolyzes roughly 8-10 times faster than 128, but 2-3 times slower than 93. More importantly, one may compare the percentage of products which arose from collapse of the initially formed ion at the bridgehead position (to give bridgehead olefin intermediates) with that which arose from collapse at the bridge position (to give cyclopropane intermediates or products); this is done in Table 13. Since the bridgehead olefins formed from 129 and 110 both are cisoid in a 6-membered ring, the change in their formation frequency must be attributable to the fact that the one from 110 is transoid in a 7-membered ring, while the one from 129 is transoid in a 6-membered ring. If this were the only

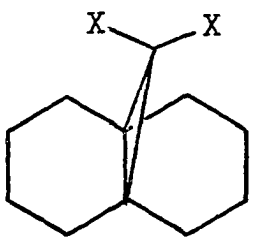
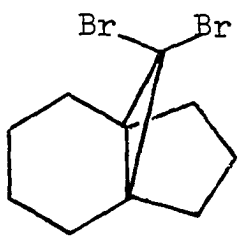
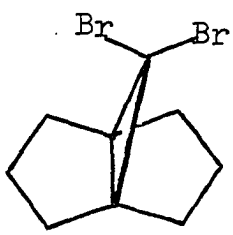
factor involved, then the energy difference between the two types of bridgehead olefins would be about 6 kcal/mole. Since the other factors involved would tend to make bridgehead collapse even more difficult in the ion derived

Scheme 16

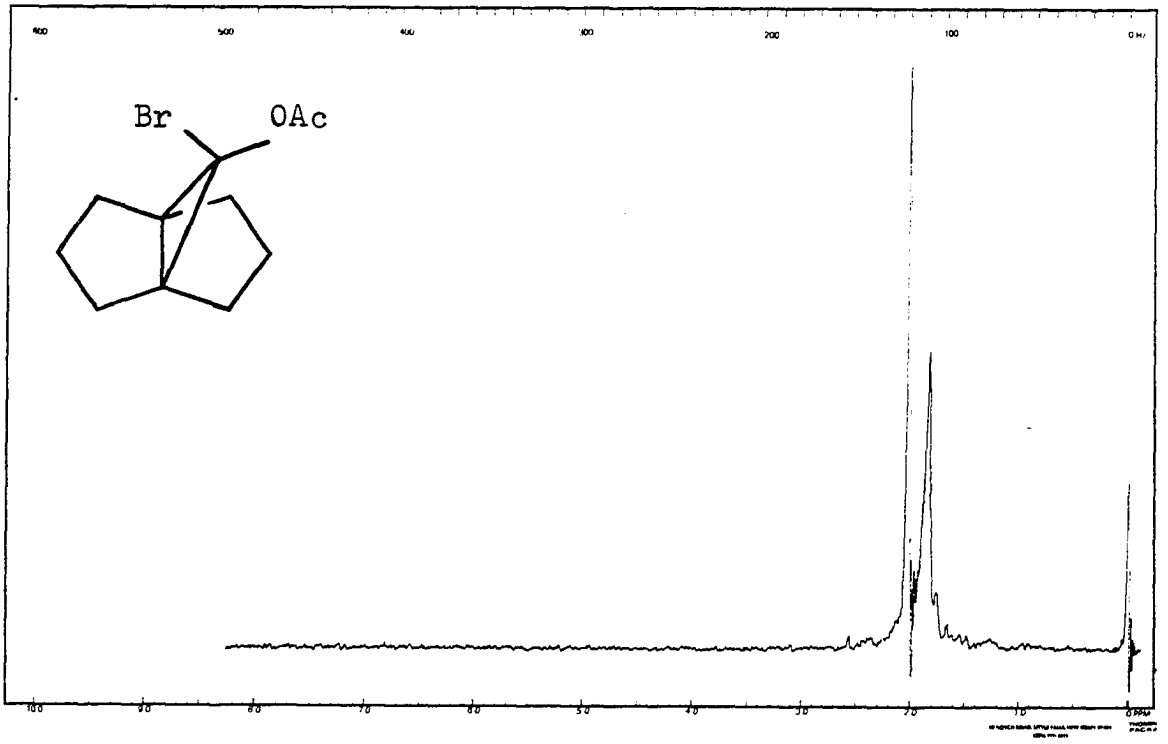


from 129, the above estimate of the energy difference is likely to be a maximum.

Table 13. Relative Product Ratios in 90% Aqueous Acetone.

Compound	Ratio of Products % br/% cyc	
 93, X = Br	1.8	
128, X = Cl	3.6	
 110	≧ 360	F ≧ 6 Kcal/mol
 129	0.024	

The Ag^+ assisted acetolysis of 129 afforded two principal products: compound 208 (ca. 0.6%), identified spectroscopically and 209, identified spectroscopically (see Fig. 58) and by its conversion to 204 (base). It was noteworthy that basic treatment of 208 led, initially,



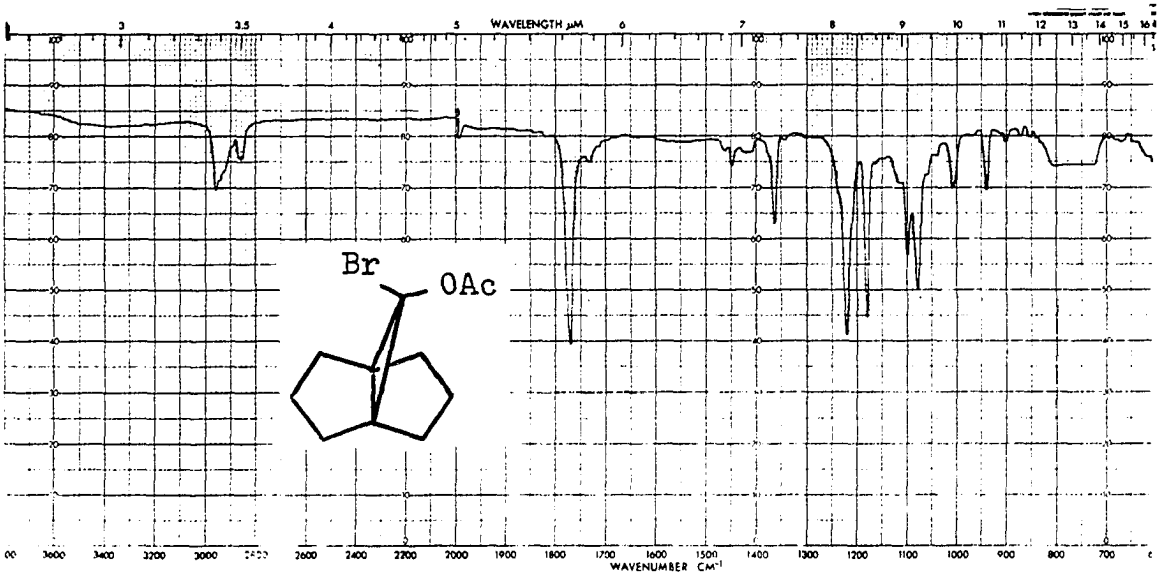
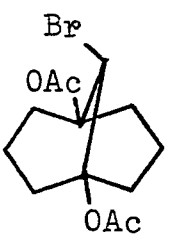


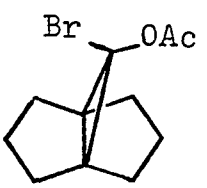
Figure 58. Pmr (Top) and Ir (Bottom) Spectra of 9-Acetoxy-9-bromotricyclo[3.3.1.$0^{1,5}$]nonane (209).

to diol 210 and hydroxyketone 211, and, after more vigorous treatment, to enone 202.

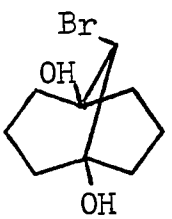
In contrast to the minor amounts of products isolated from the solvolysis of 129which were attributable to bridgehead olefin intermediates, hydrolysis of 212 in 85% aqueous acetone (Ag^+ assisted) led only to aldehyde 213 (91%, mechanistically comparable to carboxylic acids 204 and 205).



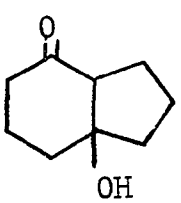
208



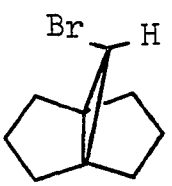
209



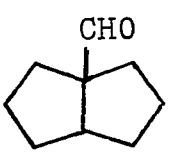
210



211



212



213

EXPERIMENTAL

The [4.3.1]Propellane System

10,10-Dibromotricyclo[4.3.1.$0^{1,6}$]dec-3-ene (33)

Propellene 33 was prepared according to the published procedure,[7] in 22-45% yield, mp 68-69.5° (acetone, lit[7] 72°), pmr: δ 5.51 (br. s. 2H), 2.33 (br. s. 4H), 2.25-1.00 (m. 6H); cmr ($CDCl_3$), δ 123.4, 55.9, 39.5, 36.8, 28.5, 26.3; ir (CCl_4): 3020 (olefinic), 1660 (C=C), 1020 (cyclopropyl C-C) cm^{-1}.

10,10-Dibromotricyclo[4.3.1.$0^{1,6}$]decane (110) Hydrogenation of 5 g of 33 was effected in 150 ml ether solution over 5% Pt-C at room pressure. A quantitative yield of 110 was isolated by filtration through celite and evaporation in vacuo. The hygroscopic product was recrystallized from pentane, mp 33-34° (sealed tube), cmr ($CDCl_3$) δ 58.6, 40.8 39.1, 27.2, 26.7 and 20.9.

11,11-Dibromotricyclo[4.4.1.$0^{1,6}$]undecane (93) Propellane 93 was prepared from catalytic hydrogenation (5% Pt-C, in ether) of 11, 11-dibromotricyclo[4.4.1.$0^{1,6}$] undeca-3,8-diene [mp 121-123°, lit[17] mp 124-125°; δ 5.65 5.35 (m. 4H) 2.8-1.0 (m. 8H)] which was itself synthesized from tetrahydronaphthalene according to the procedure described above for 33. Product 93 was obtained as a white

crystalline material after recrystallization from pentane, mp 43-44° (lit[8] 45-46°).

10α-Bromotricyclo[4.3.1.$0^{1,6}$]dec-3-ene (46f) and 10β-Bromotricyclo[4.3.1.$0^{1,6}$]dec-3-ene (42f) Propellenes 46f and 42f were synthesized via tri-n-butyltin hydride reduction of 33, utilizing Seyferth's procedure,[112] in 85% yield. The pmr spectrum showed a 3.3:1 ratio of 46f, 42f based on integration of the cyclopropyl protons (δ 2.85 for 46f and 3.16 for 42f), bp 54-58°/0.5 Torr. The epimers were separated via fractional column chromatography (neutral Woelm alumina, hexane as eluent). The pmr spectra of 46f and 42f are shown in Fig 59.

Anal. Calc'd for $C_{10}H_{13}Br$: C, 56.36; H, 6.15
Found : C, 56.68; H, 6.23

10α-Bromotricyclo[4.3.1.$0^{1,6}$]decane (45f) and 10β-Bromotricyclo[4.3.1.$0^{1,6}$]decane (41f) Partial reduction of 110 with $n\text{-}Bu_3SnH$, as described for the synthesis of 46f and 42f, led to a 4.1:1 mixture of 45f and 41f. Since all attempts to separate 45f from 41f were unsuccessful, recourse was made to the catalytic hydrogenation (5% Pt-C, ether) of 46f (to give 45f) and 42f (to give 41f). The pmr spectra of 45f and 41f are shown in Fig. 60.

Anal. Calc'd for $C_{10}H_{15}Br$: m/e 214.03571
Found : m/e 214.03533

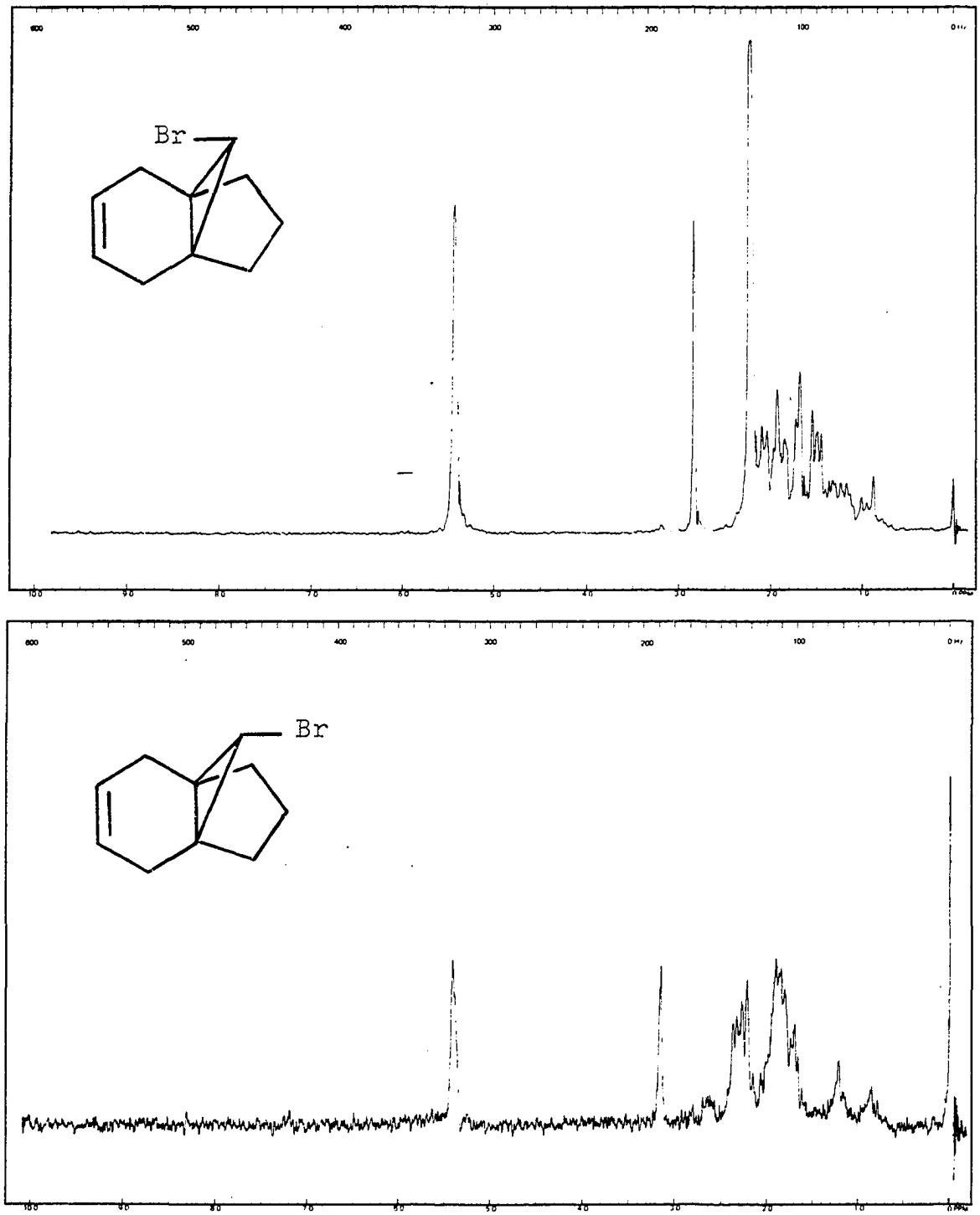


Figure 59. Pmr Spectra of 10α-Bromotricyclo[4.3.1.$0^{1,6}$]-dec-3-ene (46f,Top) and 10β-Bromotricyclo-[4.3.1.$0^{1,6}$]dec-3-ene (42f,Bottom).

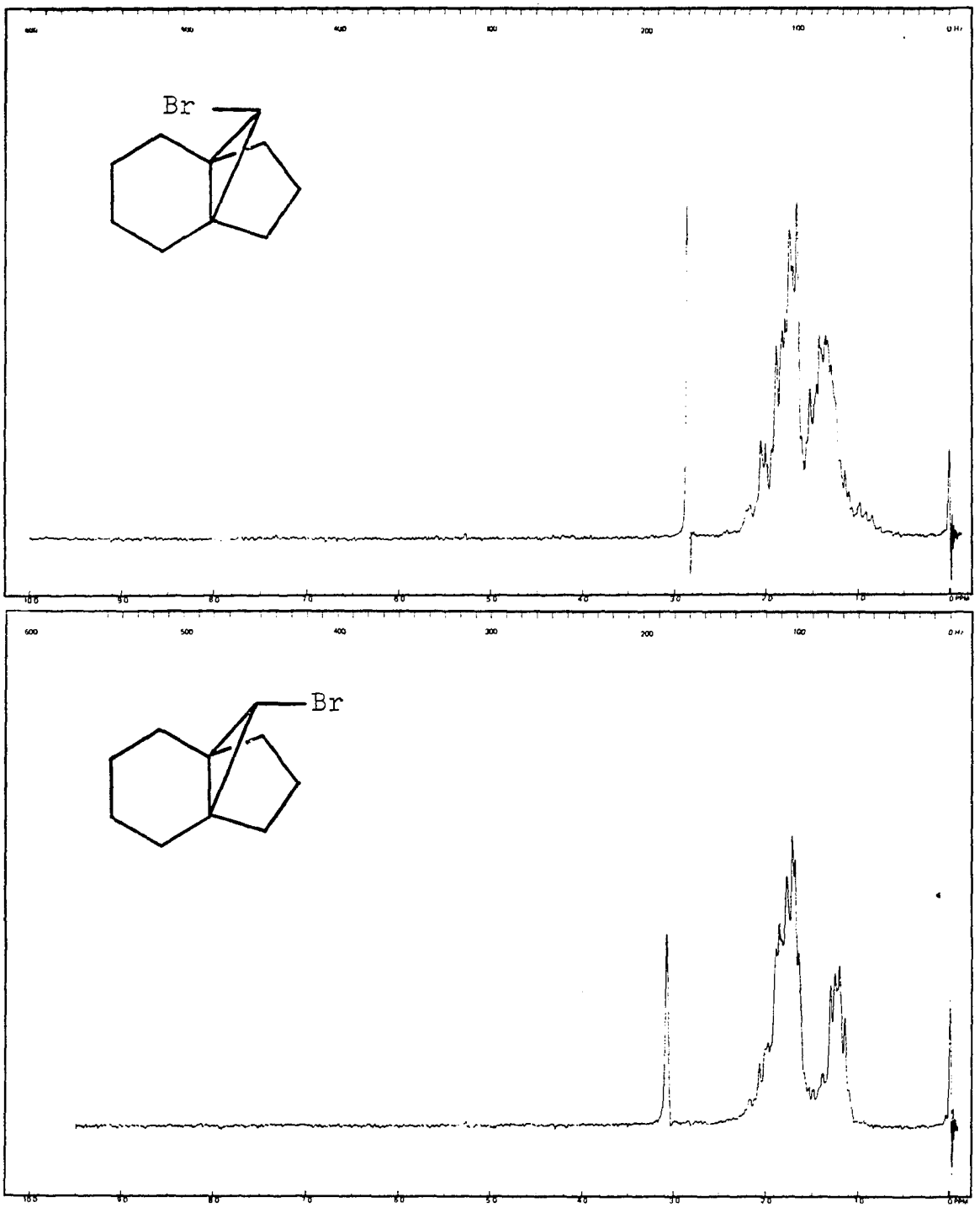


Figure 60. Pmr Spectra of 10α-Bromotricyclo[4.3.1.$0^{1,6}$]-decane (45f, Top) and 10β-Bromotricyclo-[4.3.1.$0^{1,6}$]decane (41f, Bottom).

Silver Assisted (1.1 eq) Solvolysis of 10,10-Dibromotricyclo[4.3.1.$0^{1,6}$]decane (110) in 90% Aqueous Acetone

To 0.93 g (3.16 mmol) of dibromide 110 in 6 ml 90% aq. acetone was added dropwise, over a 5 min. period, 0.70 g (3.40 mmol) of anhydrous silver perchlorate dissolved in 4 ml of 90% aq. acetone at room temperature. After stirring at room temperature for 15 min., the precipitate was filtered off by suction filtration. The solution was then concentrated in vacuo, followed by dilution with ether. The ether layer was extracted with water (three times) then 5% NaOH solution and saturated sodium chloride solution, dried over anhydrous magnesium sulfate, and concentrated on a rotary evaporator. The basic aqueous solution was acidified with 2N HCl solution followed by ether extraction, drying and solvent evaporation to give ca. 3 mg (0.6%) of hexahydroinda-8-carboxylic acid (131); ir (CCl_4): 3600-2400 (COOH), 1705 (C=O) cm^{-1}; mass spec. at 70 ev: m/e (rel. int.) 168 (35,P), 151 (100, P-OH), 123 (76, P-CO_2H). The nonacidic organic products formed a yellow oil (0.58 g) which was chromatographed on a 20 x 0.5 in. column packed with silica gel (Baker, 60-200 mesh). Elution with a mixture of ether and hexane (2/98 for fractions 1-57; 30/70 for fractions 58-64) afforded the following products (50ml fractions):

Frac.6, bicyclo[5.3.0]dec-1(7)-en-2-one (111) pmr: δ 2.75-2.20 (m. 8H), 2.15-1.40 (m. 6H); ir (CCl_4): 1644

(C=O), 1624 (C=C) cm^{-1}.

Frac. 7-17, 5-bromomethylenecyclononanone (112) pmr: δ 5.99 (s. 1H), 2.6-1.5 (m. 14H); cmr ($CDCl_3$): δ 215.2, 142.8, 106.7, 43.9, 41.4, 34.7, 33.3, 25.3, 23.9 and 23.5 (after 4,800 scans, but identical ten lines observed even after 21,000 scans); ir (film): 1702 (C=O), 1618 (C=C) cm^{-1}.

Frac. 58, 7-hydroxybicyclo[5.3.0]decan-2-one (130) mp 94-95° (hexane/ether) pmr ($CDCl_3$): δ 3.03 (t, J = 8 Hz, 1 H), 2.80-1.20 (m. 15 H); ir (CCl_4): 3600, 3450 (OH), 1707 (C=O) cm^{-1}; (see Fig. 33), lanthanide-induced shifts (LIS) for Hα demonstrated the cis ring fusion:

$$\frac{[Eu(fod)_3]}{[130]} = 0.17 \quad 0.33 \quad 0.45 \quad 1.10$$

LIS = -1.35 -2.95 -4.60 -12.3

Anal. Calc'd for $C_{10}H_{16}O_2$: m/e 168.1150

Found : m/e 168.1152

Frac. 59-64, 10-α-bromo-1,6-dihydroxybicyclo[4.3.1]decane (113) mp 154-155° (hexane/ether) (lit[106] 148-150°); pmr ($CDCl_3$): δ 4.34 (s. 1 H), 2.5-1.4 (m. 16 H); ir (CCl_4): 3570, 3455 (OH) cm^{-1}. (see Fig. 31).

Anal. Calc'd for $C_{10}H_{17}O_2Br$: C, 48.21; H, 6.88

Found : C, 48.35; H, 6.77

The yield of each product was determined by glc (column E): 112 (42%), 130 (11%), 113 (10%), 111 (3%), and 131 (0.2%).

Dehydration of 7-Hydroxybicyclo[5.3.0]decan-2-one (130) Six mg of hydroxy ketone 130 was treated with one ml of perchloric acid (70-72%) at room temperature for 2.5 hr. After work-up, ir analysis of the product indicated that enone 111 was formed.

Silver-Assisted (3.6 eq) Solvolysis of (110) in 90% Aqueous Acetone To 0.28 g (0.95 mmol) 110 in 3 ml 90% aq. acetone was added dropwise a 2 ml 90% aq. acetone solution of 0.70 g (3.40 mmol) anhydrous silver perchlorate at room temperature. After stirring for 5 hr., the usual work-up yielded a yellow oil (0.15 g). The pmr spectrum of the products indicated that no detectable diol 113 was formed; glc analysis (column E) indicated: 112 (52%), 111 (16%), 130 (4.4%) and 131 (0.2%).

Silver Assisted Solvolysis of 10-α-bromo-1,6-dihydroxybicyclo[4.3.1]decane (113) A mixture containing 20 mg (0.184 mmol) ethyl bromide and 76 mg (0.368 mmol) anhydrous silver perchlorate in 0.5 ml 90% aq. acetone was allowed to stir for 10 min. at room temperature. To the mixture was then added 45.5 mg (0.184 mmol) diol 113 in 2 ml 90% aq. acetone. After stirring for 20 min, the usual work-up gave a white solid (36 mg) which consisted of hydroxy ketone 130 and unreacted diol 113 (pmr and ir analyses). Further treatment of the above-obtained solid with 0.70 g

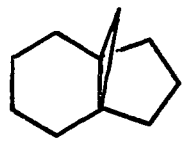
anhydrous silver perchlorate in 5 ml 90% aq. acetone for 4 hr. at room temperature, afforded, after work-up, 22 mg of a yellow oil which proved to be a 14:1 mixture of hydroxyketone 130 and enone 111 (glc analysis, column E).

Control Reaction for 5-Bromomethylenecyclononanone (112) To 30 mg (0.13 mmol) 112 in 2 ml 90% aq. acetone was added 270 mg (1.3 mmol) anhydrous silver perchlorate in 3 ml 90% aq. acetone. After stirring for 2 weeks, no detectable precipitate was observed, and ketone 112 was recovered in 91% yield.

Treatment of 110 with Acid Generated during Solvolysis To 54 mg (0.50 mmol) ethyl bromide in one ml 90% aq. acetone was added 82 mg (0.40 mmol) anhydrous silver perchlorate in one ml 90% aq. acetone. After stirring at room temperature for 25 min., 147 mg (0.50 mmol) 110 in 5 ml aq. acetone was added to the reaction mixture. The resulting mixture was allowed to stand at room temperature for 3 hr. Work-up as described for the solvolysis of 110 gave 140 mg (95%) of starting dibromide 110.

Treatment of [4.3.1]Propellane (41g) with $AgClO_4$ in Acidic Aqueous Acetone To 50 mg (0.45 mmol) ethyl bromide in one ml 90% aq. acetone was added 187 mg (0.90 mmol) anhydrous silver perchlorate in one ml 90% aq. acetone. After stirring at room temperature for 40 min.,

61 mg (0.45 mmol) 41g in one ml 90% aq. acetone was added, and the resulting mixture allowed to stir for 2 hr. at room temperature. Work-up as described for the solvolysis of 49 gave 46 mg (76%) of starting propellane 41g.



41g

2,4-Dinitrophenylhydrazone derivative of 112 Compound 135 was synthesized via a usual procedure[133] in 85% yield, mp 164-165° (chloroform); pmr ($CDCl_3$): δ 9.07 (d., 1 H, X portion of AMX pattern J_{MX} = 2.5 Hz), 8.25 (d. of d., 1H. M portion, J_{MX} = 2.5 Hz, J_{AM} = 10 Hz), 7.87 (d., 1 H, A portion, J_{AM} = 10 Hz), 5.87 (s. 1 H), 2.9-1.5 (m. 14 H), 1.25 (s. NH); ir (KBr): 3320 (NH), 1622 (C=C), 1590 (aromatic C=C), 1522, 1336 (NO_2), 836 (Ar) cm^{-1} (see Fig. 35).

Anal. Calc'd for $C_{16}H_{19}BrN_4O_4$: m/e 410.0590
Found : m/e 410.0572

Silver Assisted Solvolysis of 10-α-Bromo-1,6-dihydroxybicyclo[4.3.1]deca-3-ene (116) To 0.30 g (1.22 mmol) of diol 116 in 15 ml 90% aq. acetone was added a solution of 2.5 g (12.2 mmol) anhydrous silver perchlorate in 5 ml 90% aq. acetone. After stirring for 20 hr., the usual work-up yielded a colorless oil (195 mg, 97%), shown to

be hydroxy enone 133 which solidified upon cooling, mp 80-81.5° (pentane/ether). The structure of 133 was based on the following spectral data: pmr δ 6.05-5.80 (m. 2 H), 3.35-3.02 (m. 3 H), 2.50-1.55 (m. 9 H); ir (CCl_4): 3600, 3410 (OH), 3030 (olefinic), 1708 (C=O) cm^{-1} (see Fig. 34); cmr ($CDCl_3$): δ 209.1, 128.0, 125.9, 87.9, 62.7, 45.8, 40.1, 37.2, 24.9, 23.5.

Anal. Calc'd for $C_{10}H_{14}O_2$: m/e 166.0994
Found : m/e 166.0993

The following lanthanide induced shifts (LIS) for Hα (t, J = 8 Hz) demonstrated the cis ring fusion:

$\frac{[Eu(fod)_3]}{[133]}$ =	0.12	0.30	0.44	1.00
LIS =	-1.43	-3.90	-5.30	-11.00

Catalytic hydrogenation (10% Pd-C, ethanol) of 50 mg of 133 gave a quantitative yield of 130. The ir spectrum of the product was identical to that of an authentic sample of 130.

Buffered Acetolysis of 10,10-Dibromotricyclo-[4.3.1.$0^{1,6}$]decane (110) To 0.50 g (1.7mmol) 110 was added 10 ml glacial acetic acid containing 0.28 g (3.4 mmol) anhydrous sodium acetate. The resulting solution was sealed in an ampoule and heated at 125° for one hr. After cooling, the solution was poured into an ice cold

saturated potassium carbonate solution. The solution was then extracted three times with ether. The combined ether layers were washed with water, then saturated sodium chloride solution, dried over anhydrous magnessium sulfate, and finally concentrated in vacuo to give 0.46 g of an oil. Column chromatography (20 x 0.5 in. column packed with silica gel and eluted with ether and hexane, 2:98 for frac. 1-25, 4:96 for frac. 26-28) afforded the following products:

Frac. 5-8: 6-acetoxy-10α-bromobicyclo[4.3.1]dec-1(9)-ene (139) 83 mg (18%), mp 85.5-86.5° (aq. acetone), pmr: δ 5.85-5.47 (m. 2 H with a br. s. centered at 5.57), 2.9-0.9 (m. 15 H with a sharp singlet centered at 1.99); ir (CCl_4): 3020 (olefinic), 1734 (C=O), 1632 (C=C) and 1250 (acetate) cm^{-1} (see Fig. 6); cmr ($CDCl_3$): δ 170.4, 137.4 128.6, 84.8, 57.3, 40.4, 35.6, 32.2, 24.5, 23.1, 22.3 and 21.3.

Anal. Calc'd for $C_{12}H_{17}O_2Br$: m/e 270.0412
Found : m/e 270.0411

Chemical evidence for the structure of 139 was sought through the following four experiments:

(1) Low pressure catalytic hydrogenation of 27 mg 139 in 10 ml absolute ethanol over 10% Pd-C, followed by filtration, concentration and column chromatography (0.25 x 12 in. column, silica gel and eluted with ether and

hexane 2:98) yielded 26 mg (94%) of 141, pmr: δ 4.95 (d, J = 5 Hz 1 H), 2.8-1.2 (m. 18 H); ir (CCl_4): 1730 (C=O), 1253 (acetate) cm^{-1} (see Fig. 37); mass spec. at 16 ev: no parent ion was observed, however, a peak was found at m/e 214.0356, calc'd for $C_{10}H_{15}Br$ (P-HOAc) 214.0357.

(2) To 4.5 ml 90% aq. methanol which was 0.4 M in KOH was added 17 mg of 139. After stirring at room temperature for one hr., the solution was diluted with water, extracted with ether. The ether extracts were washed, dried over anhydrous sodium sulfate, and the solvent evaporated. This led to 12 mg (84%) 10α-bromobicyclo[4.3.1]deca-1(9)-ene-6-ol (139-OH), which had the following spectral properties: pmr: δ 5.72 (t, J = 5 Hz, 1 H), 4.85 (s. 1 H), 2.9-1.1 (m. 13 H); ir (CCl_4): 3560 (OH), 3020 (olefinic) cm^{-1}.

(3) To 0.5 ml glacial acetic acid containing 3 mg of p-toluenesulfonic acid was added 25 mg of 139 . After heating at 45° for 11 hr., the products were (pmr comparisons) mainly 10α-bromo-7-acetoxytricyclo[4.3.1.$0^{1,6}$]decane (138-exo and 138-endo), (exo/endo ratio = 1.7) and a trace of 10α-bromo-1,6-diacetoxybicyclo[4.3.1]decane (136).

(4) To 0.5 ml benzene containing 21 mg of 139 was added 50 μl of tri-n-butyltin hydride. The resulting solution was sealed in an nmr tube and heated at 125° for 10 min. The structure of the product was suggested as 6-acetoxy-tricyclo[4.3.1.$0^{1,6}$]dec-1(9)-ene (142) on the basis of its

pmr spectrum δ 5.55 (t, J = 5.5 Hz), 1.90 (s, OAc).

Frac. 9-14: 10α-bromo-7-acetoxytricyclo[4.3.1.$0^{1,6}$]decane(138-exo and138-endo), 24 mg (5.1%) in a ratio of 1.7/1.0 (exo/endo) pmr: δ 5.3-4.9 (m. 1 H), 3.18 (s. H_{10} for exo-OAc), 2.80 (s. H_{10} for endo-OAc), 1.98 (s. 3 H), 2.0-1.0 (m. 12 H); ir (film): 1733 (C=O), 1235 (acetate) cm^{-1}.

Anal. Calc'd for $C_{12}H_{17}O_2Br$: m/e 272.0412
Found : m/e 272.0422

Frac. 24-25: 5-bromomethylenecyclononanone (112) 21 mg (5.4%) showed identical spectral properties as those reported by Reese and Stebles.[105]

Frac. 26-27: 10α-bromo-1,6-diacetoxybicyclo[4.3.1]decane (136) 299 mg (53%), mp 73-74° (hexane) pmr: δ 5.14 (s. 1 H), 2.72-1.50 (m. 20 H with a sharp singlet centered at 1.98); cmr ($CDCl_3$): δ 169.6, 124.4, 83.9, 66.2, 38.1, 36.3, 22.4 and 20.9; ir (CCl_4): 1730 (C=O), 1250 (acetate) cm^{-1} (see Fig.38); mass spec. at 16 ev: no detectable parent peak (332), but observed were peaks at m/e (rel. int.), 232 (4), 230 (4), 214 (17), 212 (17), 203 (6), 201 (6), 190 (19), 188 (19), 151 (95), 133 (37) and 43 (100).

Anal. Calc'd for $C_{14}H_{21}O_4Br$: C, 50.59; H, 6.37
Found : C, 50.52; H, 6.20

The following experiment was carried out in order to obtain chemical evidence for the structure of 136: To 5 ml 90% aq. methanol, 0.4 M in KOH, was added 30 mg of 136. After stirring at room temperature for one hr., work-up as usual afforded 10 mg (45%) of 10α-bromo-1,6-dihydroxybicyclo[4.3.1]-decane (113) mp 154-155°. Prolonged treatment of 136 with the same base at 55° for 30 min., afforded quantitative enone (111) production on the basis of its pmr and ir spectra.

Frac. 28: 10α-bromo-1-hydroxy-6-acetoxybicyclo[4.3.1] decane (140) 12 mg (2.5%), mp 87-88° (ether/hexane); pmr: δ 4.66 (s. 1 H), 2.5 (s. OH), 2.35-1.45 (m. 17 H with a sharp s. centered at 1.95); ir (CCl_4): 3560, 3440 (OH), 1730 (C=O), 1234 (acetate) cm^{-1}. (see Fig. 39);mass spec. at 14 ev: no detectable parent peak (290) but observed peaks were m/e (rel. int.) 232 (12), 230 (12), 214 (7), 212 (7), 203 (19), 201 (20), 190 (37), 188 (37), 151 (100), 133 (20), and 44 (69).

Anal. Calc'd for $C_{12}H_{19}O_3Br$: C, 49.65; H, 6.60
Found : C, 49.66; H, 6.79

The following experiment was performed in order to obtain chemical evidence for the structure of 140: To 20 mg 140 was added a solution of 1 ml acetyl chloride in 2 ml pyridine. The reaction was allowed to proceed for 2 hr. at room temperature. The mixture was then poured into ice-water and

extracted with ether. The ether extracts were then sequentially washed with 10% HCl solution, saturated sadium bicarbonate solution and saturated sodium chloride solution. Drying over anhy. $MgSO_4$ was followed by evaporation of the ether to yield diacetate 136 (18 mg 78%), identical by comparison with an authentic sample.

Control Acetolysis of 136 In an nmr tube, 100 mg of diacetate 136 was dissolved in 0.5 ml glacial acetic acid (1% Ac_2O) containing two equivalents sodium acetate. The tube was heated to 125°, and the contents monitored via pmr spectrometry for a total reaction time of one hr. Only starting material was observed. After the usual work-up 93 mg (93%) of starting material was recovered.

Control Acetolysis of 112 In an nmr tube, 85 mg (0.37 mmol) of ketone 112 was dissolved in 0.5 ml glacial acetic acid containing 61 mg (0.74 mmol) anhy. sodium acetate. The tube was heated to 125°, and the contents monitored via pmr spectrometry for a total reaction time of one hr. Only starting material was observed. The reaction mixture was then worked up as described for the acetolysate from 110. This led to the recovery of 81 mg (95%) starting ketone 112.

Buffered Acetolysis of 110 in the Presence of Acetic Anhydride To 0.50 g (1.7 mmol) 110 was added a solution of 4 ml glacial acetic acid, 2 ml acetic anhydride, and

0.28 g (3.4 mmol) anhydrous sodium acetate. The resulting solution was sealed in an ampoule under a nitrogen atmosphere, and heated at 125° for one hr. Upon cooling, the reaction mixture was worked up as already described for the acetolysis of 110 without Ac_2O. There resulted 0.48 g of colorless oil, column chromatography of which afforded 97 mg (21%) 139 and 358 mg (63%) 136.

Transannular Cyclization of 5-Bromomethylenecyclononanone (112) To 5 ml acetic anhydride containing 20 mg anhydrous aluminum trichloride was added a solution of 93 mg (0.41 mmol) 112 in one ml acetic anhydride under nitrogen. The resulting mixture was heated at 150° for 2.5 hr. and then cooled prior to pouring it into a chilled saturated K_2CO_3 solution. Subsequently, the mixture was extracted 3 times with ether, followed by washing with water and saturated sodium chloride solution, drying over magnesium sulfate, and removal of solvent under reduced pressure to afford 106 mg of an oil which solidified upon cooling. Recrystallization from hexane yielded 71 mg (52%) of a white crystalline material, mp 72-74°, which was identified as diacetate 136 by comparison with the authentic material obtained from the acetolysis of 110.

Acetolysis of 33 in the Presence of Acetic Anhydride To 0.70 g (2.4 mmol) 33 was added a solution, in 5 ml of glacial acetic acid, of 0.5 ml acetic anhydride and 0.39 g

(4.8 mmol) anhydrous sodium acetate. The resulting solution was sealed in an ampoule under nitrogen and heated at 125° for 29 hr. Upon cooling, the reaction mixture was worked up as already described for the acetolysis of 110to yield 0.69 g of yellow oil. Column chromatography (0.62 x 24 in, silica gel, eluted with ether/hexane) afforded the following products in order of elution:

Frac. 2-3: 1-dibromomethylbicyclo[4.3.0]dec-3,6(7)-diene (150) 30 mg (4.3%); uv (hexane): no λ max above 200 nm; pmr ($CDCl_3$): δ 6.05 (s. 1 H), 5.75-5.45 (m. 3 H), 3.0-2.2 (m. 8 H); cmr ($CDCl_3$): δ 140.6, 126.5, 125.8, 125.2, 58.3, 57.0, 37.4, 33.2, 29.8, 27.2; ir (film): 3020, 1660, 1653, 782, 772, 755, 692,and 654 cm^{-1} (see Fig. 41).

Anal. Calc'd for $C_{10}H_{12}Br_2$: m/e 289.9306

Found : m/e 289.9298

Frac. 6-7: 10α-bromo-10β-acetoxytricyclo[4.3.1.$0^{1,6}$]dec-3-ene (151) 53 mg (8.2%); mp 51-52° (methanol); pmr ($CDCl_3$): δ 5.57 (s. 2 H), 2.7-1.1 (m. 13 H with two singlets centered at 2.40 and 2.13); cmr ($CDCl_3$): δ 169.0, 123.3, 80.1, 36.0, 33.9, 27.9, 24.8, 21.0; ir (CCl_4): 3025 (olefinic), 1772 (C=O), 1217, 1200 (acetate), 1184 and 1070 cm^{-1} (see Fig. 42).

Anal. Calc'd for $C_{12}H_{15}O_2Br$: m/e 270.0255
Found : m/e 270.0265
Calc'd : C, 53.14; H, 5.53
Found : C, 53.31; H, 5.67

The following hydrolysis was performed in order to obtain chemical evidence for the structure of 151: 14 Mg (0.052 mmol) 151 was dissolved in 90% aq. dioxane which was 0.8 M in KOH, and the solution was then stirred at room temperature for 12 hr. The reaction mixture was then diluted with water and extracted 3 times with ether. The ether extracts were washed with water, saturated NaCl solution, dried, and the solvent evaporated to yield 3 mg of an oil for which structure 164 is proposed, ir (CCl_4): 1825 cm^{-1}. The aqueous layer which remained after ether extraction was acidified and further extracted 3 times with ether. The ether solution was then washed with water, saturated NaCl solution, dried ($MgSO_4$) and stripped of solvent to yield 4 mg of cis-carboxylic acid 163; mp 78-80° (aq. acetic acid, lit[117] 80-80.5°); ir (CCl_4): 1700 cm^{-1}.

Frac. 8-11: a 1.0:8.7:4.7 (pmr analysis) mixture of isomers 152, 153-exo and 153-endo, 100 mg (15%). In a separate reaction, 1.07 g of the same mixture was obtained from the solvolysis of 7.2 g 33 under the same conditions. The mixture of isomers so obtained were separated by

careful column chromatography (0.62 x 24 in. silica gel, eluted with 0.5% ether in hexane). The spectral data for the isomers, in order of their elution, follow:

10α-Bromo-1-acetoxybicyclo[4.3.1]dec-3,6(7)-diene (152): uv (hexane): no λmax above 210 nm; pmr ($CDCl_3$): δ 5.66-5.40 (m. 4 H), 3.15-2.20 (m. 8 H), 2.07 (s. 3 H); ir (CCl_4): 3020 (olefinic), 1738 (C=O), 1663 (C=C), 1240 (acetate) cm^{-1} (see Fig. 40).

Anal. Calc'd for $C_{12}H_{15}O_2Br$: m/e 270.0255
Found : m/e 270.0254

Room pressure hydrogenation (10% Pd-C) of 20 mg 152 in 25 ml ethanol for 1 hr., followed by filtration and solvent evaporation gave 141 (19 mg, 93%) which was identical to the compound previously obtained from the hydrogenation of 139.

10α-Bromo-7exo-acetoxytricyclo[4.3.1.$0^{1,6}$]dec-3-ene (153-exo): pmr ($CDCl_3$): δ 5.56 (s. 2 H), 5.32 (t, J = 8 Hz, 1 H), 3.30 (s. 1 H), 2.5-1.0 (m. 11 H with a sharp singlet centered at 2.08); ir (CCl_4): 3030 (olefinic), 1742 (C=O), 1240 (acetate) cm^{-1} (see Fig. 44).

Anal. Calc'd for $C_{12}H_{15}O_2Br$: m/e 270.0255
Found : m/e 270.0251

The following reactions were performed in order to adduce chemical evidence for the structure of 153-exo:

(1) To 400 mg 153-exo was added 40 ml of a 0.4 M KOH in 90% aq. methanol solution. The resulting solution was

stirred for one hr. at room temperature. Work-up, as described for the hydrolysis of 151, afforded 304 mg (90%) of alcohol 165-exo, mp 84-85.5° (hexane); pmr ($CDCl_3$): δ 5.60 (s. 2 H), 4.44 (t, J = 8 Hz, 1 H), 3.32 (s. 1 H), 2.5-1.0 (m. 9 H); ir (CCl_4): 3620, 3320 (OH), 3020 (olefinic), 1662 (C=C) and 1048 (C-O) cm^{-1} (see Fig. 47).

Anal. Calc'd for $C_{10}H_{13}OBr$: m/e 228.0150

Found : m/e 228.0150

(2) Room pressure hydrogenation (5% Pt-C) of 36 mg mixture of 153-exo and 153-endo in 25 ml ether for 1 hr., followed by usual work-up as described for 152 afforded 35 mg mixture of saturated analog 138-exo and 138-endo by comparison with the authentic material obtained from the acetolysis of 110.

(3) To 90 mg alcohol 165-exo in 4.5 ml acetic acid was added 42 mg chromium trioxide. After stirring for 2 hr. at room temperature, 2 ml isopropyl alcohol was added to reduce excess oxidant. Subsequently, the resulting solution was diluted with water, treated with solid K_2CO_3 until the solution become basic, and then extracted with ether. The ether solution was washed with water, dried ($MgSO_4$) and stripped to give 72 mg (80%) oil which solidified upon cooling and was identified as 10α-bromotricyclo[4.3.1.$0^{1,6}$]dec-3-en-7-one (166) mp 74-75° (aq. methanol), pmr ($CDCl_3$): δ5.58 (s. 2 H), 3.40 (s. 1 H), 3.1-1.2 (m. 8 H); ir (CCl_4):

3030 (olefinic), 1735 (C=O) cm^{-1} (see Fig. 45).

Anal. Calc'd for $C_{10}H_{11}OBr$: m/e 225.9993

Found : m/e 225.9986

(4) To 30 mg (0.13 mmol) alcohol 165-exo was added 0.5 ml dry pyridine containing 50 mg p-toluenesulfonyl chloride (recrystallized from hexane). Placement of the resulting solution in the freezer (ca. -20°) overnight led to the precipitation of pyridinium hydrochloride. However, since attempts at isolation of 165-exo-OTs had failed (the tosylate is apparently too reactive), the pyridine solution was merely diluted with 0.5 ml HMPA. To this was added 83 mg (1.3 mmol) $NaBH_3CN$, followed by stirring for 6 hr. at room temperature. The reaction mixture was then diluted with water and extracted with ether three times. The combined ether layers were washed with dil. HCl, dil. $NaHCO_3$ solution, water and saturated NaCl solution, dried and concentrated to yield 21 mg of oil. Pmr analysis showed ca. 40% conversion to the known compound 46f (vide supra).

(5) To 40 mg (0.18 mmol) ketone 166 in 10 ml of a 1:1 mixture of DMF-sulfolane was added 47 mg (0.25 mmol) p-toluenesulfonylhydrazine, 5 mg of p-toluenesulfonic acid and 100 mg (1.6 mmol) $NaBH_3CN$. The resulting mixture was heated for 20 hr. at 110°. Work-up consisted of dilution with water, extraction with cyclohexane, drying and evaporation. However, no desired product was obtained

utilizing Hutchins procedure.[134]

(6) To 30 mg (0.13 mmol) ketone 166 in 1 ml ethanol was added 37 mg (0.20 mmol) p-toluenesulfonylhydrazine. The solution was heated for 2 hr. at 60°. The tosylhydrazone was isolated after work-up as described by Hutchins,[134] 34 mg (65%), mp 222-224° (decomp., recrystallized from ethanol). The tosylhydrazone was dissloved in 2 ml methylene chloride and cooled to -10°. Catecholborane[137] (0.11 ml, 0.10 mmol) was added and the solution was stirred for 1.5 hr. Sodium acetate (40 mg, 0.3 mmol) was than added and the resulting mixture was allowed to stir for 24 hr. at room temperature. After diluting with water, extraction with ether, drying ($MgSO_4$) and evaporation gave a yellow solid which did not show the desired product on the basis of its pmr spectrum.

10α-Bromo-7endo-acetoxytricyclo[4.3.1.$0^{1,6}$]dec-3-ene (153-endo): pmr ($CDCl_3$): δ 5.62 (s. 2 H), 5.39 (d. J = 3.5 Hz, 1 H), 2.92 (s. 1 H), 2.8-1.2 (m. 11 H with a sharp s centered at 2.10); ir (CCl_4): 3030 (olefinic), 1742 (C=O), 1660 (C=C), 1240 (acetate) cm^{-1} (see Fig. 43).

Anal. Calc'd for $C_{12}H_{15}O_2Br$: m/e 270.0255

Found : m/e 270.0251

The following reactions were carried out in order to adduce chemical evidence for the structure of 153-endo:

(1) To 63 mg (0.23 mmol) 153-endo was added 4.5 ml of a

0.4 M KOH in 90% aq. methanol solution. Under the same conditions, as previously described for 153-exo, 48 mg (91%) alcohol 165-endo was obtained, mp 90-91° (hexane); pmr ($CDCl_3$): δ 5.63 (s. 2 H), 4.29 (d. J = 3.5 Hz, 1 H), 2.90 (s. 1 H), 2.8-1.1 (m. 9 H); ir (CCl_4): 3620, 3590 (OH), 3020 (olefinic), 1655 (C=C), and 1120 (C-O) cm^{-1} (see Fig. 46).

Anal. Calc'd for $C_{10}H_{13}OBr$: m/e 228.0150
Found : m/e 228.0148

(2) To 30 mg alcohol 165-endo in 1.3 ml acetic acid was added 14 mg chromium trioxide. Under the same conditions as previously described for 165-exo, 20 mg (75%) ketone 166 was found, mp 73-75°. This material had the same ir and pmr spectra as that obtained from the oxidation of 165-exo.

Frac. 16-27: 10α-bromo-1,6-diacetoxybicyclo[4.3.1] dec-3-ene (154) 480 mg (61%), mp 84-85.5° (hexane); pmr ($CDCl_3$): δ 5.60 (s. 1 H), 5.49 (t. J = 3 Hz, 2 H), 3.1-1.5 (m. 16 H with a sharp s. centered at 2.05); cmr ($CDCl_3$): δ 169.6, 124.4, 83.9, 66.2, 38.1, 36.3, 22.4, 20.9; ir (CCl_4): 3020 (olefinic), 1738 (C=O), 1242 (acetate) cm^{-1} (see Fig. 48).

Anal. Calc'd for $C_{14}H_{19}O_4Br$: C, 50.78; H, 5.77
Found : C, 50.91; H, 5.73

The following experiment was performed in order to establish the chemical evidence for the structure of 154: Room pressure hydrogenation (10% Pd-C) of 30 mg 154 was executed in 25 ml ethanol for 1 hr. Work-up, as described for 152, afforded 27 mg (90%) saturated compound 136 on the basis of its pmr spectrum.

Attempted Dehydrogenation[100] of Tricyclo[4.3.1.$0^{1,6}$]dec-3-ene (175) To 80 mg propellene 175 in an nmr tube was added one ml acetonitrile solution containing 450 mg silver nitrate and 12 drops of pyridine. The mixture turned dark immediately and was heated for a week at 80°. No desired product was detected via pmr spectrometry. However, an AB quartet at δ 0.38 (J = 5 Hz) and a broad singlet at δ 5.87 were observed. (see Results and Discussion)

Synthesis of 10β(α)-Acetoxytricyclo[4.3.1.$0^{1,6}$]decane (173, 186) via Oxygenation To 0.88 g (41 mmol) 76 dissolved in 6 ml dry THF in a 100 ml Schlenk flask was added dropwise 26 ml (42 mmol) n-butyllithium (1.6 M in hexane) under nitrogen. After stirring at r.t. for one hr. (during which time the solution turned orange), the solution was cooled to -78°, and O_2 bubbled in for 1 hr. Saturated NH_4Cl solution was then added to quench the reaction, followed by threefold extraction with ether. The combined ether layers were washed with water,

saturated NaCl solution, dried ($MgSO_4$) and concentrated to give a yellow oil which was further heated at 90° in vacuo (1.5 Torr) to pump off the n-butanol. The pmr spectrum of the resulting crude product showed two equally intense peaks at δ 2.98 and 3.17 which were attributed to the epimeric cyclopropyl hydrogens of (186-OH) and (173-OH).

The above-obtained alcohols were dissolved in a mixture of 5 ml acetic anhydride and 10 ml dry pyridine, and stirred at room temperature for 20 hr. The mixture was then poured over ice-water, followed by extraction with ether. The ether solution was washed with dil. HCl, dil. $NaHCO_3$ solution, water and saturated NaCl solution, dried, concentrated, and column chromatographed (silica gel, eluted with 2% ether in hexane) to afford 0.10 g of unidentified product(s) (probably cyclopropyl ring-opened aldehyde(s)) [ir(CCl_4): 1735, 1670, 1230 cm^{-1}; pmr: δ 9.60 (s), 9.40 (s), and 2.65-0.40 (m)] and 0.34 g (43%) of a mixture of 173 and 186. Attempts to separate the two epimers by glc (column B) were unsuccessful. The purified mixture gave the following data: ir (CCl_4): 3030 (olefinic), 1754, 1740 (C=O), 1235 (acetate) cm^{-1}; pmr: δ 3.72 (s), 3.63 (s), 2.00 (s), 1.96 (s), 2.3-0.9 (m) (see Fig. 52).

Anal. Calc'd for $C_{12}H_{18}O_2$: C, 74.18; H, 9.35
Found : C, 74.23; H, 9.23

Kinetic Buffered Acetolysis Measurements-General Procedure A 0.004-0.012 M solution of the appropriate bromide, which was also 0.012 M in sodium acetate, was prepared in a 50 ml volumetric flask, utilizing the required amount of glacial acetic acid to which had been previously added 1% acetic anhydride. Seven 7 ml samples were pipetted into glass ampoules which had been flushed with nitrogen gas. After sealing, the ampoules were transferred to a constant temperature bath (125 ± 1°) and a timer was immediately started. After 3 minutes, the first ampoule was removed from the bath and quickly plunged into an ice-water bath to quench the reaction; this was used as the zero-time sample. After warming to room temperature, the ampoule was opened and two 2.99 ml aliquots were removed with a calibrated pipet. The aliquots were then titrated with a standard solution of perchloric acid in acetic acid (0.0108 M) which contained ca. 4% of acetic anhydride, using crystal violet as the indicator. The color of the solution changed from violet to pure blue at the end point. A blank solution was also prepared in order to aid in determining the end point of the titration. The molarity of the standard perchloric acid was determined by titrating three aliquots with the primary standard, potassium acid phthalate, in glacial

acetic acid using crystal violet as the indicator. The rate constants were obtained from the integrated first order rate equation

$$\log \frac{V_o - V_\infty}{V_t - V_\infty} = \frac{K_1}{2.303} t,$$

where V_t = volume of titrant needed at the elapsed time t, V_∞ and V_o are the corresponding volumes at the completion of reaction (ten half-lifes) and at time equal to zero, respectively. All kinetic data are summarized in Table 3; the raw data are given in Tables 14 and 15.

The [4.4.1]Propellane System

11,11-Dichlorotricyclo[4.4.1.$0^{1,6}$]undecane (128)

11,11-Dichlorotricyclo[4.4.1.$0^{1,6}$]undec-3,8-diene was prepared in 56% yield from tetrahydronaphthalene and chloroform (60% ^{13}C reagent, from Merck, was diluted to 12% with regular chloroform) in the presence of potassium t-butoxide in pentane, as described by Vogel, et al.,[8] mp 86-88° (methanol). Hydrogenation over 5% Pt-C in ether, as described for 110, afforded 128 in 99% yield mp 36.5-38° (acetone/methanol). High resolution mass spectroscopy at 70 ev: m/e (rel. int.) 217 (4.2, P-1), 218 (100, P), 219 (20.5, P+1), 220 (62.8, P+2), 224 (10.9, P+4). The enrichment at C_{11} was calculated as follows: First was

Table 14. Kinetic Data for Buffered Acetolysis of Some Cyclopropyl Bromides at 125°.

Compound	t, min.	Titer,[a] ml.	10^6K, sec^{-1}	
110	0	3.02	-	
	5	2.48	2180	
	10	2.26	1870	
	15	2.13	1720	
	20	2.05	1630	
	25	1.99	1610	
	150	1.89	-	Ave. 1800±180
33	0	3.36	-	
	60	2.61	79.1	
	120	2.10	74.5	
	360	1.12	62.0	
	600	0.60	66.0	
	720	0.50	65.3	
	1470	0.32	-	Ave. 69.4±5.9
41f	0	0.31	-	
	30	2.79	133	
	60	2.44	122	
	90	2.19	113	

[a]Average value for two runs.

Table 14 (Continued)

Compound	t, min.	Titer,[a] ml.	10^6K, sec^{-1}	
41f	120	2.02	105	
	150	1.88	97.5	
	1230	0.86	-	Ave. 118±9.3
42f	0	3.30	-	
	780	2.87	6.25	
	1380	2.65	5.75	
	2760	2.27	5.59	
	6820	1.59	-	Ave. 5.86±0.26

Table 15. Kinetic Data for Buffered Acetolysis of Some Cyclopropyl Bromides at 100°.

Compound	t, min.	Titer,[a] ml.	10^6K, sec^{-1}
110	0	2.20	-
	60	1.55	372
	120	1.41	316

[a]Average value for two runs.

Table 15.(Continued)

Compound	t, min.	Titer,[a] ml.	$10^6 K$ sec^{-1}
110	180	1.36	285[b]
	300	1.33	250[b]
	1560	1.32	- Ave. 344±28
33	0	2.36	-
	1620	1.24	10.2
	3060	0.86	10.0
	4440	0.64	12.2[b]
	5760	0.54	7.1[b]
	14400	0.37	- Ave. 10.1±0.2

[b]Discarded value is not included in the average.

subtracted from P+1 the percentage due to the natural abundance of deuterium from 16 hydrogens. The resulting value is the total ^{13}C contribution P+1, which, when divided by the sum of itself and the parent ion, followed by multiplication by 100, gives the percent total ^{13}C in the molecule. If one then subtracts from this percentage that due to the ^{13}C natural abundance of 10 carbons, the resultant (5.8%) is the percentage of ^{13}C enrichment in C_{11} of 128; cmr ($CDCl_3$, rel area per carbon): δ 78.9 (4.9; C_{11}), 29.9

(1.4; C_2, C_5, C_7, C_{10}), 27.5 (1.2; C_1, C_6), 20.8 (1.0; C_3, C_4, C_8, C_9).

Silver Assisted Solvolysis of ^{13}C-enriched 128 in 90% Aqueous Acetone To 4.35 g (21.0 mmol) anhydrous silver perchlorate in 4 ml 90% aqueous acetone was added dropwise a solution of 0.92 g (4.2 mmol) of 5.8% ^{13}C-enriched 128 in 6 ml 90% aqueous acetone. The resulting milky mixture was allowed to stir at room temperature for 23 hr. The purple precipitate was then filtered off and washed with ether. The filtrate was diluted with more ether and washed with water three times, then saturated $NaHCO_3$ solution, and finally saturated NaCl solution. After drying over anhydrous Na_2SO_4, removal of solvent in vacuo left 0.78 g of yellow oil which was chromatographed on silica gel (0.75 x 24 in. column). Elution with a mixture of ether and hexane (1/99 for fractions 1-16; 3/97 for fractions 17-21; 10/90 for fractions 22-25; 20/80 for fractions 26-35) afforded the following products (50 ml fractions):

Frac. 16, 6-chloromethylenecyclodecanone (189) mp 45.5-46° (aq. methanol); pmr: δ 5.87 (s. 1 H), 2.6-1.5 (m. 16 H); ir (CCl_4): 1710 (C=O), 1620 (C=C) cm^{-1} (see Fig. 53 and 54); high resolution mass spec. at 70 ev: Calc'd for $C_{11}H_{17}OCl$ m/e 200.0968, found m/e (rel. int.) 200.0975

(5, P), 184 (22, P-16), 183 (14, P-17), 182 (72, P-18), 164 (100, P-36). Due to the weak signals for the P and P+1 ions, the relative intensities of the peaks at 183 and 182 were used to calculate the ^{13}C-enrichment of ketone 189. The data indicated that if all of the excess (i.e. above natural abundance) ^{13}C were at one position (e.g. C_{11}), then there was 5.8% ^{13}C at that position; cmr ($CDCl_3$): gave only one peak at δ 113.1 attributable to the enriched α-chloro olefinic carbon; no other peaks could be observed due to lack of pure material.

Frac. 21, bicyclo[5.4.0]undec-1(7)-en-2-one (94) pmr: δ 2.75-1.95 (m. 8 H), 1.9-1.4 (m. 8 H); ir (CCl_4): 1662 (C=O), 1632 (C=C) cm^{-1}; high resolution mass spec. at 70 ev: m/e (rel. int.) 163 (4.5, P-1), 164 (100, P), 165 (19.2, P+1), 166 (1.7, P+2); the percentage of ^{13}C at C_α (of the α,β-unsaturated enone system), assuming all the excess ^{13}C was at that position, was calculated to be 5.3%; cmr ($CDCl_3$, rel. area): δ 205.4 (0.84, $C_{C=O}$), 153.2 (1.00, C_β), 135.3 (5.06, C_α), 41.7 (1.24), 34.1 and 33.9 (1.94), 24.8 (1.08), 24.4 (1.36), 22.7 (1.21), 22.1 (1.23), 21.4 (1.26); thus the percentage of ^{13}C at C_α was computed to be 5.6%.

Frac. 25, 7-hydroxybicyclo[5.4.0]undecan-2-one (193) pmr: δ 3.7 (m. OH), 2.7-1.0 (m. 17 H); ir (CCl_4): 3450

(OH), 1705 (C=O) cm^{-1} (see Fig. 55); cmr ($CDCl_3$): δ 215.1 ($C_{C=O}$), 72.9 (C_{OH}), 62.3 (tertiary carbon α to carbonyl, enriched), no other peaks could be observed due to lack of pure material. The following reaction was performed in order to adduce chemical evidence for the structure of 87: To 40 mg 193 was added 1 ml conc. HCl solution and the resulting reddish solution was stirred for 5 hr. at room temperature. Ether extraction followed by washing with dil. $NaHCO_3$ solution, water, drying ($MgSO_4$) and evaporation gave a yellow oil which showed an identical ir spectrum to that of enone 94.

Frac. 27, unknown compound A with the following spectral properties: pmr: δ 4.3 (m), 3.5 (m), 2.6-1.1 (m), mass spec. at 16 ev: m/e 336; ir (CCl_4): 1710 cm^{-1}.

Frac. 30, a mixture of cis-decalin-9-carboxylic acid (190) and bicyclo[4.4.0]dec-5(6)-ene-1-carboxylic acid (191) mp 168-175°; pmr: δ 10.8 (br. s.), 5.5 (m), 2.4-1.1 (m); ir (CCl_4): 3600-2400, 1695 cm^{-1}; cmr ($CDCl_3$): δ 184.6 (C_{COOH}, enriched), 181.7 (C_{COOH}, enriched), no other peaks could be observed due to lack of pure material.

Frac. 35, unknown compound B with the following spectral properties: pmr ($CDCl_3$): δ 2.8-0.7 (m); ir (film): 3660, 3550, 1740 and 1670 cm^{-1}; mass spec. at 16 ev: m/e 238.

The yield of above products was determined by glc (column C): 189 (28%), 94 (31%), 139 (6%), 190 and 191 (4%), unknown A (4.5%), unknown B (4%).

Treatment of Enone 94 under Ag^+-Assisted Hydrolysis Conditions To a mixture of 770 mg (37 mmol) anhydrous silver perchlorate and 78 mg (0.73 mmol) ethyl bromide in one ml 90% aq. acetone was added 120 mg (0.73 mmol) of 5.06% ^{13}C enriched enone 94 (obtained from the above-described hydrolysis). The mixture was allowed to stir for two days at room temperature. Work-up, as described for the hydrolysis of 128 led to 110 mg (92%) of starting enone. High resolution mass spect. analysis revealed 4.92% ^{13}C enrichment; cmr ($CDCl_3$, rel. area): δ 205.4 (0.81), 153.1 (1.00), 135.3 (5.10), 41.7 (1.52), 34.1 and 33.9 (1.78), 24.8 (1.20), 24.3 (1.04), 22.7 (1.06), 22.1 (1.22), 21.4 (1.08).

Silver Assisted Solvolysis of 128 in 90% Aqueous Acetone To 1.62 g (7.42 mmol) 128 in 15 ml 90% aq. acetone was added 7.70 g (37.2 mmol) silver perchlorate in 10 ml 90% aq. acetone. After stirring at r.t. for 22 hr., the mixture was diluted with ether. The ether solution was then washed with water and 3 times with 5% NaOH solution. The combined basic extracts were acidified with

conc. HCl solution to yield a white precipitate which was extracted into ether, dried (Na_2SO_4) and concentrated to afford 239 mg (18%) of acids 190-192 (vide infra for separation and determination of the ratios of these acids). The ether solution which remained after base extraction was worked up as described for ^{13}C enriched 128 to give 960 mg oil which was chromatographed to give three major products, 189, 94 and 193, comparable to those obtained from the solvolysis of enriched 128 according to their spectral properties (pmr and ir spectra); cmr spectral data for 189 94, 190 and 191 are collected as follows:

6-Chloromethylenecyclodecanone (189) cmr ($CDCl_3$, rel. area): δ 214.3 (0.25, $C_{C=O}$), 141.4 (0.43, $C_{C=C}$), 113.1 (1.00, $C_{C=CHCl}$), 43.1 (1.28), 37.8 (1.21), 31.2 (2.31), 30.9 (0.56), 24.5 (1.21), 23.2 (1.53), 22.9 (0.96), 22.5 (0.69).

Bicyclo[5.4.0]undec-1(7)-en-2-one (94) cmr ($CDCl_3$, rel. int.): δ 205.4 (1.02, $C_{C=O}$), 153.2 (1.00, C_β), 135.3 (0.62, C_α), 41.8 (0.95), 34.1 (1.34), 33.9 (0.40), 24.8 (1.10), 24.4 (0.92), 22.8 (0.98), 22.2 (0.97), 21.4 (0.99).

Cis-Decalin-9-carboxylic acid (190) and Bicyclo[4.4.0]dec-5(6)-ene-1-carboxylic acid (191): cmr ($CDCl_3$): δ 182.7 (1.55, C_{COOH}) 181.4 (1.23, C_{COOH}), 137.7 (1.50, $C_{C=C}$), 123.1 (1.65, $C_{C=CH}$), 65.9 (3.14), 48.3 (1.00), 28.2 (1.10),

36.4 (1.26), 35.7 (1.30), 34.3 (1.29), 31.7 (2.27), 30.7 (1.05), 29.4 (1.18), 28.0 (2.32), 25.4 (1.85), 22.9 (2.95), 21.1 (1.84), 15.2 (2.07).

Treatment of Ketone 189 under Silver Assisted Hydrolysis Conditions To 37 mg (0.34 mmol) ethyl bromide in one ml 90% aq. acetone was added 350 mg (1.7 mmol) $AgClO_4$ in 2 ml 90% aq. acetone. After stirring at room temperature for 30 min, 68 mg (0.34 mmol) unenriched ketone 189 in one ml 90% aq. acetone was added to the mixture. After an additional 24 hr. at room temperature, the reaction mixture was worked up as described for 128 to yield 60 mg (88%) starting ketone 189 (identified by ir spectroscopy). None of the other solvolysis products was detected.

Silver Assisted Solvolysis of 128 in 99% Aqueous Acetone To 2.40 g (11.6 mmol) anhy. $AgClO_4$ in 10 ml 99% aq. acetone was added dropwise 0.50 g (2.3 mmol) 128 in 10 ml 99% aq. acetone. After stirring at r.t. for 23 hr., work-up as already described for 128 gave 0.45 g of oil which was chromatographed on silica gel. Elution with pure hexane afforded 230 mg (46% recovery) of 128. Elution with 1% ether in hexane gave 103 mg (42% based on unrecovered 128, 189. Elution with 2% ether in hexane afforded 23 mg (11%) 94. Finally, elution with 10-40% ether in hexane gave 28 mg (12%) hydroxy ketone 193 and 45 mg (20%) carboxylic acids 190-192.

Silver Assisted Solvolysis of 11,11-Dibromotricyclo-[4.4.1.$0^{1,6}$]undecane (93) in 90% Aqueous Acetone To 1.00 g (3.24 mmol) 93 in 10 ml 90% aq. acetone was added dropwise a 5 ml solution of 4.5 g (21.8 mmol) anhydrous $AgClO_4$ in 90% aq. acetone. After stirring at room temperature for one hr., work-up as described for 128 yielded 0.50 g of yellow oil. When the pmr spectrum was obtained, it revealed a singlet at δ 5.95, which was attributed to the olefinic proton of 187. Ir spectroscopy also indicated a carbonyl absorption at 1710 cm^{-1}. Glc-mass spec. analysis (column A at 50-180°) showed a peak with the same retention time and mass spectrum as that of an authentic sample obtained from the acetolysis of 38 (vide infra). Glc yields were 94 (65%), 187 (0.4%). Three other products were observed by glc analysis, but no further characterization was attempted.

Silver Assisted Solvolysis of 93 in Various Concentrations of Aqueous Acetone-General Procedure Aqueous acetone mixtures were prepared, by volume, by adding the appropriate volume of distilled water (utilizing a graduated syringe or pipette) to a volumetric flask and then filling the flask with acetone. Reagent grade acetone was obtained from Fisher Scientific Company (note that this acetone contained 0.5% water, which was taken into consideration when preparing the aqueous solutions). The

following procedure, described for 90% aq. acetone, was typical: To 140 mg (0.455 mmol) 93 in 3 ml 90% aq. acetone was added 940 mg (4.55 mmol) anhy. $AgClO_4$ in 4 ml 90% aq. acetone. After stirring for 4 hr. at room temperature, the mixture was diluted with ether. The ether solution was washed subsequently with water and three times with 5% NaOH solution. The combined basic extracts were then acidified with conc. HCl solution, followed by ether extraction, drying over anhy. Na_2SO_4 and evaporation of solvent to yield 28 mg (34%) of carboxylic acids 190, 191 and 192, (vide infra for determination of the ratios of these acids). The ether solution which remained after base extraction was washed with dil. HCl solution, water and saturated NaCl solution, dried over anhy. $MgSO_4$ and concentrated to give 46 mg oil, to which was added 15.5 mg nitrobenzene as an internal standard for glc analysis (column B). Only a trace of hydroxy ketone 193 was detected due to the β-elimination caused by the basic work-up. To verify this, an ether solution of 193 was extracted several times with a 5% NaOH solution. Drying and solvent evaporation left a quantitative yield of enone 94 (glc and ir analyses). Total analyses of the products obtained from the solvolysis of 93 in various concentrations of aq. acetone are summarized in Table 12.

Determination of the Ratio of Carboxylic Acids (190-192). Use of the Methyl Esters One of the acids 192 was found to be insoluble in CCl_4 and $CDCl_3$. On this basis, it was possible to isolate the hydroxy carboxylic acid 192, utilizing CCl_4, mp 191-194; pmr (acetone-d_6, TMS): δ 9.5 (s. 1 H), 2.5-0.9 (m. 17 H); ir (KBr): 3400-2400 (COOH), 1705 (C=O), 1182 (C-O) cm^{-1} (see Fig. 56); cmr (acetone-d_6, rel. int.): δ 174.3 (0.11, C_{COOH}), 80.3 (0.24, C_{C-OH}), 50.3 (0.25, C_α to carboxylic acid), 27.3 (1.55), 25.3 (1.22), 21.9 (1.04), 19.8 (1.00).

Anal. Calc'd for $C_{11}H_{18}O_3$: m/e 198.1256
Found : m/e 198.1255

The remaining CCl_4 solution was concentrated in vacuo to give a semi-solid (55 mg) and then diluted with 20 ml ethanol and subjected to room pressure catalytic (10% Pd-C) hydrogenation. The reduced product (57 mg) was obtained, after work-up as described for hydrogenation of 139, and revealed a similar ir spectrum[128] (especially the characteristic peak at 1255 cm^{-1} for cis fused carboxylic acid) to that known for cis-decalin-9-carboxylic acid 190, mp 120-122° (acetone, lit[135] 121.8-123°).

In order to determine the ratios of 190-192, an ethereal solution of the mixture of the acids was titrated with diazomethane to yield the methyl esters 190a-192a; pmr ($CDCl_3$, rel. int.) three singlets at δ 3.70 (1.0,

CO_2CH_3 of 191a), 3.66 (3.0, CO_2CH_3 of 190a), 3.62 (1.6, CO_2CH_3 of 192a); glc analysis (column H, at 140°): retention time 33, 60 and 66 min. for 190a, 191a and 192a, with a ratio of 3.6:1.0:1.2, respectively. The assignment of the peaks was based on those of each ester prepared from the corresponding pure acid 190 and 192 with diazomethane.

Treatment of 93 with Acid Generated during Solvolysis To 49 mg (0.455 mmol) ethyl bromide in one ml 90% aq. acetone was added 85 mg (0.415 mmol) anhy. $AgClO_4$ in one ml 90% aq. acetone. After stirring at room temperature for 30 min., 140 mg (0.455 mmol) 93 , dissolved in 5 ml aq. acetone, was added to the reaction mixture. The resulting mixture was allowed to stand at room temperature for 4 hr. Work-up, as previously described for the hydrolysis of 93, afforded 136 mg (97%) of starting dibromide 93.

Treatment of [4.4.1]Propellane (198) with $AgClO_4$ in Acidic Aqueous Acetone To 30 mg (0.27 mmol) ethyl bromide in one ml 90% aq. acetone was added 112 mg (0.548 mmol) anhy. $AgClO_4$ in one ml 90% aq. acetone. After stirring at room temperature for 30 min., 41 mg (0.274 mmol) 198 in one ml 90% aq. acetone was added, and the resulting mixture allowed to stir for 2 hr. at room temperature. Work-up, as described for the hydrolysis of 93, gave 28 mg (70%) of starting propellane 198.

Buffered Acetolysis of 93 A solution of 1.10 g (3.58 mmol) 93 and 0.60 g (7.32 mmol) anhydrous sodium acetate in 6 ml glacial acetic acid was heated in a sealed tube at 125° for 32 hr. After cooling, the mixture was poured into ice-water and neutralized with solid sodium carbonate. The solution was then extracted with ether several times. The combined ether extracts were dried over anhydrous Na_2SO_4, followed by evaporation of solvent to yield 0.71 g brown oil. Next, 0.70 g of the oil was column chromatographed (silica gel). Elution with hexane afforded 330 mg (30% recovery) 93 and 70 mg (20%) 188; elution with 2% ether in hexane gave partial separation of enone 94, ketone 187, and two unidentified acetates. Compound 94 was identified by spectral (ir and pmr) comparison with a sample obtained from the solvolysis of 93 in aq. acetone. 6-Bromomethylenecyclodecanone (187), pmr: δ 5.95 (s. 1 H), 1.5-2.5 (m. 16 H); ir (film): 1710 (C=O) cm^{-1} (see Fig. 53 and 54).

Anal. Calc'd for $C_{11}H_{17}OBr$: m/e 244.0463

Found : m/e 244.0473

Benzocycloheptene (188): pmr: δ 6.95 (br. s. 4 H), 2.70 (m. 4 H), 1.7 (m. 6 H), ir (film): 3040, 1500, 1460, 750 cm^{-1}; uv (95%, C_2H_5OH): 271 (ϵ=380) nm [lit[68b] 271 (ϵ=292)]. Unidentified acetate A: pmr: δ 2.2-1.2 (m. with a sharp

singlet at 2.0); ir (CCl_4): 1740, 1710, 1240 cm^{-1}. unidentified acetate B: pmr: δ 2.1-0.6 (m. with a singlet at 1.98); ir (CCl_4): 1740, 1240 cm^{-1}. Glc analysis of the remaining 10 mg oil (column C) indicated the following composition (on the basis of unrecovered 93): 187 (19%), 94 (36%), 188 (21%) and unidentified acetates (ca. 18%)

Attempted Transannular Cyclization of 6-Chloromethylenecyclodecanone(189) To 5 ml acetic anhydride containing 50 mg anhy. $AlCl_3$ was added a solution of 50 mg (0.25 mmol) 189 in one ml acetic anhydride under nitrogen. The resulting mixture was heated at 145° for one hr. and then worked up as previously described for the transannular cyclization of 113. There resulted 53 mg of oil which was apparently an enol acetate on the basis of its ir spectrum (1768 cm^{-1}). The oil was treated with 5 ml 90% aq. methanolic KOH solution (0.3 M) at room temperature for 30 min. After work-up as described for the hydrolysis of 139, 41 mg (82%) of ketone 189 was recovered.

The [3.3.1]Propellane System

Silver Assisted Solvolysis of 9,9-Dibromotricyclo-[3.3.1.$0^{1,5}$]nonane(129) in 90% Aqueous Acetone in the Presence of Pyridine To 11.2 g (53.5 mmol) anhydrous

$AgClO_4$ and 4.23 g (53.5 mmol) dry pyridine in 20 ml 90% aq. acetone was added dropwise 3.0 g (10.7 mmol) 129 in 50 ml 90% aq. acetone over a 30 min period. The mixture turned brown rapidly. After stirring at room temperature for 24 hr., the precipitate was filtered off followed by dilution with ether. The solution was washed with water three times, then with saturated NaCl solution, and dried over anhydrous Na_2SO_4. After evaporation in vacuo left 4.84 g of yellow oil which was chromatographed (1 in.x 6 ft.nylon tubing, silica gel-Woelm grade for dry-column chromatography) with 2% ether in hexane. The following products were obtained in order of elution, i.e. the greatest R_f is first:

Tricyclo[3.3.1.$0^{1,5}$]nonan-9-one (203) 17 mg (1.2%); pmr: δ 2.5-1.1 (m); ir (CCl_4): 1824 (C=O), 1050 (cyclopropyl C-C) cm^{-1} (see Fig. 57); uv (CH_2Cl_2): λ_{max} 325 (ϵ = 27), 336 (ϵ = 22) nm; cmr ($CDCl_3$): δ 174.1, 32.8, 30.7, 30.4; cmr ($CDCl_3$, containing 2.5 equiv. CrAcAc): δ 173.6, 35.3, 33.8, 29.9.

Anal. Calc'd for $C_9H_{12}O$: m/e 136.0888

Found : m/e 136.0883 (0.2)

Calc'd for C_8H_{12} : m/e 108.0939

Found : m/e (rel. int.) 108.0938 (1.2)

Calc'd for C_7H_8O : m/e 108.0575

Found : m/e (rel. int.) 108.0575 (1.0)

Bicyclo[4.3.0]non-1(6)-en-2-one (202) 31 mg (2.1%); pmr: δ 2.7-1.6 (m); ir (CCl_4): 1668, 1632 cm^{-1}; uv (CH_2Cl_2): λ_{max} 250 (log ε = 4.23) nm [lit[136] 250 (log ε = 3.95)].

Anal. Calc'd for $C_9H_{12}O$: m/e 136.0888

Found : m/e 136.0886

A mixture of cis-bicyclo[3.3.0]octane-1-carboxylic acid (204) and bicyclo[3.3.0]oct-4(5)-ene-1-carboxylic acid (205) 1.42 g (86%); mp 30-38°; pmr (rel. int.) δ 11.3 (s. COOH, 6.2), 5.36 (m. CH = C, 1.0), 2.9-1.1 (m); ir (CCl_4): 3500-2400 (COOH), 1695 (C=O) cm^{-1}; cmr ($CDCl_3$): δ 186.0, 183.4, 151.9, 122.2, 65.2, 59.8, 49.8, 38.1, 37.6, 37.0, 35.2, 34.0, 26.8, 26.3, 23.8. The following reactions were carried out in order to adduce chemical evidence for the structure of 204 and determine the ratio of 204 and 205: (1) Room pressure catalytic hydrogenation of 50 mg of the mixture of 204 and 205 in 20 ml ethanol over 10% Pd-C, followed by filtration and evaporation afforded a white crystalline material, mp 43-44° (lit[127] 40-43°); pmr: δ 12.1 (s. 1 H), 2.65 (m. 1 H), 2.4-1.0 (m. 12 H); ir (CCl_4): 3500-2400 (COOH), 1693 (C=O) cm^{-1}; cmr ($CDCl_3$): δ 186.0, 59.8, 49.8, 38.1, 34.0, 26.3.

Anal. Calc'd for $C_9H_{14}O_2$: m/e 154.0994

Found : m/e 154.0996

(2) Esterification of 204 and 205 was performed by adding ethereal diazomethane solution to 10 ml ethereal solution containing 100 mg of the mixture of 204 and 205 until the yellow color persisted in the reaction mixture. After work-up as described for 190 and 191, the corresponding methyl esters 204a and 205a were obtained in excellent yield (98%); pmr ($CDCl_3$, rel. int.): δ 5.62 (m. CH=C of 205a, 1.0), 3.67 (s. OCH_3 of 205a, 3.0), 3.62 (s. OCH_3 of 204a, 16), 2.8-1.1 (m. aliphalic H); ir (CCl_4): 1730 (C=O), 1165 (CO_2CH_3) cm^{-1}; mass spec. at 16 ev: m/e (rel. int.) 168 (30), 166 (6), 140 (35), 137 (20), 136 (14), 127 (100), 109 (49), 108 (26), 107 (18); glc analysis (column H) failed to give ratio of 204a and 205a, probably due to the decomposition of the latter in the column.

Attempted Synthesis of Methanol Hemiketal of Tricyclo [3.3.1.$0^{1,5}$]nonan-9-one (203) A solution of 10 mg 203 and 5 ml anhydrous methanol was allowed to stir at room temperature for 16 hr. The excess methanol was evaporated under reduced pressure while the water bath was kept under 30°, giving 9 mg oil which showed no formation of hemiketal according to its ir and pmr spectra, but rather showed starting ketone 203. Thi oil was treated with 5 ml anhydrous

methanol at refluxing temperature (ca. 70°) for 8 hr. Again, no desired product was obtained, but a rearrangement product was observed, 7 mg (70%), pmr: δ 5.35 (m), 2.8-1.1 (m); ir (CCl_4): 1700 (C=O), 1640 (C=C) cm^{-1}. The structure of the product was tentatively assigned as bicyclo[3.3.1] non-1(2)-en-9-one (206).

Attempted Hydrogenation of 203 A 10 ml absolute ethanol solution containing 10 mg 203 and 2 mg 5% Pt-C was hydrogenated at 50 psi for two hr. After filtering off the catalyst and evaporating the solvent under reduced pressure, there remained 8 mg oil which was identified as mostly starting ketone 203, and possibly some desired product (according to its ir spectrum, 1730 (C=O) cm^{-1}. The tentative structure is bicyclo[3.3.1]nonan-9-one.

Attempted Photolysis of 203 A 100 ml pentane solution containing 10 mg 203 was degassed and irradiated at room temperature with a 450 watt mercury lamp through a filter (pyrex sleeve ACE glass cat. 6515-44). The solvent was removed under reduced pressure to give an oil showing only starting ketone 203 via ir analysis. When the oil was irradiated without filter for an additional 5 hr period, the product obtained gave a broad carbonyl absorption at 1720 cm^{-1}, and other peaks (1100, 1025 cm^{-1}). Glc analysis (column D) showed none of the expected product, bicycl[3.3.0] oct-1(5)-ene.

Reaction of 203 with Potassium Hydroxide To 5 mg 203 was added 5 ml 90% aqueous methanolic KOH solution (0.5 M) and allowed to stir at room temperature for 15 hr. After evaporating under reduced pressure, the residue was diluted with water and acidified with conc. HCl solution. The milky solution was extracted three times with ether. The combined ethereal solution was washed with water, saturated NaCl solution, dried and concentrated under reduced pressure. The resulting oil (4 mg), which solidified upon cooling, mp 40-44°, was identified as bicyclo[3.3.0] octane-1-carboxylic acid (204) on the basis of its ir spectrum.

Silver Assisted Solvolysis of 129 in 99% Aqueous Acetone To 4.80 g (17.9 mmol) anhydrous $AgClO_4$ in 30 ml 99% aq. acetone was added dropwise 1.00g(3.58 mmol) 129 in 20 ml 99% aq. acetone. After stirring at room temperature for 20 min., work-up as described for the solvolysis of 129 in 90% aq. acetone afforded 0.58 g of yellow oil which was diluted with 100 ml ether. The acids 204 and 205 were not completely removed by extraction with saturated $NaHCO_3$ solution. Thus, the ethereal solution. was extracted with 5% NaOH solution. Acidification of the aqueous solution followed by ether extraction, drying and solvent evaporation afforded 343 mg (62%, note that low

yield is due to a mechanical loss in work-up) carboxylic acids 204 and 205. The organic layer remaining after base extraction was washed with water, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to yield 98 mg oil, which was chromatographed to afford 42 mg (4.2% recovery) 129 34 mg (7%) 203 and 15 mg of a mixture of enone 202 and 5-bromomethylenecyclooctanone (207). The evidence for the structure of 207 is a pmr singlet at δ 5.80, an ir carbonyl absorption at 1690 cm^{-1} and a molecular ion at m/e 216.0156 (calc'd for $C_9H_{13}OBr$: m/e 216.0150).

Treatment of 129 with Acid Generated during Solvolysis To 49 mg (0.455 mmol) ethyl bromide in one ml 90% aq. acetone was added 85 mg (0.415 mmol) anhydrous $AgClO_4$ in one ml 90% aq. acetone. After stirring at room temperature for 30 min., 127 mg (0.455 mmol) 129 dissolved in 5 ml 90% aq. acetone, was added to the mixture. The resulting mixture was stirred for 12 hr. at room temperature, and then worked up as described for the hydrolysis of 129 to yield 118 mg (92%) starting dibromide 129.

Treatment of Tricyclo[3.3.1.$0^{1,5}$]nonane (214) with $AgClO_4$ in Acidic Aqueous Acetone To 53 mg (0.494 mmol) ethyl bromide in one ml 90% aq. acetone was added 204 mg (0.988 mmol) anhydrous $AgClO_4$ in 2 ml 90% aq. acetone.

After stirring at room temperature for 30 min, 60 mg (0.494 mmol) 214 dissolved in 2 ml 90% aq. acetone, was added to the mixture. Further stirring of the resulting slurry for 17 hr. at room temperature, followed by work up as described for the hydrolysis of 129 gave 17 mg (28%) starting propellane 214.

Treatment of 214 with $AgClO_4$ in Neutral Aqueous Acetone To 17 mg (0.139 mmol) 214 in one ml 90% aq. acetone was added 30 mg (0.145 mmol) anhydrous $AgClO_4$ in one ml 90% aq. acetone. After stirring at room temperature for 4 hr., work-up as described for the hydrolysis of 129 gave neither starting material nor any other identifiable monomeric products.

Silver Assisted Solvolysis of 129 in 95% Aqueous Acetone in the Absence of Pyridine To 11.2 g (54.0 mmol) anhydrous $AgClO_4$ in 30 ml 95% aq. acetone was slowly added 3.0 g (10.7 mmol) 129 dissolved in 50 ml 95% aq. acetone. After stirring for 12 hr at room temperature, work-up as described for the solvolysis of 129 in 90% aq. acetone in the presence of pyridine afforded 1.46 g (89%) carboxylic acid 204 and 205 and 72 mg yellow oil, which showed a trace amount of cyclopropanone 203 in the ir spectrum. However, no further separation was attempted.

Silver Assisted Acetolysis of 129 To 0.74 g (3.58 mmol) anhydrous $AgClO_4$ in 20 ml of a mixture of acetic acid and acetic anhydride (80:20) was added dropwise 1.00 g (3.58 mmol)129, in 30 ml of the aforementioned solvent, over a period of 15 min. After stirring the resulting mixture at room temperature for an additional 10 min., it was stored in the freezer overnight. Work-up was performed as described for the acetolysis of 93 to afford 0.73 g of yellow oil, which showed a pmr singlet at δ 5.60 and an ir absorption at 1745 cm^{-1}. The mixture was chromatographed (silica gel, eluted with 1-10% ether in hexane) to yield 436 mg (44% recovery)129, 7 mg (0.6%) 9-bromo-1,5-diacetoxybicyclo[3.3.1]nonane (208) and 79 mg (15%) 9-bromo-9-acetoxytricyclo[3.3.1.$0^{1,5}$]nonane (209). The new compounds gave the following properties:

Diacetate 208: mp 183° (decomp.); pmr: δ 5.60 (s. 1 H), 2.8-1.2 (m. with a singlet at 2.04); ir (CCl_4): 1740 (C=O), 1240, 1220 (acetate) cm^{-1}; mass spec. at 16 ev: m/e (rel. int.), 320 (P+2, 10), 318 (P, 10), 280 (22), 278 (39), 276 (22), 218 (89), 216 (92), 150 (76), 138 (56), 136 (100), 109 (72), 108 (72).

Bromoacetate 209: mp 70-71° (aq. methanol); pmr: δ 2.5-1.2 (m. with a sharp singlet at 2.0); ir (CCl_4): 1770 (C=O), 1220, 1180 (acetate) cm^{-1} (see Fig. 58); mass spec. at 70 ev: m/e (rel. int.), 260 (P+2, 0.3), 258 (P, 0.3),

217 (0.8), 215 (0.8), 137 (8), 136 (4), 135 (3), 126 (4), 108 (100), 93 (32), 80 (45), 43 (60); also found: m/e 108.0939 (calc'd for C_8H_{12}: m/e 108.0939).

A second solvolysis, similar to that described above, involved the reaction of 0.50 g (1.79 mmol) 129 with 0.37 g 1.79 mmol) anhydrous $AgClO_4$ in 30 ml of the aforementioned acetic acid/acetic anhydride mixture at room temperature for 22 hr. After work-up as above, the 0.30 g yellow oil obtained was subjected to base catalyzed hydrolysis as described for 151 to give 7 mg carboxylic acid 204 (identified by ir spectroscopy). The organic layer remaining after base extraction and drying afforded 198 mg oil which was chromatographed to give 186 mg (37% recovery) 129 and 10 mg of a mixture (two spots on TLC) of 9-bromo-1,5-dihydroxybicyclo[3.3.1]nonane (210) and 6-hydroxybicyclo[4.3.0]nonan-2-one (211) on the basis of the following spectral data, pmr: δ 3.58 (s), 3.40-3.15 (m), 2.8-1.2 (m); ir (CCl_4): 3570 (OH), 1725 (C=O), 1165 (tertiary C-O) cm^{-1}. Part of the mixture (5 mg) was then refluxed in 2 ml 90% aq. methanolic KOH solution (0.4 M) for 10 min. The product (2 mg), obtained after work-up as described for the elimination of hydroxyketone 193, showed a doublet [1668 (C=O) and 1632 (C=C) cm^{-1}] in the ir spectrum, and Rf = 0.38 (TLC, 1:1 CH_2Cl_2/hexane), and

the same pmr spectrum (HX-90 FT-spectrometer) as an authentic sample of enone 202.

Silver Assisted Solvolysis of 9-Bromotricyclo-[3.3.1.$0^{1,5}$]nonane (212) in 85% Aqueous Acetone To 414 mg (2.0 mmol) anhydrous $AgClO_4$ in 2 ml 85% aq. acetone was added one ml of an 85% aq. acetone solution of 40 mg (0.2 mmol) 212. After stirring at room temperature for 20 min., work-up as described for the hydrolysis of 129 afforded 25 mg (91%) of bicyclo[3.3.0]octane-1-carboxaldehyde (213), pmr: δ 9.40 (s. 1 H), 2.7-1.1 (m. 13 H); ir (CCl_4): 2695 (aldehydic C-H), 1730 (C=O) cm^{-1};

Anal. Calc'd for $C_9H_{14}O$: m/e 138.1045

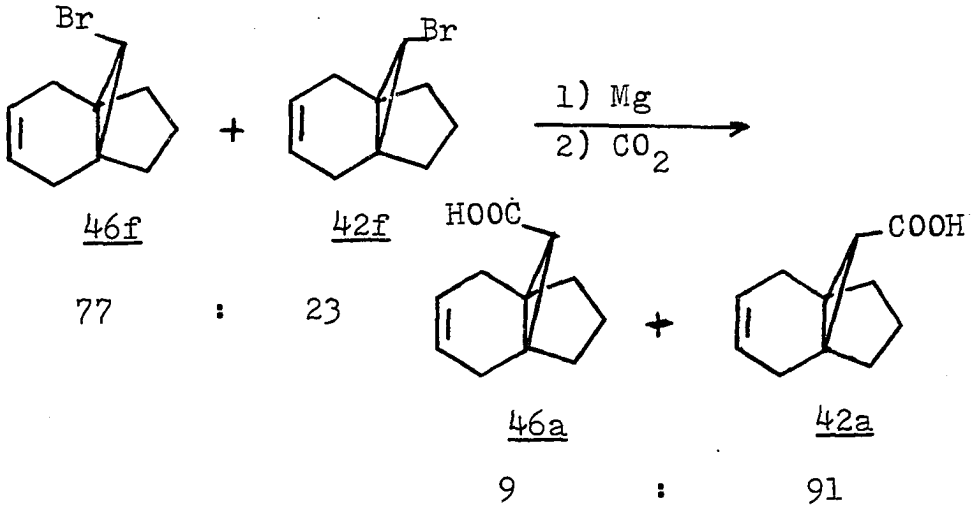
Found : m/e 138.1046

Additionally, a trace amount of carboxylic acid 190 was detected in the mass spec. (m/e 154).

PART III:
STUDIES OF CERTAIN CYCLOPROPYL ANIONS AND RADICALS

INTRODUCTION

In the course of the syntheses of norcaradienylcarbinyl derivatives, we chanced to observe that a 77 to 23 mixture of bromopropellanes 46f and 42f was converted to a 9:91 mixture of the corresponding carboxylic acids 46a and 42a via carbonation of the Grignard reagent (see Eq. 23). The stereoselective formation of 46a and 42a led us to investigate the nature of the cyclopropyl radical(s) and cyclopropyl anion(s) formed in the propellane system.



46f 42f 46a 42a

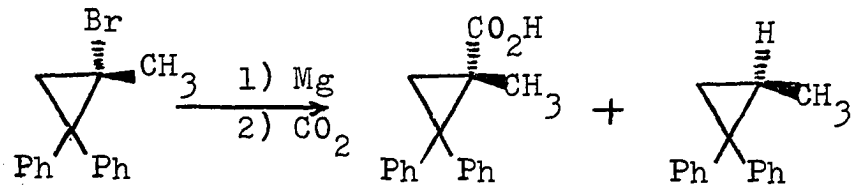
77 : 23 9 : 91

(23)

Mechanism of Grignard Reagent Formation

It has been well established by many workers that Grignard formation occurs by a free radical mechanism.[138-140] Walborsky and Young[141] reported the first example of a Grignard product formed with net retention of configuration

from an optically active cyclopropyl bromide 215, (see Eq. 24), and suggested that the extensive racemization observed in the products occurred in the Grignard formation step and not after the Grignard reagent was formed; the Grignard reagent was presumed to form with net retention.



215 216 217 (24)

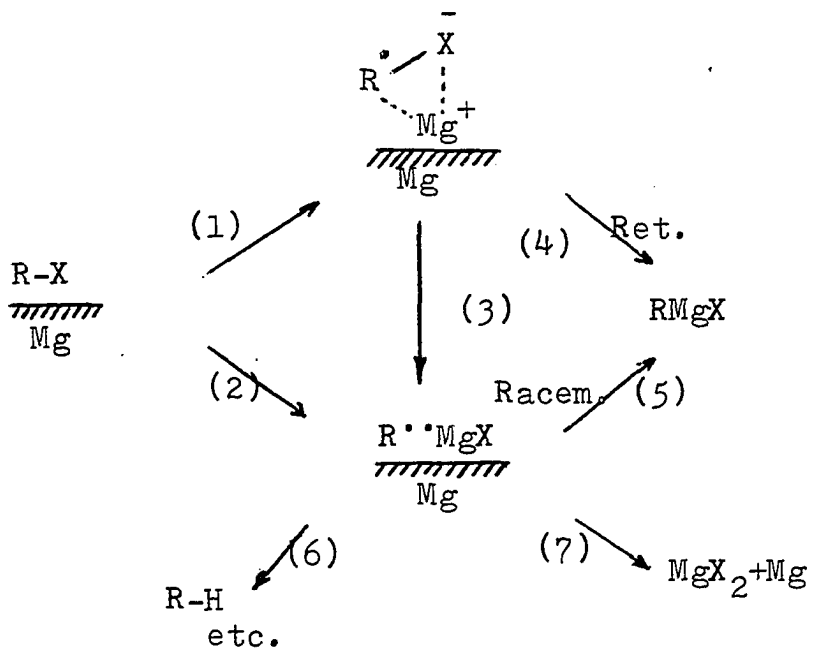
opt. purity %

98±2% 12±2% 10±2%

In the same study, deuterolysis of the Grignard reagent resulted in 78% and 52% deuterium incorporation when THF and ether were used as solvent, respectively. These data indicate that reaction with solvent in the Grignard formation step does occur and that diethyl ether is cleaved to a greater extent than THF. However, Walborsky's recently published results in perdeuterated ether,[142] shown in Table 16, suggest that solvent cleavage becomes more important in THF than in ether, i.e. solvent cleavage is an important source of that hydrocarbon which

is formed. Furthermore, it is also of interest that the yield of the acid 216 is highter in THF-d_8 than in ordinary THF and the optical purity of 216 drops slightly in THF-d_8. Likewise, the yield of Grignard reagent is drastically reduced in ether while the yield of side products increases. The authors proposed the following mechanistic pathways (see Scheme 17) for Grignard reagent formation in order to explain their results.

Scheme 17



The processes were assumed to take place on the surface of the magnesium metal. Interaction of the cyclopropyl halide and magnesium by pathway (1) gives a tight

radical anion which collapses with radical cation by pathway (4) to Grignard reagent with complete retention of configuration. Alternatively collapse may proceed by pathway (3) to a loose radical pair, which may also be formed directly from magnesium by pathway (2). Racemization therefore takes place in the loose radical pair to give racemic Grignard reagent by pathway (5). However,

Table 16. Formation and Carbonation of the Grignard Reagent from 215 in Various Solvents.

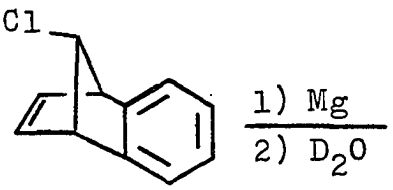
Solvent	Temp. °c	Acid 216 yield,%	Acid 216 opt. purity%	Hydrocarbon, 217 overall yield of RH + RD, %	Hydrocarbon, 217 RD %	Hydrocarbon, 217 opt. purity,%
Et_2O	35	26	20.4	22.9	-	3.7
THF	65	70	18.5	6.0	-	6.2
Et_2O-d_{10}	35	25	18.2	20.2	6.7	4.6
THF-d_8	65	88	13.0	1.0	29.2	10.3
THF-d_8	65	93	13.2	1.4	28.1	7.7

the cyclopropyl radical may abstract a hydrogen from a solvent molecule or from other alkyl halide molecules present on the surface of the metal. Ethyl ether is known to be one of the poorer solvents for the formation of radical anions;[143] therefore more of the loose radical pair might be formed in ether than in THF. Consequently,

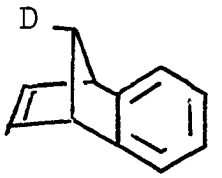
more hydrocarbon 217 would be produced in ether. More recently, Whitesides, et al.,[144] reported that the rate determining step for formation of Grignard reagents involves electron transfer from the magnesium metal to alkyl halide., presumbly forming an unstable radical anion.[145] However, Bodewitz and coworkers[146] presented direct evidence, via CIDNP phenomena, that radicals are true intermediates in the formation of ethylmagnesium and iso-butylmagnesium bromide in THF and of ethylmagnesium iodide in di-n-butyl ether.

Moreover, Ford and Buske[147] investigated the reaction of 218 with magnesium in THF followed by deuterolysis. The major product (220, 90%) was formed via overall retention (see Eq. 25). Unfortunately, no conclusive results were obtained from the syn epimer (221) under the same conditions. In any event, the authors rationalized the highly stereoselective formation of the Grignard reagent as due to a large barrier to pyramidal inversion of 7-benzonorbornadienyl free radicals and carbanions, formed via an electron transfer free radical surface mechanism. It is interesting to note that when 219 or 222 was reduced by $n\text{-Bu})_3SnD$, the isomeric distribution of deuterium in the product (220/223=43/57) was nearly identical in both cases, irrespective of the geometry of the starting bromide[148] (see

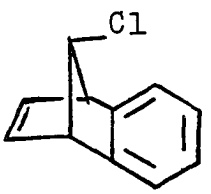
Eq. 26 and 27). This may indicate a lower inversion barrier in the radical than in the anion.



218

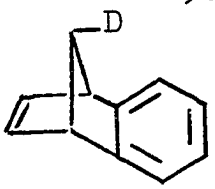


220 90%



221

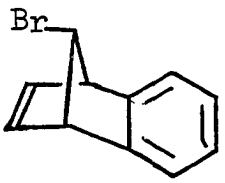
+



10%

223

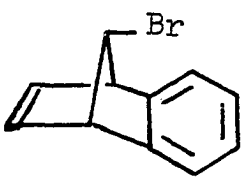
(25)



219

220 + 223 (26)

43% 57%



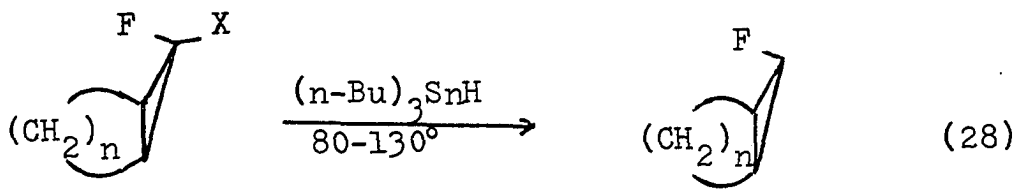
222

220 + 223 (27)

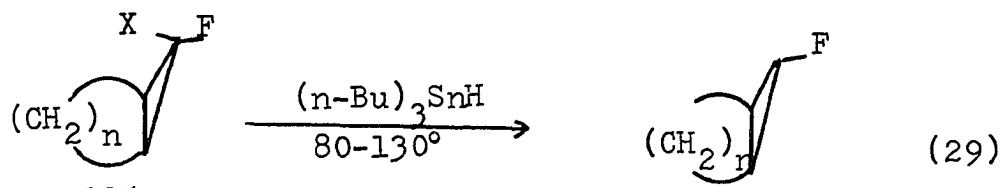
43% 57%

Generation of Cyclopropyl Radicals

Since the geometry of the cyclopropyl radical has long been a subject of interest, attempts to intercept the nonplanar radical have been made; a number of these have been unsuccessful.[149-151] However, stereospecific reduction of gem-halofluorocyclopropanes 224 or 225 with tri-n-butyltin hydride to produce completely retained fluorocyclopropane products has been cited as evidence for a pyramidal structure for the fluorocyclopropyl radical[152] (see Eq. 28 and 29). This conclusion was reasonable since there is evidence that the reduction of alkyl halides with organotin hydride involves a free radical chain



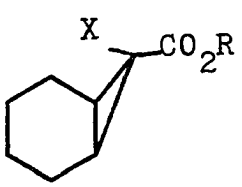
224 (28)



225 (29)

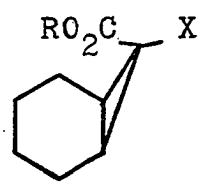
n=3,4
X=Cl,Br

mechanism.[153-156] Most recently, the assumptiom regarding the pyramidal structure for the fluorocyclopropyl radical has been confirmed by studying the brominative decarboxylation and thermal decomposition of 226, 228, 227, 229 respectively. The results shown in Tables 17 and 18 led to the conclusion that the 7-fluoro-7-norcaryl radical is configurationally stable, but the chloro and proton analogs are not.[157]



X=F,Cl,H

226 [a]R=H
227 [b]R=O-t-Bu



228 R=H
229 R=O-t-Bu

In connection with this, thermolysis and photolysis of the t-butyl peroxyester precursors 230 and 231 indicated that the equilibration of radicals determines the products; essentially identical endo/exo ratios were obtained from either starting chloride, although the ratio varied with conditions (from 0.4 to 2.0).[158,159]

Table 17.Brominative Decarboxylation of Acids at 77°.

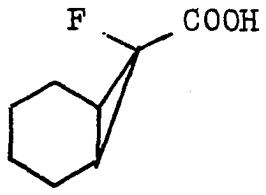
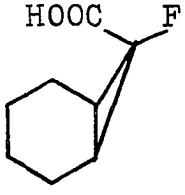
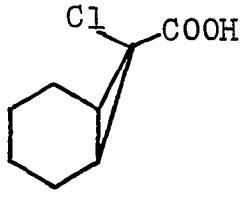
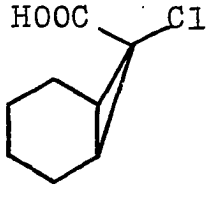
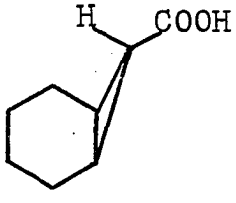
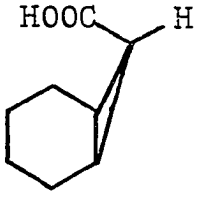
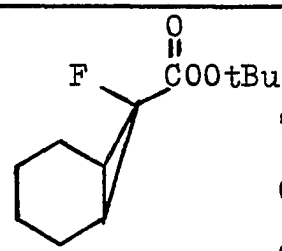
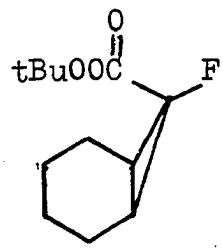
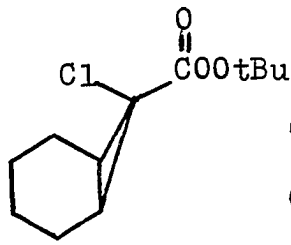
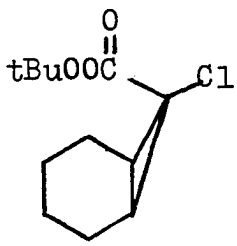
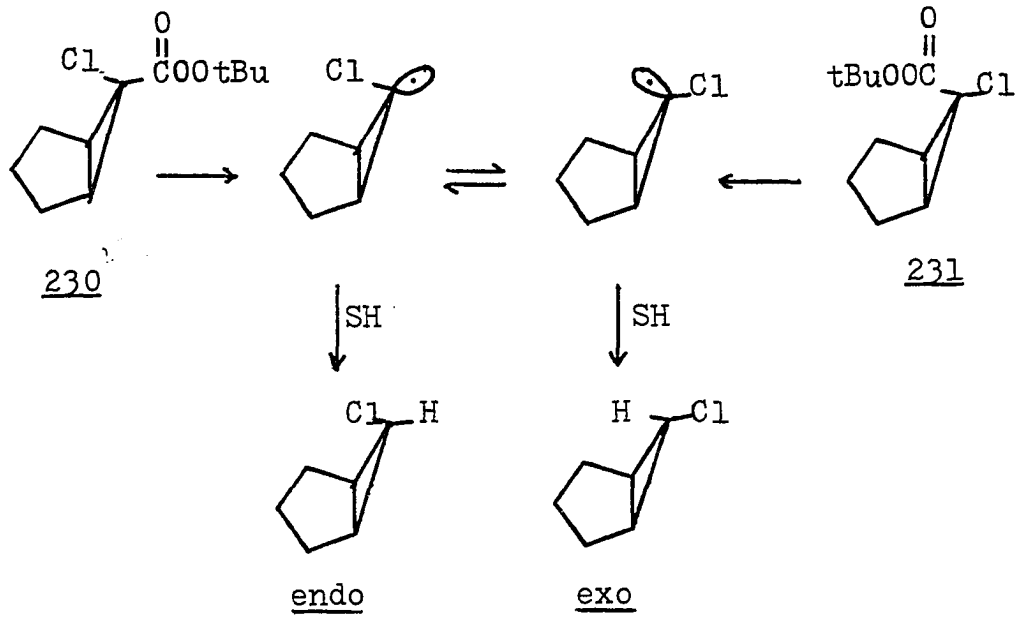
Compound	Yield, %	Isomer Ratio	
		Retn.	Invn.
	75	100	0
	71	100	0
	73	72	28
	74	43	57
	73	84	16
	76	15	85

Table 18. Thermal Decomposition of Peroxy Esters.

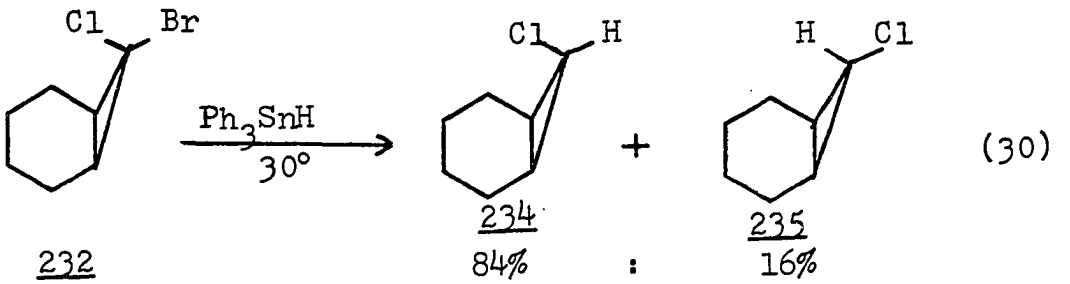
Compound	Solvent	Yield, %[a]		Isomer Ratio	
		RCO_2H	RH or RBr	Retn.	: Invn.
	Toluene	13	61	94	6
	Cumene	15	65	96	4
	$CBrCl_3$	-	53	100	0
	Toluene	16	65	90	10
	Cumene	16	58	93	7
	$CBrCl_3$	-	49	100	0
	Toluene	17	64	78	22
	Cumene	18	56	80	20
	$CBrCl_3$	-	38	82	18
	Toluene	18	68	23	77
	Cumene	19	55	21	79
	$CBrCl_3$	-	47	18	82

[a] R stands for 7-fluoro or 7-chloro-7-norcaryl group



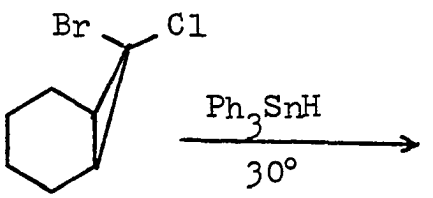
Solvent (toluene or diisopropylbenzene) is the source of hydrogen in the above case. If the hydrogen donor is a more reactive one such as triphenyltin hydride, the approach of tin hydride to the intermediate radicals becomes important, and may compete with complete equilibration of the cyclopropyl radical, as in the reduction of 232 and 233.[160] The former yielded more retentive product than did the latter. (see Eq. 30 and 31)

In a related study, Ando and coworkers[161] reported that the isomeric products were nearly identical for



(30)

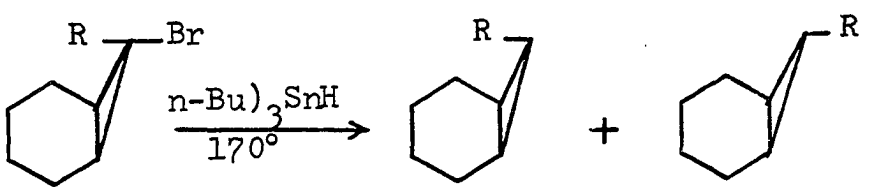
232 → 234 84% : 235 16%



(31)

233 → 234 69% : 235 31%

reduction of 236 and 237 (see Eq. 32). This is probably due to the p-π conjugation between methoxycarbonyl or cyano group and the cyclopropyl radical center which lowers the energy barrier for inversion. The predominant formation of endo product 238 must be due to the greater steric repulsion in the hydrogen transfer from the tin hydride to the endo side of the radical relative to the exo side.



(32)

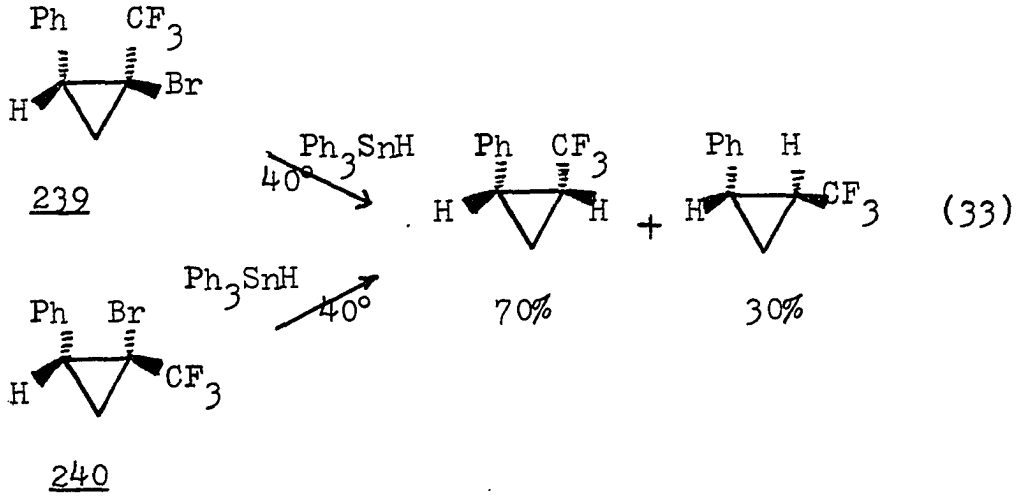
236 R = CO_2CH_3

237 R = CN

238 90% 10%

91% 9%

Nevertheless, reduction of 239 or 240 with a large excess of neat triphenyltin hydride at 40° gave a mixture of two isomers of the same composition irrespective of the geometry of the starting material.[162] (see Eq. 33)



(33)

In general, the configurational stability of free radicals can be regarded as being dependent on the s character of the odd-electron orbital.[163] Since the s character of the carbon orbital forming the C-F bond in the α-fluorocyclopropyl radical decreases relative to that of the C-H bond in the cyclopropyl radical, the s character of the odd-electron orbital increases. It may be expected that the more electronegative the α substituent is, the

less rapidly the inversion of the cyclopropyl radical will occur.[157] In fact, the energy barrier for inversion of some cyclopropyl radicals was calculated via CNDO/2[160] and MINDO/3;[164] the results, given below, were in accord with the above reasoning.

Inversion Barrier Kcal/mol			
CNDO/2	10.5	4.0	0.8
MINDO/3	5.9	4.6	-

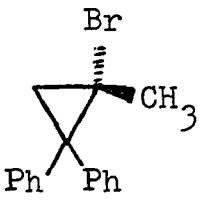
It should be noted that organotin hydrides are considered to be extremely reactive toward radicals;[155,165] with the reactivity of the various tin hydrides as follows:[156c]

$$(n\text{-Bu})_3SnH < (n\text{-Bu})_2SnH_2 < Ph_3SnH < Ph_2SnH_2$$

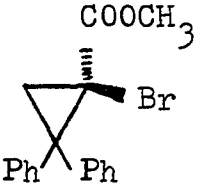
Thus the more reactive hydrides may be better able to trap some cyclopropyl radicals before equilibration occurs.

However, Altman and Nelson[166] carried out the reduction of two optically active cyclopropyl bromides, 241 and 215 in a large excess of neat triphenyltin hydride and

reported that net inversion had occurred. This is in direct contrast to the results of Jacobus and Pensak[167] who reduced pure 215 with sodium dihydronaphthalide in dimethoxyethane and obtained 29% optically pure product with net retention of configuration. Although they were dealing with two different reagents, radical intermediates were involved in both cases. One possible explanation[166] would be that the radical undergoes rapid inversion, but that the front side is blocked by the bulky triphenyltin bromide (radical cage pair) and reduction thus gives net inversion in Altman's case.



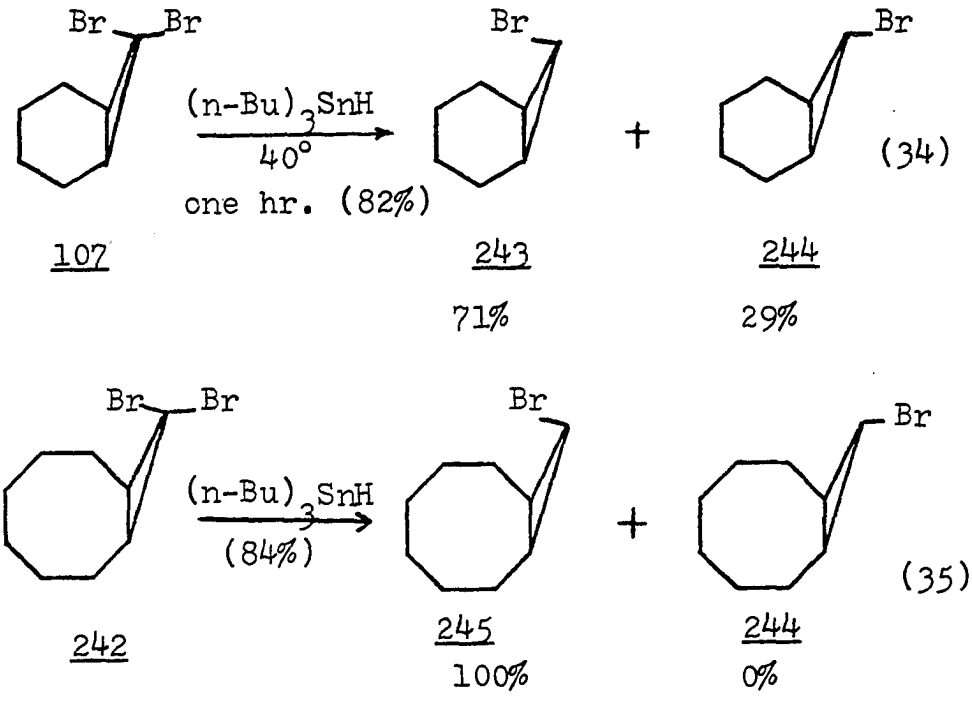
215



241

Indeed, when the reducing agent was changed to di-n-butyltin dihydride, net retention in the reduction of optically active 215 and 241 was observed.[168] Cage reduction of a rapidly inverting cyclopropyl radical was proposed.[168]

The original work on the preparation of monohalocyclopropane with tri-n-butyltin hydride[112] provides the results shown in Eq. 34 and 35.



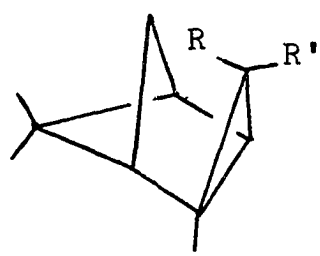
Seyferth and coworkers[112] have argued that steric factors overweigh other considerations, such as planar or rapidly inverting cyclopropyl radicals, in terms of the observed product distribution. However, when the same dibromo compounds, 107 and 242, were treated with excess Na-DMSO, they yielded the opposite composition of the monobromo products 243-246.[169] see (Eq. 36 and 37) The mechanism was postulated as involving nucleophilic displacement on bromine to give a bromocyclopropyl carbanion intermediate which then is protonated by solvent.

Recently, Hatem and Waegell[170] studied the reduction of the cyclopropane derivatives 247 and 248; n-Bu)$_3$SnH or

$$\underline{107} \xrightarrow[25°,\ 2.5\ hr\ (72\%)]{Na,\ DMSO} \underline{243}\ (1\text{-}10\%) + \underline{244}\ (90\text{-}99\%) \qquad (\underline{36})$$

$$\underline{242} \xrightarrow[(71\%)]{Na,\ DMSO} \underline{245}\ (5\%) + \underline{246}\ (95\%) \qquad (\underline{37})$$

Na-DMSO gave solely the anti-monohalo product 249. Tin hydride reduction was thought to proceed through a radical intermediate which formed by attack from the less hindered direction and then rapidly inverted. The inverted radical abstracted hydrogen from tin hydride. However, either an anion or radical mechanism was suggested by the authors for the Na-DMSO reduction.[170] Likewise, treatment of 248 with lithium aluminum deuteride in refluxing ether gave only 250 together with some cyclopropane ring-opened products. A radical mechanism was proably also involved in the reduction of 248 with LAD.[171]



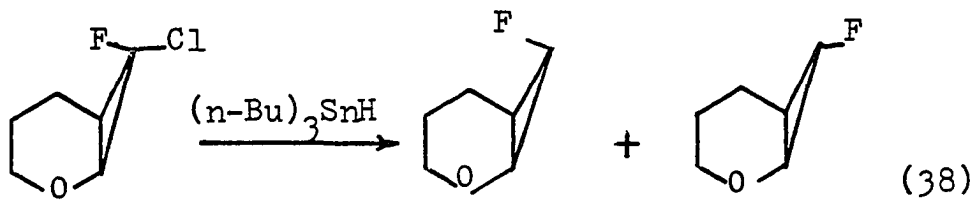
247 [a] R = R' = Cl

248 [b] R = Cl, R' = Br

249 [c] R = H, R' = Cl

250 [d] R = D, R' = Cl

The effect of β-substituents on the configurational stubility has also been probed. It was reported[172] that an isomeric mixture of fluorocyclopropanes was obtained in the reduction of 251 with $(n\text{-Bu})_3SnH$, despite the configurational stability of the fluorocyclopropyl radical described previously (see Eq. 38).

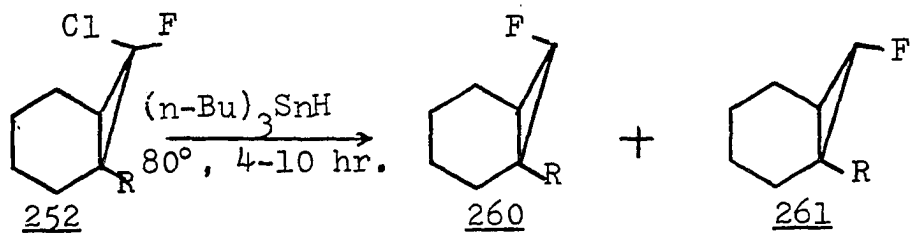


(38)

	Temp.		
	± 80°	84%	16%
251	130°	65%	35%
	165°	5%	95%

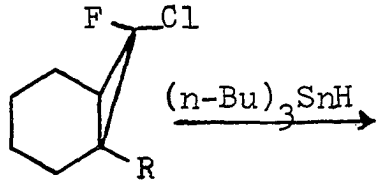
In a parallel study, the stereospecificity of the reduction of 252a-c and 253a-c with tin hydride has been found to decrease in the order a > c > b, (see Eq. 39 and 40), suggesting that the configurational stability of the α-fluorocyclopropyl radical is affected by the nature of the β-substituents.[173] It appears that β-methyl and β-methoxy groups have the effect of stabilizing and destabilizing the 7-fluoro-7-norcaryl radical, respectively.

Normally, cyclopropyl radicals unsubstituted at the α-carbon will undergo rapid ring inversion to give an epimeric mixture of products.[174-176] However, when 254 was treated with lithium naphthalenide in THF at -78°,



(39)

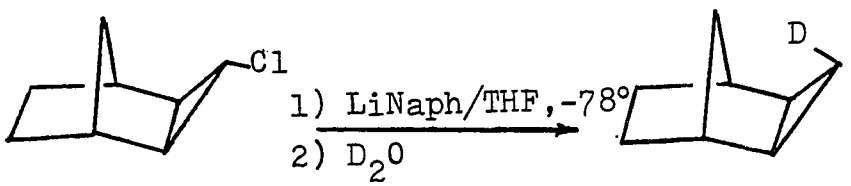
252	260	261
[a]R = Me	0%	100%
[b]R = OMe	12%	88%
[c]R = H	2%	98%



260 + 261 (40)

253		
[a]R = Me	100%	0%
[b]R = OMe	94%	6%
[c]R = H	100%	0%

followed by deuterolysis, predominantly inverted product ($\geq$100/1) was obtained[177] (see Eq. 41). One possible explanation is that the initially formed anti radical 255 is less stable than the syn radical 256 due to greater steric interaction (H_3-H_8) in 255 (see Scheme 18). Alternatively, 256 could be reduced much faster than 255.



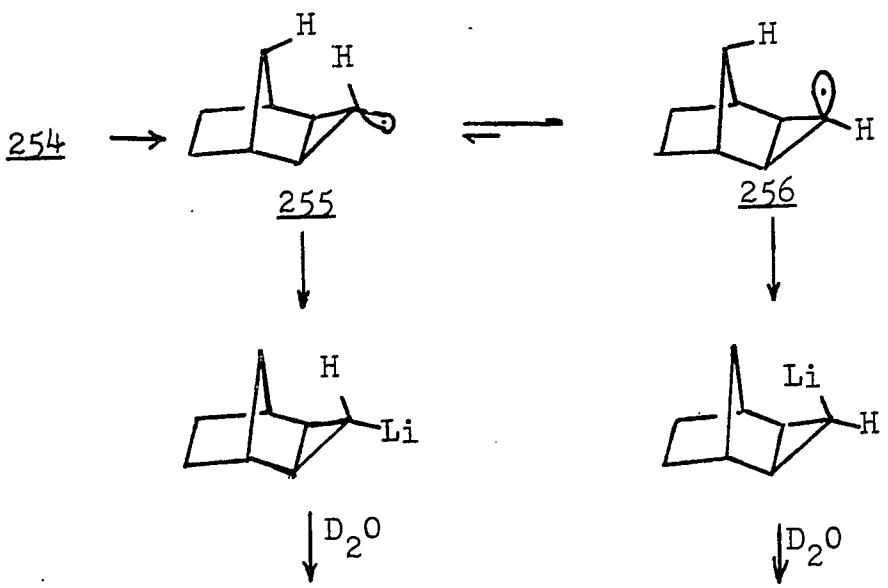
100%

254

+ (41)

≤ 1%

Scheme 18



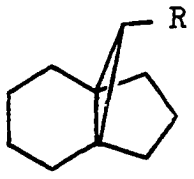
retained product

inverted product

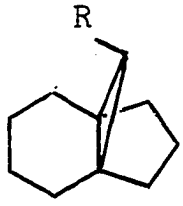
RESULTS AND DISCUSSION

Formation of Cyclopropyl Anions

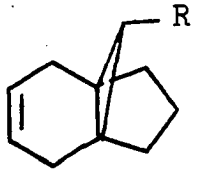
Our studies of the Grignard reaction of 46f and 42f prompted us to investigate the nature of the carbanions associated with 46f and 42f. Walborsky and coworkers[174] have published results involving an intermediate cyclopropyl carbanion derived from an optically active bromide 215 and n-butyllithium. They found that on treatment of the resultant tertiary cyclopropyllithium compound with carbon dioxide, bromine, iodine or water, products were obtained in which the configuration, as well as the optical activity, had been completely retained. No effect on the optical purity of the products could be found upon varying the temperature, solvent or reaction time, although the lithium derivative was found to react with solvent in the order 1,2-dimethoxyethane> THF >diethyl ether. These results indicate that 1-methyl-2,2-diphenylcyclopropyllithium is configurationally more stable than alkyllithiums[175] (sp^3) and stilbenyllithium[176] (sp^2) which have been shown to either racemize or isomerize under comparable conditions.



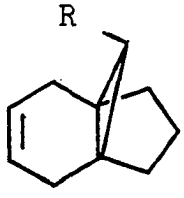
41



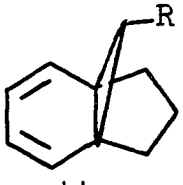
45



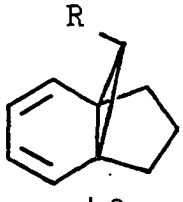
42



46



44



48

a, R=CO_2H

b, R=CO_2CH_3

g, R=H

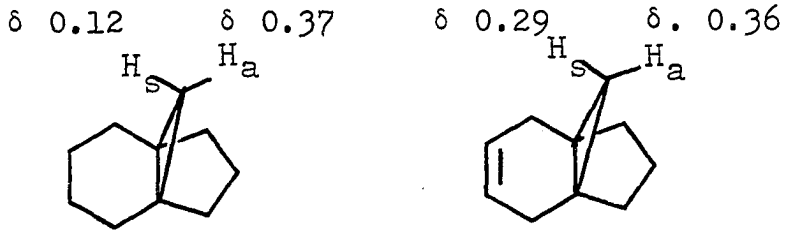
h, R=D

i, R=Li

j, R=OH

k, R=$OCOCH_3$

Evidence pertaining to the stability of secondary cyclopropyl carbanions[177,178, 179] has also appeared in the literature. In order to check the configurational stability of the secondary cyclopropyl carbanions related to 46f 42f and their saturated analogs, the lithio derivatives were generated. Treatment of 45f with n-butyllithium in ether followed by deuterolysis yielded deuterated product 45h with complete retention of configuration within the error limits of pmr analysis (see Eq. 42). Only one cyclopropyl proton signal was observed in the pmr (δ 0.34) and attributed to Ha in 45h. The assignment of stereochemistry of 45h can be compared to the published data[8] as shown.



41g 42g

However, the same lithio derivative 45i was converted to the carboxylic ester 45b via the usual procedure. The pmr spectrum of the product obtained displayed one methyl ester signal (δ 3.55, see Fig.61) and glc analysis indicated one component due to 45b (ret. time = 8.3 min, checked with an authentic sample). β-Epimer 41b was prepared independently, and showed a ret. time = 9.4 min,

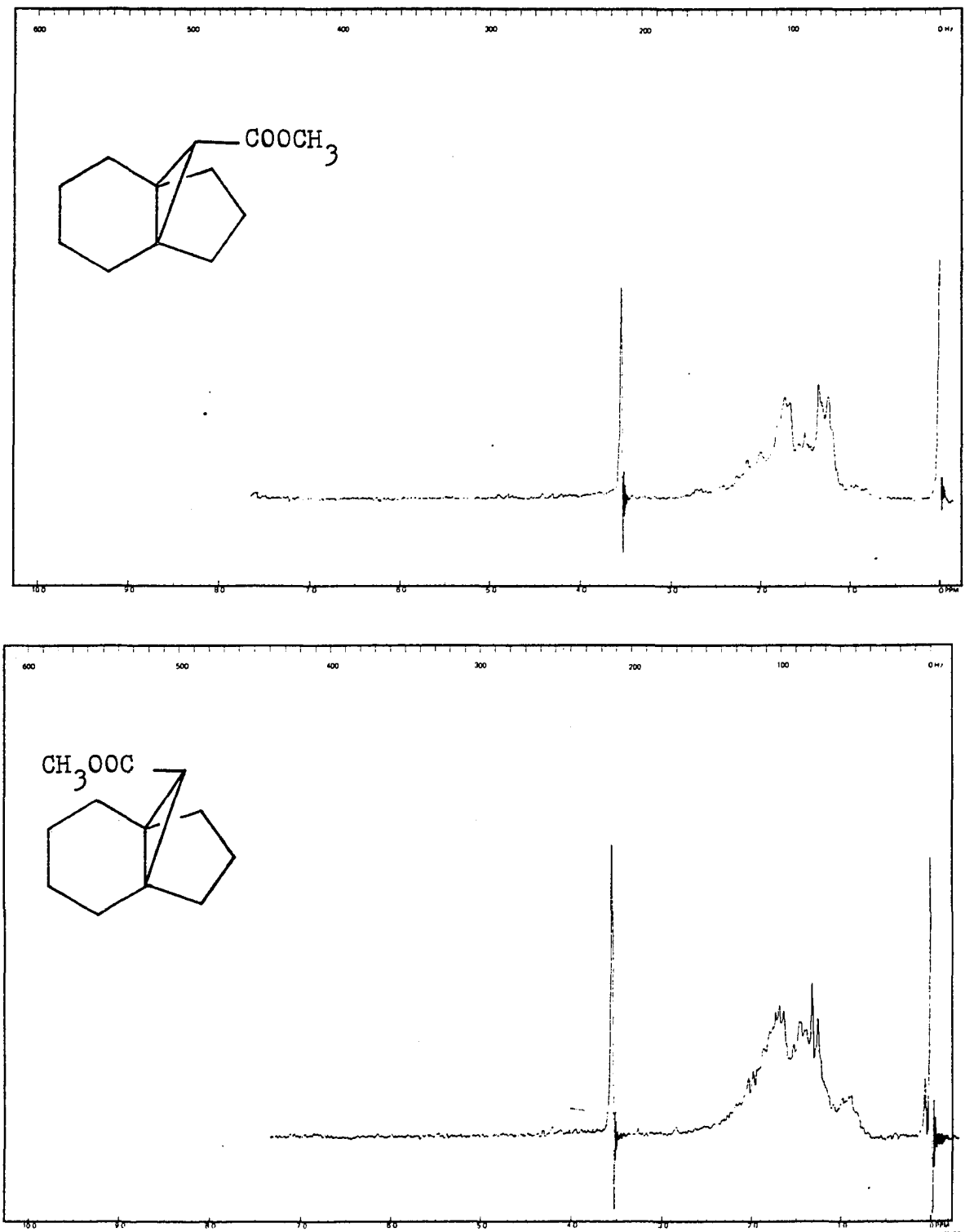
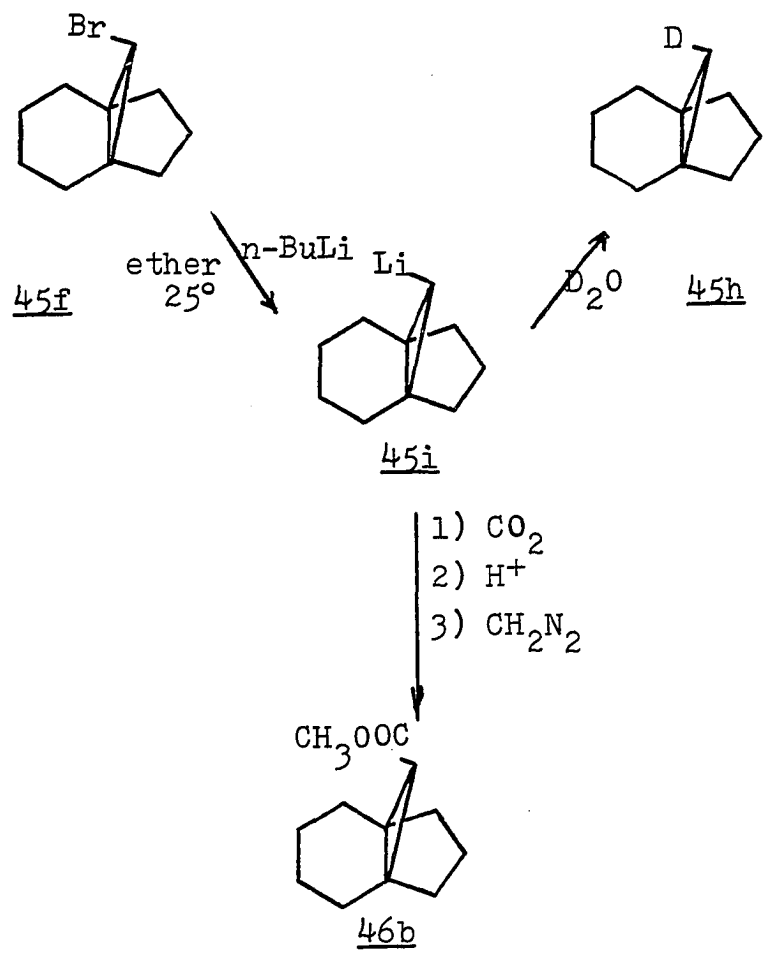


Figure 61. Pmr Spectra of 10-Methoxycarbonyltricyclo-[4.3.1.$0^{1,6}$]decane: 41b (Top) and 45b (Bottom).



(42)

whereas the pmr spectrum revealed a very similar chemical shift for the methyl ester (δ 3.55, see Fig.61).

Unsaturated analog 46f was treated in the same manner, and the results indicated that over-all retention of configuration in the products had occurred. Since the small chemical shift difference between the cyclopropyl protons of 42g leads to singlet at δ 0.32, the product obtained from the deuterolysis of cyclopropyllithium 46i

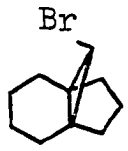
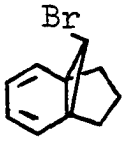
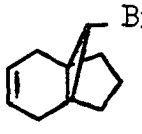
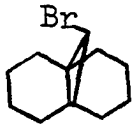
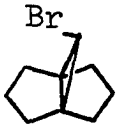
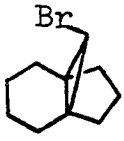
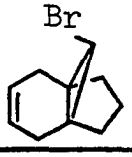
was hydrogenated to 41g in order to analyze the deuterium distribution. On the other hand, the methyl ester protons of 46b are quite different from those of 42b (δ 3.47 and 3.52 respectively, see Fig. 5 in Part I). Also product 46b showed a different glc retention time from that of 42b (11.8 and 10.0 min respectively). The reaction between cyclopropyl bromide 46f (or 45f) and n-BuLi may well involve a four-centered transition state in order to result in halogen-metal interchange with complete retention of configuration.[141]

Formation of Cyclopropyl Radicals Enroute to Cyclopropyl Anions-Grignard Formation

The Grignard reagents were prepared from the reaction between epimerically pure cyclopropyl bromide and magnesium metal in refluxing THF in the presence of magnesium bromide (formed when 1,2-dibromoethane was added to the mixture). Deuterolysis, followed by work-up and column chromatography, gave monodeuterated products in 30-84% yield. The samples were purified by glc prior to high resolution mass spectrometric (HRMS) analysis. Based on the integrated ratio of the two cyclopropyl proton signals (pmr spectroscopy) and the deuterium incorporation data from HRMS, the

percentage of each deuterated species was calculated and is summarized in Table 19. From the data, it is apparent that over-all stereoselective formation of anti-deutero product has occurred, regardless of the stereochemistry of the starting bromides or the presence of double bonds in the 6-membered ring. Less than 100% D-incorporation in the products may be explained in several ways, including solvent cleavage, proton abstraction from reactant molecules, and reaction of the Grignard reagent with H_2O contaminant. In order to check for solvent cleavage, the reactions were studied in perdeuterated THF. The resulting D-incorporations in the products seem to be less than expected. However, the values are reasonable if the primary solvent deuterium isotope effect (K_H/K_D = ca. 2.5) is taken into account. From the previous discussion, it is clear that once cyclopropyl carbanions are formed they are configurationally stable,[141] i.e., epimerization from one cyclopropyl carbanion to another is probably a high energy process. When the reaction was carried out under reflux in THF for 2 hr. instead of 20 min., almost identical product ratios were obtained (see Table 20). Also, an exchange experiment was performed. When the cyclopropyllithium 46i, prepared from 46f and n-BuLi, was added to a THF solution of excess magnesium bromide, the

Table 19. Deuterolysis of Grignard Reagents.

Run	Bromide	Solvent	Yield of RD		Isomer Ratio	
			RD & RH (%)	in H.C. (%)	anti-D	syn-D[a]
1		THF	45	63	94	6
2		THF	84	71	93	7
3		THF	30	43	99	1
4		THF	76	61	100	0
5		THF	59	63	-	-
6		THF	38	68	-	-
7		THF-d_8	74	15	-	-
8		THF-d_8	78	0	-	-

[a] Syn configuration = to D syn to 6-membered ring

Table 20. Stability of Grignard Reagent from 46f.

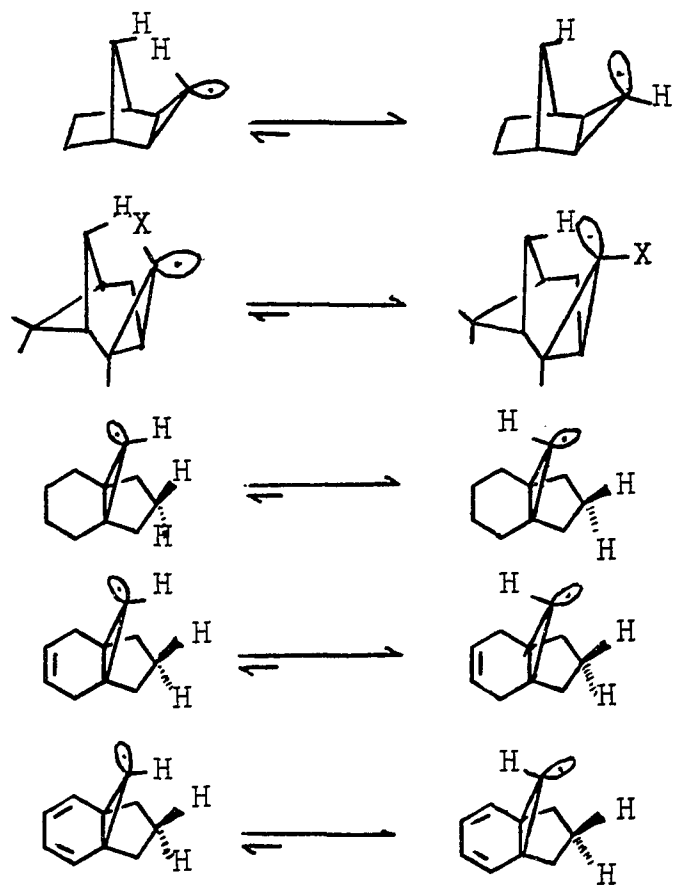
Condition	Yield,%	D%	Isomer Ratio	
			Invn.	: Retn.
Mg/THF reflux, 0.3 hr.	84	71	93	7
Mg/THF reflux, 2.0 hr.	77	69	92	8
1) n-BuLi/THF, 25°				
2) $MgBr_2$ reflux, 1.5 hr.	57	44	0	100

Table 21. Effect of Hydroperoxide (in THF-d_8) on the Deuterium Incorporation in the Product.

Run	Bromide	THF-d_8	D%	
			by HRMS	by PMR
1	45f	with ROOD	64	48
2	45f	with ROOD	45	27
3	45f	without ROOD	15	-
4	46f	with ROOD	54	37
5	46f	with ROOD	49	25
6	46f	without ROOD	0	-

intense yellow color characteristic of the organolithium compound disappeared immediately. After heating for 1.5 hr, usual deuterolysis and work-up produced 57% yield of hydrocarbon ([4.3.1]propell-3-ene) which contained 44% 46h (i.e., 44% D-incorporation with complete retention of configuration). The low D-incorporation from the alkyllithium reaction in THF could be due to solvent cleavage, as precedented by Walborsky and Young[141]. The above two experimants show that the Grignard reagent formed from 46f in indeed stable under the reaction conditions and thus the inverted product 42h, formed form the reaction of 46f with magnesium, does not arise from inversion of the syn cyclopropylmagnesium bromide. Therefore, inversion must take place at the cyclopropyl radical stage, which is one of the intermediates involved in the formation of the Grignard reagent. It should be noted that the overall inversion in the formation of the Grignard reagents observed in this study is in contrast to the results by Walborsky and Aronoff[142]. In that case, net retention of configuration led him to conclude that a surface electron transfer type of mechanism for Grignard reagent formation (see Scheme 17) predominated. In our case, the secondary cyclopropyl radicals apparently diffuse away from the metal surface, and are then free to rapidly invert (the

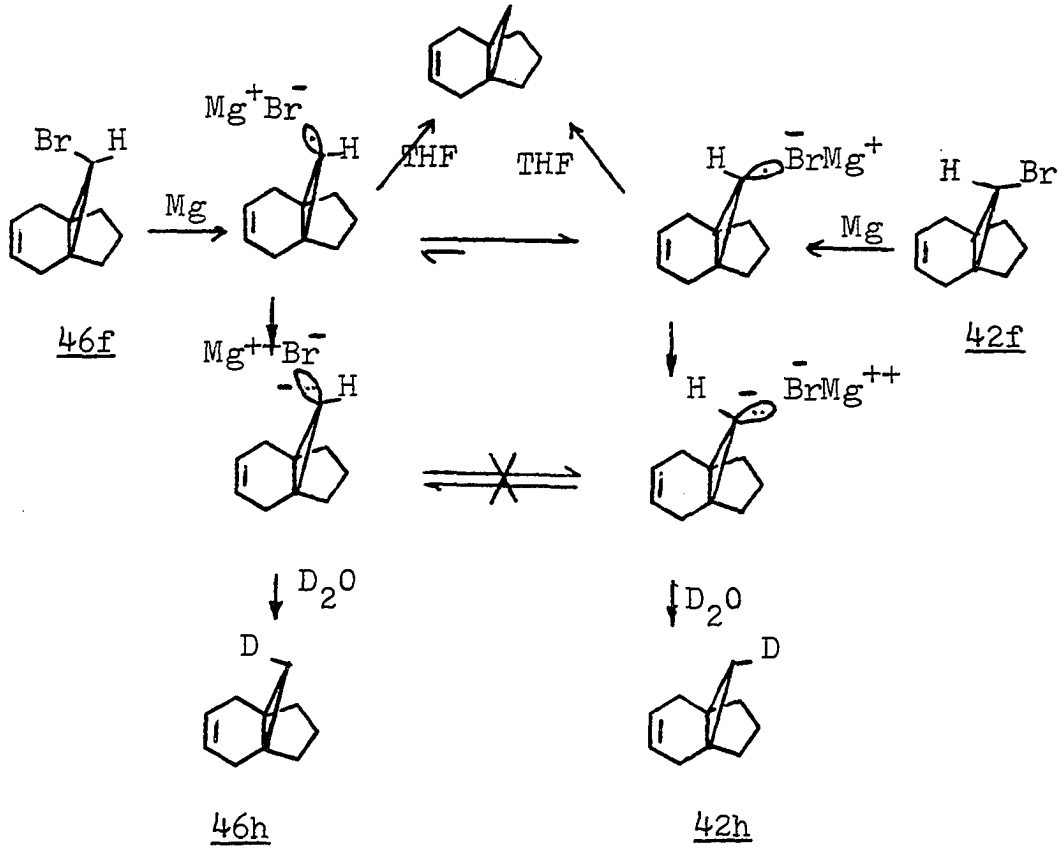
rate of inversion of cyclopropyl radical itself is 10^8-10^{10} sec^{-1}[159]). Assuming the rate of electron transfer to the epimeric radicals is equal (and this need not be the case), then the more stable (inverted) radical is being reduced. In fact, <u>anti</u> radicals in the [4.3.1]propellane system are probably more stable than the <u>syn</u> radicals, as judged by two very simular cases reported by Freeman[177] et al., and Hatem and Waegell[170,171] (but with the same reservations on relative rates of reduction of the epimeric radicals).



(less stable) (more stable)

The argument is that nonbonding interaction between two hydrogens is worse than one hydrogen and one half-filled orbital. The possibility of an S_N2 displacement of magnesium bromide by D_2O is ruled out on the basis of the stereoretained product obtained from the reaction between β-epimer 42f and magnesium in THF. It seems reasonable to propose that the pathway for Grignard formation and deuterolysis in the [4.3.1]propellane system is as shown in Scheme 19 (where the Grignard reagent is written in the ionic form only for illustrative purposes).

Scheme 19



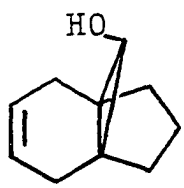
The above scheme explains the stereoselective formation of 42h and the source of side product 42g. However, one disturbing fact from the THF-d_8 experiments is that the D-incorporations are higher than expected (see Table 21) if the commercial perdeuterated solvent is used without purification. After some consternation, the solvent was tested with potassium iodide starch paper which indicated the presence of a peroxide, presumbly the perdeuterated peroxide from THF.

A more interesting point was uncovered from the observation that the D-incorporations measured by the HRMS method (from reactions in THF-d_8) are higher than that obtained by the pmr method (for which it was assumed that one isomer predominated in the mixture and the D-incorporation was then calculated from the integration of the cyclopropyl proton signals). The pmr D-incorporation values calculated for the experiments in undeuterated THF do not deviate much from those calculated from HRMS data. This suggests that in the THF-d_8 experiments the cyclopropyl radical may partly rearrange intramolecularly via hydrogen transfer (this could be a source of low D-incorporation in the THF cases). Such a process would decrease the D-incorporation in the products as indicated from the pmr of the cyclopropyl region, but the calculation

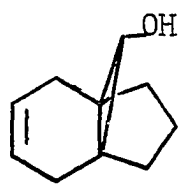
from HRMS data will give the total D-incorporation in the molecule. Further study of this point should be pursued.

Formation of Cyclopropyl Radicals from Cyclopropyl Anions-Oxygenation

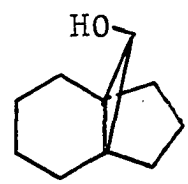
Our need to synthesize cyclopropanols 46j, 42j, 45j, and 41j for the "partially opened" cyclopropyl cation work led us to investigate the mechanism of the oxygenation of cyclopropyllithium derivatives. This convenient new method for synthesis of cyclopropanols was published by Longone and Wright.[180] However, the stereochemical course of the oxygenation step was not elucidated.



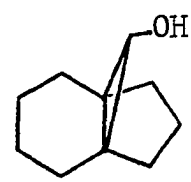
46j



42j



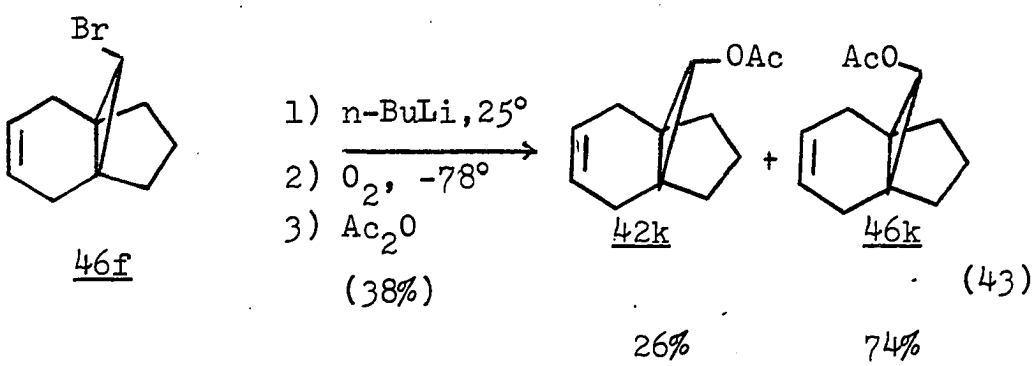
45j



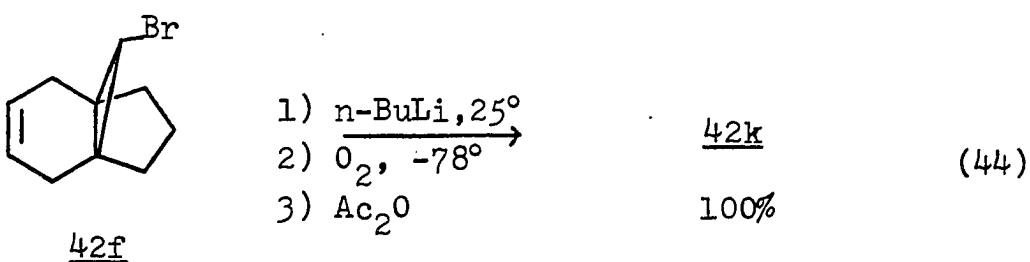
41j

The exchange reaction between cyclopropyl bromide and n-BuLi has been shown to be stereoretentive (vide supra). After the lithio derivative was cooled to -78°, oxygen was bubbled through the solution for about one hr. The resultant mixture of cyclopropanols and n-butanol was then acetylated directly (see Eq. 43, 44 and 45). Pmr spectra

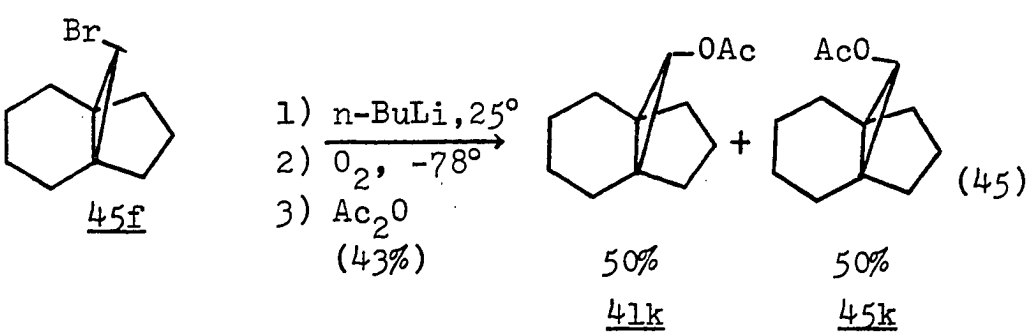
of the products indicated that there was obtained a 26:74 mixture of 42k and 46k from 46f and pure 42k from 42f. The stereochemistry of the acetates was assigned according to the arguments described in Part II (also see Fig. 50, 51 and 52 in part II).



(43)



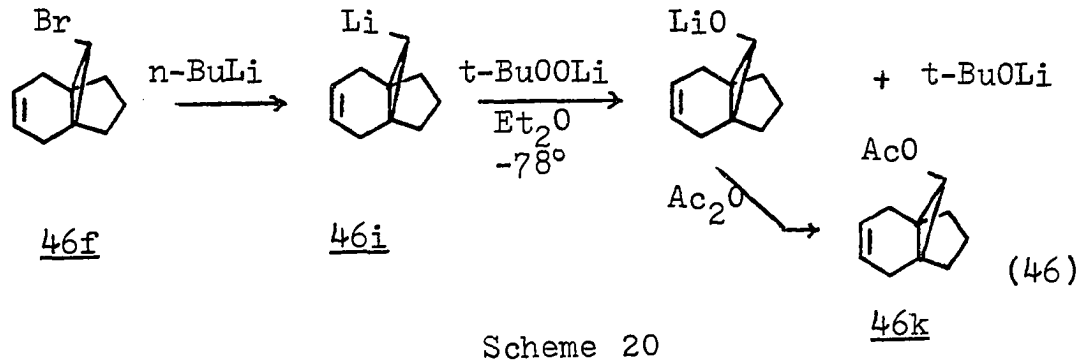
(44)



(45)

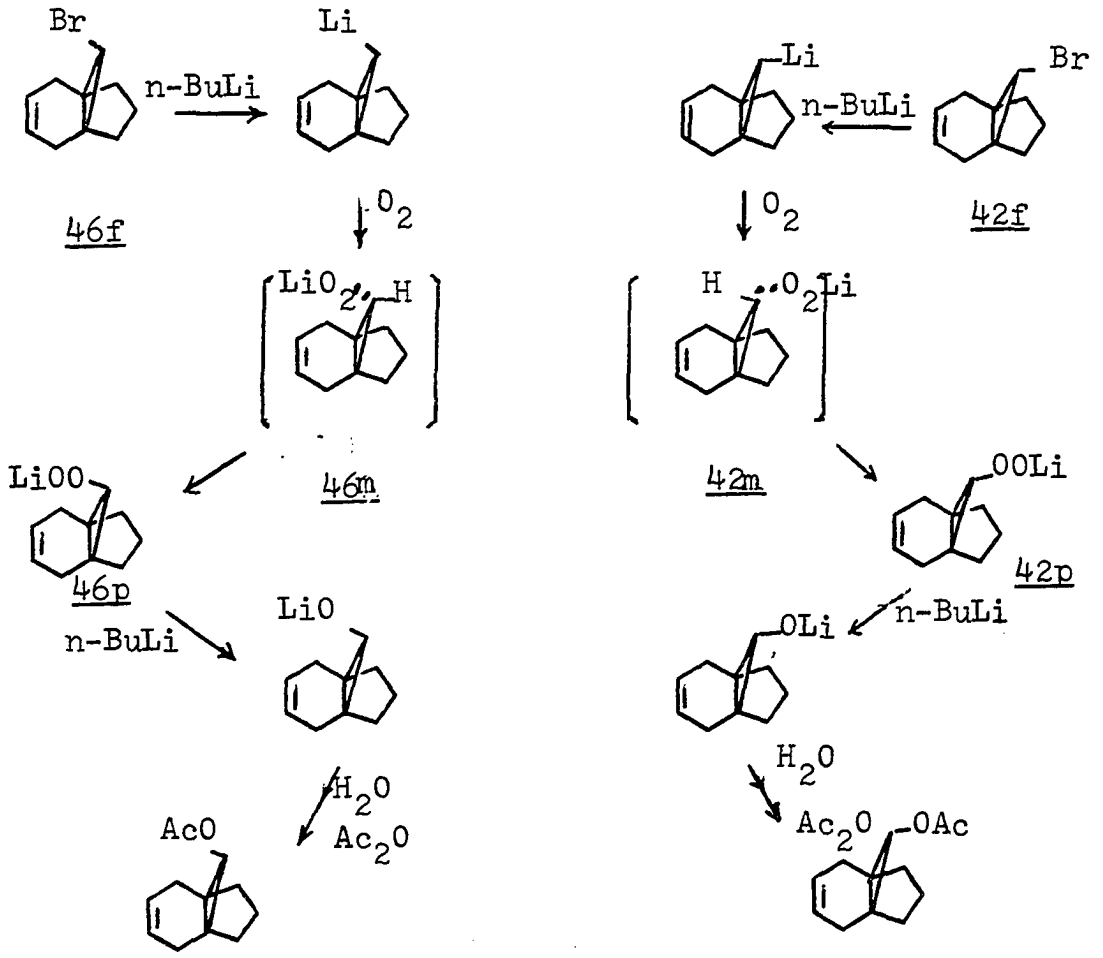
While the exclusive formation of 42k from 42f might lead one to consider direct collapse of the cyclopropyllithium with oxygen, the epimeric mixture obtained from 46f strongly implies an electron transfer mechanism, which would proceed via an intermediate cyclopropyl radical-lithium superoxide ion pair; the life time of this radical pair would allow epimerization at C_{10}.[181] However, one must exclude the possibility that 42k arises via an S_N2 displacement[182] by $LiO_2^{\cdot}$ (formed from the reaction of n-BuLi and O_2) on 46f. To this end, a 5-fold excess of n-BuLi and 46f were cooled to -78° and O_2 bubbled through; 46f was almost quantitatively recovered.[172] Thus oxygenation of cyclopropyllithiums apparently occurs via the same electron transfer mechanism already observed for simple alkyl magnesiums.[183] Since the initial product formed from the collapse of a cyclopropyl radical with superoxide is a hydroperoxide salt, but the obtained product is an alcohol, a step involving the transformation of hydroperoxide to alkoxide salt must occur. When a solution of t-BuOOLi in ether, prepared by adding n-BuLi to dissolved t-BuOOH, was dropped into an ethereal solution of the cyclopropyl lithium derivative of 1a at -78° and the resultant mixture acetylated, pmr analysis of the product showed that only syn-acetate 46k was formed (see Eq. 46). This indicates

that the reaction of the cyclopropyllithium with an alkyl hydroperoxide salt occurs via an S_N2 displacement by the organolithium. The inversion of stereochemistry at cyclopropyl carbon must have occurred in the primary oxygenation step.



46f 46i 46k (46)

Scheme 20



However, within the context of Scheme 20 we cannot tell whether 42m is more stable than 46m or whether 42m collapses to 42p more rapidly than 46m does to 46p; note that the conversion of 46m to 42m involves more than simply inversion of a cyclopropyl radical.[181] A strictly analogous result is obtained from the oxygenation of the cyclopropyllithium derived from saturated analog 45f.

Formation of Cyclopropyl Radicals from Tin Hydride Reduction

So far, all evidence seems to support a radical mechanism for the tin hydride reduction of gem-dihalocyclopropanes.[156]

Initiation: $SnH + Q\bullet \longrightarrow Sn\bullet + QH$

Propagation: $Sn\bullet + RX \xrightarrow{K_1} R\bullet + SnX$ (47)

$R\bullet + SnH \xrightarrow{K_2} RH + Sn\bullet$ (48)

Termination $R\bullet + R\bullet \longrightarrow R\text{-}R$

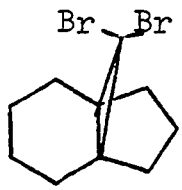
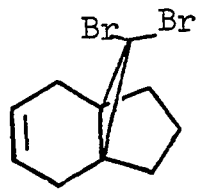
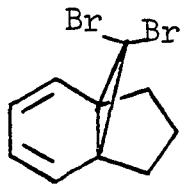
$R\bullet + Sn\bullet \longrightarrow R\text{-}Sn$

$Sn\bullet + Sn\bullet \longrightarrow Sn\text{-}Sn$

Cyclopropyl radical intermediates formed in reaction (47) tend to epimerize or fragment. If reaction (48) is sufficiently fast, simple reduction products will result; otherwise rearranged or fragmented products may form.

Addition of tri-n-butyltin hydride to an equimolar quantity of dibromocyclopropane derivatives 110, 33 and 257 resulted in a mixture of isomeric monobromocyclopropane products. The results are summarized in Table 22.

Table 22. Reduction of gem-Dibromocyclopropanes with n-Bu)$_3$SnH at 25°.

Compound	Yield, %	Isomeric Ratio	
		anti-Br	: syn-Br[a]
 110	79	20	80
 33	84	23	77
 257	65	13	87

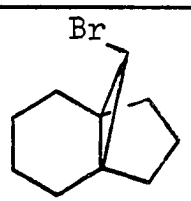
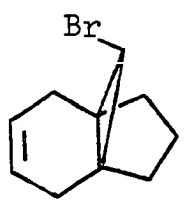
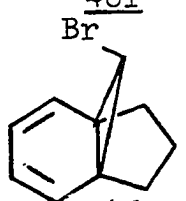
[a] Syn configuration refers to the Br syn to the 6-membered ring

Seyferth, et al.,[112] reported that reduction of 7,7-dibromonorcarane with tin hydride gave a 29:71 mixture of anti-Br and syn-Br product. The similarity of the stereochemical results from this work and Seyferth's seems to suggest that syn-bromocyclopropyl radicals are either more stable than anti ones or bulky n-Bu)$_3$SnH molecules preferentially attack the anti side. It should be noted that none of the results can determine which of the two bromines has been removed by tri-n-butyltin radical. From a model of compound 110, it appears that the anti side of the cyclopropyl radical may be blocked by $H_{8\ exo}$. This would imply that approach from the side of the 5-membered ring is not sterically less hindered than approach from the other side. If true, then the steric explanation used for the reaction of tin hydride with the cyclopropyl radical in the 7,7-dibromonorcane case cannot be used to explain the stereoselective formation of syn-Br products in our system.

Since it has been fairly well established that α-fluoro- or α-chlorocyclopropyl radicals are much more stable than the corresponding unsubstituted cyclopropyl radicals,[157] it is of interest to investigate the stereochemistry of collapse of some unsubstituted cases. The results of reduction of some monobromocyclopropanes with

n-Bu)$_3$SnD are shown in Table 23. These results are consistent with the idea that anti cyclopropyl radicals (with respect to the 6-membered ring) in the [4.3.1]propellane system are sterically more stable than the epimeric radicals, as previously proposed for the Grignard studies. However, further studies are needed to confirm this hypothesis.

Table 23. Reduction of Monobromocyclopropanes with n-Bu)$_3$SnD in benzene at 85°.

Compound	Isomer Ratio	
	anti-H :	syn-H[a]
 45f	6	94
 46f	9	91
 48f	5	95

[a]Syn configuration refers to the H syn to the 6-membered ring

EXPERIMENTAL

Reagents

Magnesium chips (99.99%) were purchased from Alfa Inorganics, Beverly, Mass.; tetrahydrofuran-d_8 (99% D) and lithium aluminum deuteride-d_4 (99% D) were purchased from Stohler Isotope Chemicals, Rutherford, N. J.; deuterium oxide (99.75% D) was obtained from J. T. Baker Chemical Co., Phillipsburg, N. J.; n-butyllithium (1.6 M in hexane) originated from Foote Mineral Co. Exton, Penn.

Synthesis

Tri-n-butyltin Deuteride was synthesized in 87% yield from tri-n-butyltin chloride, utilizing lithium aluminum deuteride reduction according to the method described by Van Der Kerk, et al.;[184] b.p: 74°/0.45 torr.

10α-Bromotricyclo[4.3.1.$0^{1,6}$]deca-2,4-diene (48f)

A 50 ml methylene chloride solution containing 2.80 g (12.8 mmol) 46f and 5.8 g (25.6 mmol) 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) was placed in a tube and sealed with a torch. The mixture turned a yellowish green color after heating at 70° for four days. Upon cooling, the tube was opened and the solid was filtered off follow-

ed by washing the solid with hexane. The residue obtained after concentration in vacuo was chromatographed (neutral alumina, hexane as eluent) to give 0.82 g (49% on the basis of unrecovered 46f) of white crystals, mp 43-44.5° pmr: δ 5.88 (m. 4 H, AA'BB' pattern), 3.37 (s. cyclopropyl H , 2.5-1.0 (m. 6 H), (see Fig.62); ir (CCl_4): 3040 (olefinic C-H), 2965, 2935, 2870, 1445, 1252, 1050 (cyclopropyl C-C), 625 (C-Br) cm^{-1}.

Anal. Calc'd for $C_{10}H_{11}Br$: m/e 210.0044
Found : m/e 210.0028

10,10-Dibromotricyclo[4.3.1.$0^{1,6}$]deca-2,4-diene (257)

In a manner identical to that described for 48f, compound 257 was synthesized in 36% yield on the basis of unrecovered 33; mp 71-73° (methanol); pmr: δ 5.86 (m. 4 H, AA'BB' pattern), 2.8-1.3 (m. 6 H) (see Fig.62); ir (CCl_4): 3040 (olefinic C-H), 2970, 2940, 2870, 1445, 1170, 1155, 1040 (cyclopropyl C-C), 635 (C-Br) cm^{-1}; uv (C_6H_{12}): λ_{max} 235 (ϵ = 1600) nm;

Anal. Calc'd for $C_{10}H_{10}Br_2$: m/e 287.9150
Found : m/e 287.9149

11-Bromotricyclo[4.4.1.$0^{1,6}$]undecane (258) To 2.48 g (8.05 mmol) of dibromide 93 cooled with an ice bath was added 2.32 g (7.96 mmol) of n-Bu)$_3$SnH with stirring. After reaction for 3.5 hr. at room temperature, 1.39 g (76%) of

258 was obtained from vacuum distillation at 76-82°/0.2 torr; pmr: δ 3.0 (s. 1 H), 1.1-1.9 (m. 16 H) (see Fig.63); ir (film): 3040 (cyclopropyl C-H), 1075 (cyclopropyl C-C) cm^{-1};

Anal. Calc'd for $C_{11}H_{17}Br$: m/e 228.0514
Found : m/e 228.0514

9-Bromotricyclo[3.3.1.$0^{1,5}$]nonane (259) The procedure described for the preparation of 258 was employed. Monobromide 259 was obtained in 80% yield from 129, bp. 50-59°/0.5 torr; pmr: δ 3.15 (s. 1 H), 1.5-2.2 (m. 12 H) (see Fig.63); ir (film): 3050 (cyclopropyl C-H), 1080 (cyclopropyl C-C) cm^{-1};

Anal. Calc'd for $C_9H_{13}Br$: m/e 200.0201
Found : m/e 200.0197

Formation of Cyclopropyl Radicals Enroute to Cyclopropyl Anions

General Procedure for Reaction between Cyclopropyl Bromide and Magnesium in THF or THF-d_8 The organic bromides were chromatographed (neutral alumina, hexane) and dried over anhy. $MgSO_4$ before use. Tetrahydrofuran (THF) was freshly distilled from lithium aluminum hydride.

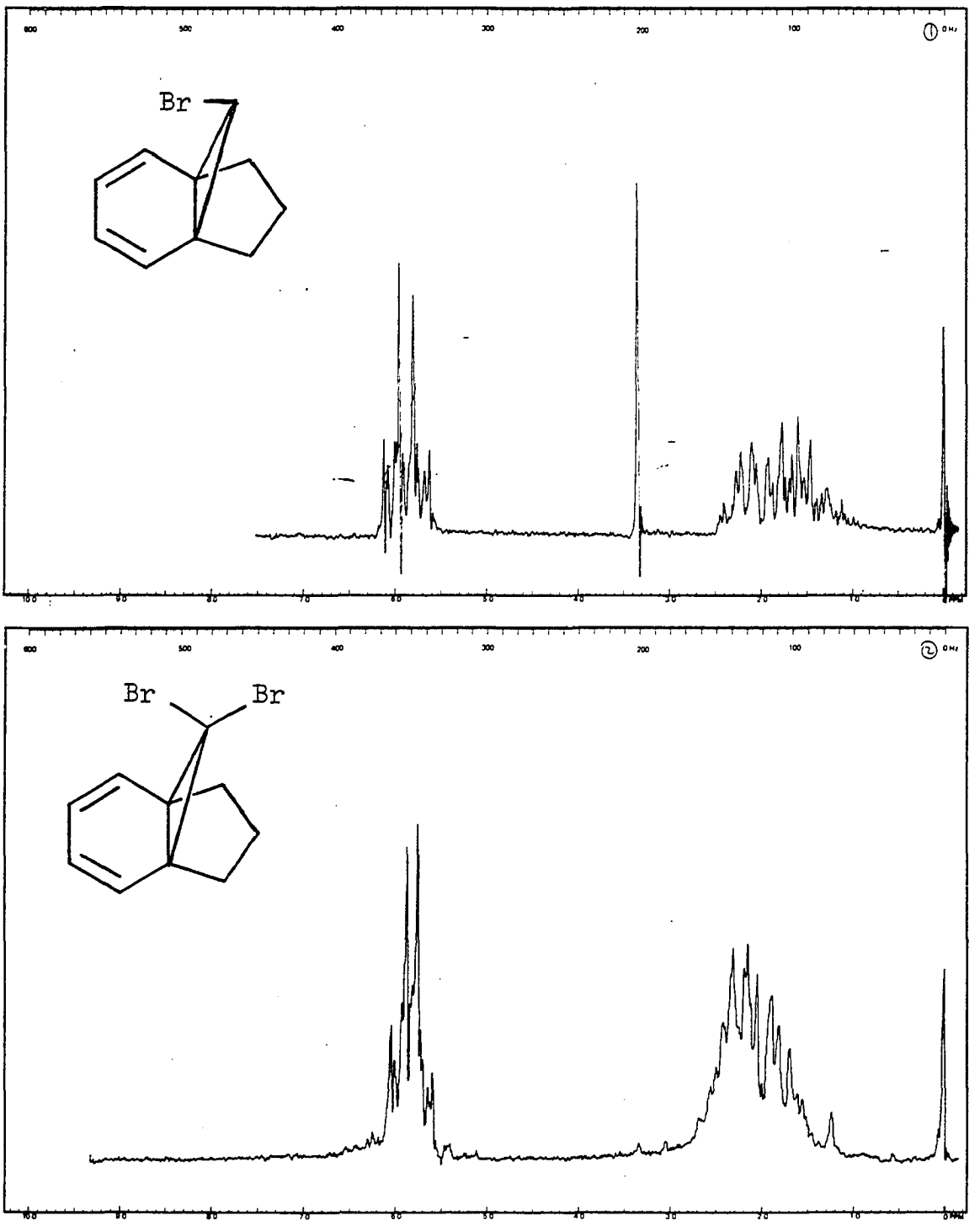


Figure 62. Pmr Spectra of 10α-Bromotricyclo[4.3.1.$0^{1,6}$]-deca-2,4-diene: 48f (Top) and 10,10-Dibromotricyclo[4.3.1.$0^{1,6}$]deca-2,4-diene: 257 (Bottom).

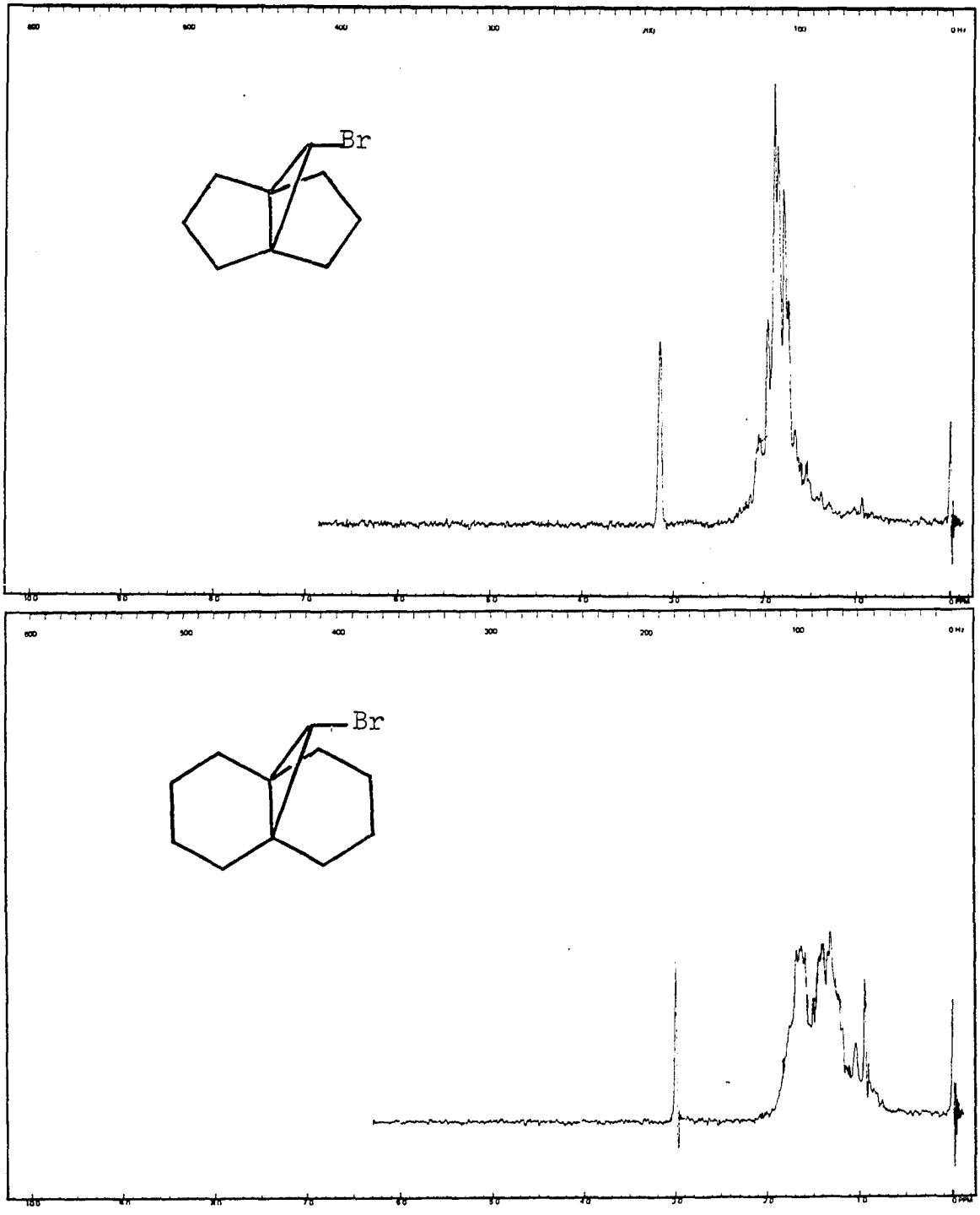


Figure 63. Pmr Spectra of 9-Bromotricyclo[3.3.1.$0^{1,5}$]-nonane: 259 (Top) and 11-Bromotricyclo-[4.4.1.$0^{1,6}$]undecane: 258 (Bottom).

A 25 ml three neck flask was equipped with nitrogen gas inlet, rubber serum cap and condenser whose top was attached to a mercury bubbler with tygon tubing. The system was flamedried under a flow of nitrogen. After cooling to room temperature, approximately 0.1 g of magnesium chips, together with a stirring bar, were placed in the flask under N_2. After the syringing in of 1 mmol of cyclopropyl bromide dissolved in 2 ml of freshly distilled THF was complete, the resultant mixture was heated to reflux. Meanwhile, 0.1 ml of 1,2-dibromoethane was syringed into the mixture. Once the gas (ethylene) started to evolve, the oil bath was removed. After the reaction subsided, the mixture was reheated at 70° for an additional 20 min. Heating was then terminated and the reaction mixture was quenched by adding 0.5 ml of D_2O. After stirring at room temperature for 5 min, the mixture was diluted with water followed by several extractions with hexane. The combined extracts were washed with saturated sodium chloride solution, and dried over anhy. $MgSO_4$. Removal of solvent under reduced pressure gave 30-84% (see Table 19) yield of deuterated and undeuterated hydrocarbons which were subjected to glc (column C) prior to product analysis. D-Incorporations of the products were calculated from the relative intensity of the mass spectral

signals of P (parent) and P+1 ions. Isomer ratios were obtained from the D-incorporation data and the deuteration patterns of the cyclopropyl protons, as revealed by integration of the pmr signals of $H_{10\underline{anti}}$ (δ 0.35, J = 4.8 Hz) and $H_{10\underline{syn}}$ (δ 0.12, J = 4.8 Hz). The results are shown in Table 4, (run 1-6).

When the solvent was changed to perdeuterated THF, the Grignards were hydrolyzed, rather than deuterolyzed. In runs 1, 2, 4 and 5 of Table 21, commercial THF-d_8 was used directly. In two cases, the THF-d_8 was treated with KOH pellets overnight, then distilled under reduced pressure before use (see run 3 and 6 in Table 21).

Stability of the Grignard Reagent from 46f In a manner analogous to the above procedure, the Grignard was formed and further heated for 2 hr. at 70°. The product (77% yield) showed 69% D-incorporation, with a 92:8 ratio of anti-D to syn-D product.

Exchange of Cyclopropyllithium with Magnesium Bromide A 50 ml flame dried three-necked flask was equipped with rubber serum cap, nitrogen gas inlet and an addition funnel. To the funnel was added 0.29 g (1.37 mmol) 46f in 2 ml of freshly distilled THF and 4.4 ml (7 mmol) n-BuLi (1.6 M in hexane). The mixture was shaken occasionally at

room temperature for 30 min., and then was dropped into the flask which had been charged with magnesium bromide in 10 ml of dry THF (the magnesium bromide was generated *in situ* from 2.82 g (15 mmol) 1,2-dibromoethane and 0.5 g magnesium chips). The reaction was exothermic, but was allowed to stir for an additional 30 min., during which time the intense yellow color characteristic of the organolithium reagent faded away. The mixture was then heated for an additional 1.5 hr. at 65-70°. Deuterolysis (1 ml) followed by the usual work-up and silica gel column chromatography afforded 104 mg (57%) of product 46h with 44% D-incorporation. The deuterium was found to be 100% *syn*, within the error limits of pmr analysis.

Formation of Cyclopropyl Anions

Reaction of 10α-Bromotricyclo[4.3.1.$0^{1,6}$]decane (45f) and n-Butyllithium To 0.214 g (1.0 mmol) 45f in 2 ml freshly distilled THF was added 2.5 ml (4.5 mmol) n-BuLi (1.6 M in hexane) under nitrogen. After stirring for one hr. at r.t., the resulting mixture was quenched by adding 1 ml D_2O, then diluted with hexane. The hexane solution was washed with water, saturated NaCl solution, dried and evaporated under reduced pressure to afford 0.118 g (87%) oil which was identified as 45h via pmr spectroscopy, a singlet at δ0.37 and no detectable peak at δ0.12 was observed.

General procedure for Carbonation of Cyclopropyllithium Derivatives To 0.427 g (2.0 mmol) 45f in 3 ml freshly distilled THF was added dropwise 5 ml (9.0 mmol) n-BuLi (1.6 M in hexane). The mixture was stirred for 30 min. at room temperature and poured over ca. 10 g dry ice under N_2. After stirring for one hr., the excess CO_2 was allowed to evaporate. The residue was acidified with 2N HCl solution, followed by ether extraction. The combined ethereal layers were extracted with 2N NaOH solution. Acidification of the basic extracts gave a milky precipitate which was again extracted into ether. Drying and removal of solvent gave 65 mg (37%) solid. Treatment of the resultant carboxylic acid with diazomethane in ether afforded a methyl ester. Glc analysis (column F at 92°) showed the presence of essentially one component (retention time, Rt = 8.3 min) which was identified as syn ester 45b by comparison of pmr and Rt with those of an authentic sample. (see Fig. 61).

Carboxylic acid 46a was synthesized in the same manner (32% yield). Its methyl ester 46b displayed an Rt = 11.8 min. with the same glc column. No epimeric ester 42b, which was prepared from pure anti carboxylic acid 42a was detected by pmr or glc analysis (Rt = 10.0 min). The pmr and ir spectra are shown in Fig. 5 and 6 in part I.

Formation of Cyclopropyl Radicals from Cyclopropyl Anions

Oxygenation of 10α-Bromotricyclo[$4.3.1.0^{1,6}$]dec-3-ene (46f) To a solution of 100 mg (0.47 mM) 46f in 20 ml Et_2O contained in a flame-dried, N_2-swept 50 ml Schlenk flask was added a solution of 4.98 mM nBuLi in 3 ml hexane and 10 ml Et_2O. The resulting mixture was allowed to stir for 3/4 - 1 hr., after which it was cooled to -78°. O_2 was then bubbled into the solution (fritted glass bubbler) for 1 hr. This was followed by addition of aqueous NH_4Cl to the reaction mixture (at $\leq$ 0°). After shaking in a separatory funnel, the layers were separated and the aqueous layer further extracted with Et_2O. Combination of the ethereal layers was followed by drying (K_2CO_3) and solvent evaporation.

The crude mixture of 46j, 42j and nBuOH was then dissolved in ca. 5 ml dry pyridine, to which was added ca. 1 ml Ac_2O. The solution was heated to 75° for 1 hr., followed by cooling, addition of H_2O, and extraction with Et_2O. The Et_2O extracts were then washed with 1N HCl until the wash remained acidic. Drying of the ether layer was followed by rotoevaporation using a hot water bath (ca. 75°) to evaporate the nBuOAc. The resulting crude oil was analyzed by nmr. The only methine peaks seen proved to be

those for 46k and 42k in the ratio of 2.8:1. It was assumed that this ratio also applied to the alcohols 46k and 42k.

Separation and purification of 46k and 42k was achieved by chromatography on silica gel (of 355 mg crude material). Both acetates were eluted with 4% Et_2O/96% hexane, with 42k coming through first. The total isolated yield of cyclopropyl acetates was 38%.

46k : pmr ($CDCl_3$): δ 5.50 (narrowly split mult., olefinic H), 3.82 (s, cyclopropyl H), 2.13 (s, 4 allylic H), 2.1-1.2 (m, 6 aliphatic H), δ 1.90 (s, OAc); ir ($CDCl_3$): 3020 (m), 1740 (s), 1665 (w), 1250 cm^{-1} (s):

Anal. Calc'd for $C_{12}H_{16}O_2$: m/e 192.1150
Found (70eV) : m/e 192.1160

42k : pmr ($CDCl_3$): δ 5.50 (narrowly split mult., olefinic H), 3.95 (s, cyclopropyl H), 2.8-1.5 (m, 4 allylic + 6 aliphatic H), 2.07 (s, OAc); ir ($CDCl_3$): 3020 (m), 1735 (s), 1654 (w), 1245 cm^{-1} (s);

Anal. Calc'd for $C_{12}H_{16}O_2$: m/e 192.1150
Found (70eV) : m/e 192.1160

Oxygenation of 10β-Bromotricyclo[4.3.1.$0^{1,6}$]dec-3-ene (42f) In a manner exactly analogous to that described for 46f, 50 mg (0.23 mM) 42f were oxygenated and acetylated. To within the error limits of pmr analysis, the only detectable product was 42k.

10α-Hydroxytricyclo[4.3.1.$0^{1,6}$]deca-3-ene (46j)

In 1 ml of a 5% KOH in 25% aqueous MeOH solution were dissolved 16 mg pure 46k. The mixture was heated for 2 hr. at 50°, followed by dilution with H_2O and extraction with Et_2O. After drying (K_2CO_3), filtering and evaporating the solvent, ca. 5 mg of solid white product were recovered. The ir ($CDCl_3$) showed peaks at 3590 (sharp, free OH), 3540 (sharp, intramolecularly hydrogen-bound OH) and 3430 cm^{-1} (broad, intermolecularly hydrogen-bound OH).

10β-Hydroxytricyclo[4.3.1.$0^{1,6}$]deca-3-ene (42j)

In the manner described above, a 50 mg sample of pure 42k was hydrolyzed (in 1 ml of the basic solution, and for only 40 min. at 50°); 13 mg of product were recovered. The ir ($CDCl_3$) showed peaks at 3600 (sharp, free OH) and 3430 cm^{-1} (broad, intermolecularly hydrogen-bound OH).

Oxygenation of 10α-bromotricyclo[4.3.1.$0^{1,6}$]decane. (see Part II).

Reaction of 10α-lithiotricyclo[4.3.1.$0^{1,6}$]deca-3-ene (46i) with lithium t-butylhydroperoxide 100 mg 46f were converted to the corresponding organolithium 46i exactly as described for the oxygenation of 46f. Subsequently, an addition funnel above the Schlenk flask containing 46i was charged with 5 mM nBuLi in 3 ml hexane and 5 ml Et_2O. To this were cautiously added 5 mM (90 mg) of tBuOOH (previously dried, over K_2CO_3, in pentane) in 5 ml Et_2O (a

syringe was utilized). The resulting ethereal solution of LiOO*t*Bu was then added dropwise to the solution of 46i (which had been cooled to -78°). Thus the only way 46j and/or 42j could form would be via reaction with *t*-BuOOLi. The work-up and subsequent acetylation of the product mixture was performed as described for the oxygenation of 46f. To within the error limits of pmr analysis, the only cyclopropyl acetate formed was 46k.

Formation of Cyclopropyl Radicals from Tin Hydride Reduction

General Procedure for Reduction of Dibromocyclopropane Derivatives with n-Bu)$_3$SnH Reduction was carried out in a manner similar to the procedure developed by Seyferth, *et al.*[112] To 2.92 g (10mmol) of dibromo compound 33 was added dropwise 2.91 g (10 mmol) of (n-Bu)$_3$SnH at room temperature. The reaction was initially exothermic and was allowed to stir for 2-3 hr. A mixture of monobromocyclopropanes was obtained in 84% yield bp. 75-80°/1.3 torr. The ratio of the isomers was determined by integration of the pmr signals for the cyclopropyl protons (δ 2.85 for46f and 3.16 for42f) as 3.3 to 1.0 (46f:42f). In an identical manner,110 produced a 4.1:1.0 mixture of 45f and 41f in 79% yield. Also,257 yielded a 6.8:1.0 mixture of 48f and

44f in 65% yield.

General Procedure for Reduction of Bromocyclopropanes with n-Bu)$_3$SnD In an nmr tube, 83 mg (0.39 mmol) of 45f was mixed with 114 mg (0.39 mmol) of (n-Bu)$_3$SnD in 0.5 ml of benzene. The mixture was heated at 85° for 4 days and monitored by pmr spectroscopy until no more starting materials were left. After removal of solvent, column chromatography (neutral alumina, hexane as eluent) afforded a colorless oil (45f and 41h) which showed two singlets for the cyclopropyl protons at δ 0.35 and 0.14 respectively, with a ratio of 1 to 16 (or 6% to 94%).

Likewise, compound 46f gave a 1 to 10 (or 9% to 91%) mixture of 46h and 42h. Propellane 48f resulted in a 1 to 19 (or 5% to 95%) mixture of 48h and 44h.

BIBLIOGRAPHY

1. E. Buchner, Ber. Dtsch. Chem. Ges., 21, 2637 (1888), and subsequent papers.

2. W. V. E. Doering, G. Laber, R. Vonderwahl, N. F. Chamberlain and R. B. Williams, J. Amer. Chem. Soc., 78, 5488 (1956).

3. For review: G. Maier, Angew. Chem. Int. Ed. Engl., 6, 402 (1967).

4. W. V. E. Doering and M. J. Goldstein, Tetrahedron, 5, 53 (1959).

5. R. Huisgen and G. Juppe, Chem. Ber., 94, 2332 (1961).

6. G. Wittig, H. Eggers and P. Duffner, Liebigs Ann. Chem., 619, 10 (1958).

7. E. Vogel, W. Wiedemann, H. Kiefer and V. F. Harrison, Tetrahedron Lett., 673 (1963).

8. E. Vogel, W. Wiedemann, H. Roth, J. Eimer and H. Günther, Justus Liebigs Ann. Chem., 759, 1 (1972).

9. E. Vogel, W. Maier and J. Eimer, Tetrahedron Lett., 655 (1966).

10. E. Vogel and W. A. Böll, Angew. Chem. Int. Ed. Engl., 3, 642 (1964).

11. E. Vogel and H. D. Roth, Angew. Chem. Int. Ed. Engl., 3, 228 (1964).

12. M. Dobler and J. D. Dunitz, Helv. Chim. Acta., 48, 1429 (1965).

13. H. Günther, H. Schmickler, H. Königshofen, K. Recker and E. Vogel, Angew. Chem. Int. Ed. Engl., 12, 243 (1973).

14. H. Günther, H. Schmickler, E. Bremser, F. A. Straube and E. Vogel, Angew. Chem. Int. Ed. Engl., 12, 570 (1973).

15. L. H. Knox, E. Velerde and A. D. Cross, J. Amer. Chem. Soc., 85, 2533 (1963); 87, 3727 (1965).

16. E. Vogel, W. A. Böll and M. Biskup, Tetrahedron Lett., 1569 (1966).

17. E. Vogel, W. Grimme and S. Korte Tetrahedron Lett., 3625 (1965).

18. W. Grimme, H. Hoffmann and E. Vogel, Angew. Chem. Int. Ed. Engl., 4, 354 (1965).

19. E. Vogel, M. Biskup, A. Vogel, V. Haberland and J. Eimer, Angew. Chem. Int. Ed. Engl., 5, 603 (1966).

20. E. Vogel, W. Schrock and W. A. Böll, Angew. Chem. Int. Ed. Engl., 5, 732 (1966).

21. W. Grimme, M. Kaufhold, U. Dettmeier and E. Vogel, Angew. Chem. Int. Ed. Engl., 5, 604 (1966).

22. W. A. Böll, Angew. Chem. Int. Ed. Engl., 5, 733 (1966).

23. P. Radlick and W. Rosen, J. Amer. Chem. Soc., 88, 3461 (1966).

24. (a) E. Ciganek, J. Amer. Chem. Soc., 87, 652 (1965); 89, 1454, 1458 (1967); (b) C. J. Fritchie Jr., Acta. Cryst., 20, 27 (1966).

25. (a) D. M. Gale, W. J. Middleton and C. G. Krespan, J. Amer. Chem. Soc., 87, 657 (1965); 88, 3617 (1966); (b) J. B. Cambert, L. J. Durham, P. Lepoutere and J. D. Roberts, J. Amer. Chem. Soc., 87, 3896 (1965).

26. (a) R. Huisgen and F. Mietzsch, Angew. Chem. Int. Ed. Engl., 3, 83 (1964); (b) R. Huisgen, F. Mietzsch, G. Boche and H. Seidl, Chem. Soc. Spec. Publ., 19, 3 (1964); (c) E. Ciganek, J. Amer. Chem. Soc., 87, 1149 (1965).

27. E. Ciganek, J. Amer. Chem. Soc., 93, 2207 (1971).

28. T. Mukai, H. Kubota and T. Toda, Tetrahedron Lett., 3581 (1967).

29. M. Regitz, H. Scherer and W. Anschütz, Tetrahedron Lett., 753 (1970).

30. (a) D. Schönleber, Chem. Ber., 102, 1789 (1969);

(b) D. Schönleber, Angew. Chem. Int. Ed. Engl., 8, 76 (1969).

31. M. Jones Jr., Angew. Chem. Int. Ed. Engl., 8, 76 (1969).

32. H. J. Reich, E. Ciganek and J. D. Roberts, J. Amer. Chem. Soc., 92, 5166 (1970).

33. G. E. Hall and J. D. Roberts, J. Amer. Chem. Soc., 93, 2203 (1971).

34. M. Görlitz and H. Günther, Tetrahedron, 25, 4467 (1969).

35. T. Tsuji, S. Teratake and H. Tanida, Bull, Chem. Soc. Jap., 42, 2033 (1969).

36. W. von E. Doering and M. R. Willcott III., unpublished calculation; M. R. Willcott III., Ph.D. Dissertation, Yale University, 1963.

37. R. Huisgen, G. Boche, A. Dahmen and W. Hechte, Tetrahedron Lett., 5215 (1968).

38. E. Ciganek, J. Amer. Chem. Soc., 89, 1454 (1967).

39. R. Hoffmann, Tetrahedron Lett., 2907 (1970).

40. H. Günther, Tetrahedron Lett., 5173 (1970).

41. G. D. Sargent, N. Lowry and S. D. Reich, J. Amer. Chem. Soc., 89, 5985 (1967).

42. P. von R. Schleyer and G. W. van Dine, J. Amer. Chem. Soc., 88, 2321 (1966).

43. P. Warner, unpublished results.

44. E. E. Van Tamelen and M. Schamma, J. Amer. Chem. Soc., 76, 2315 (1954).

45. C. S. Rondestvedt Jr. and C. D. Ver Nooy, J. Amer. Chem. Soc., 4882 (1955).

46. S. P. Acharya and H. C. Brown, J. Amer. Chem. Soc., 89, 1925 (1967).

47. E. Heftmann "Chromatography" 2nd ed, Reinhold Publishing Corp., New York, N.Y., 1967, p 485-488.

48. (a) L. A. Paquette and G. L. Thompson, J. Amer. Chem. Soc., 95, 2364 (1973); (b) G. L. Thompson, W. E. Heyd and L. A. Paquette, J. Amer. Chem. Soc., 96, 3177 (1974).

49. (a) P. Warner and S-L. Lu, J. Amer. Chem. Soc., 95, 5099 (1973); (b) P. Warner and S-L. Lu, Tetrahedron Lett., 3455 (1974).

50. (a) M. J. S. Dewar and P. J. Grisdale, J. Amer. Chem. Soc., 84, 3548 (1962); (b) M. J. S. Dewar and A. P. Marchand, J. Amer. Chem. Soc., 88, 354 (1966).

51. T. Sasaki, S. Eguchi, M. Ohno and T. Umemura, Chem. Lett., 503 (1972).

52. (a) C. F. Wilcox, L. W. Loew and P. Hoffmann, J. Amer. Chem. Soc., 95, 8192 (1973); (b) R. S. Brown and T. G. Traylor, J. Amer. Chem. Soc., 95, 8025 (1973).

53. (a) W. D. Stohrer and J. Daub, Angew. Chem. Int. Ed. Engl., 13, 86 (1974); (b) J. Daub and W. Betz, Tetrahedron Lett., 3451 (1972); (c) S. Kohen and S. J. Weininger, Tetrahedron Lett., 4403 (1972).

54. (a) E. J. Corey and G. H. Posner, J. Amer. Chem. Soc., 90 5615 (1968); (b) R. T. Arnold, J. Amer. Chem. Soc., 61, 1405 (1939).

55. L. J. Bellamy, "The Infra-red Spectra of Complex Organic Molecules," John Wiley, 2nd ed, New York, N.Y., 1958 p 78.

56. S. Kohen and S. J. Weininger, Tetrahedron Lett., 4403 (1972).

57. Diazomethane was prepared according to the method of F. Arndt, Org. Syn., Coll. Vol. II, 165 (1943).

58. A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," 2nd ed, John Wiley and Sons Inc., New York, N.Y., 1961, p. 27-50.

59. W. F. Bruce, J. Amer. Chem. Soc., 63, 301 (1941).

60. J. Vaughan, G. J. Welch and G. J. Wright, Tetrahedron, 21, 1665 (1965).

61. J. D. Roberts and V. C. Chambers, J. Amer. Chem. Soc., 73, 5034 (1951).

62. P. v. R. Schleyer and R. D. Nicholas, J. Amer. Chem. Soc., 83, 182 (1961).

63. C. S. Foote, J. Amer. Chem. Soc., 86, 1853 (1964).

64. P. v. R. Schleyer, J. Amer. Chem. Soc., 86, 1856 (1964).

65. C. N. Depuy, L. G. Schnack and J. W. Hauser, J. Amer. Chem. Soc., 88, 3343 (1966).

66. R. B. Woodward and R. Hoffmann, "The Conservation of Orbital Symmetry," Verlag Chemie, Weinheim, West Germany, 1971, p 46.

67. R. B. Woodward and R. Hoffmann, J. Amer. Chem. Soc., 87, 395 (1965).

68. P. v. R. Schleyer, W. F. Sliwinski, G. W. Van Dine, U. Schöllkopf, J. Paust and K. Fellenberger, J. Amer. Chem. Soc., 94, 125 (1972), and earlier literature cited therein.

69. P. v. R. Schleyer, T. M. Su, M. Saunders and J. C. Rosenfeld, J. Amer. Chem. Soc., 91, 5174 (1969).

70. P. v. R. Schleyer, G. W. Van Dine, U. Schöllkopf and J. Paust, J. Amer. Chem. Soc., 88, 2868 (1966).

71. U. Schöllkopf, K. Fellenberger, M. Patsch, P. v. R. Schleyer, T. Su and G. W. Van Vine, Tetrahedron Lett., 3639 (1967).

72. K. B. Wiberg and T. Nakahira, Tetrahedron Lett., 1773 (1974).

73. W. Kutzelnigg, Tetrahedron Lett., 4965 (1967).

74. J. A. Landgrebe and L. W. Becker, J. Amer. Chem. Soc., 90, 395 (1968).

75. D. B. Ledlie and E. A. Nelson, Tetrahedron Lett., 1175 (1969).

76. D. B. Ledlie and W. H. Hearne, Tetrahedron Lett., 4837 (1969).

77. D. T. Clark and G. Smale, Chem. Commun., 1050 (1969).

78. G. Köbrich, Angew. Chem. Int. Ed. Engl., 12, 464 (1973).

79. G. L. Buchanan, Chem. Soc. Rev., 3, 41 (1974).

80. R. Keese, Angew. Chem. Int. Ed. Engl., 14, 528 (1975).

81. J. Bredt, Liebigs Ann. Chem., 437, 1 (1924).

82. F. S. Fawcett, Chem. Rev., 47, 219 (1950).

83. J. R. Wiseman, J. Amer. Chem. Soc., 89, 5966 (1967).

84. J. R. Wiseman and J. A. Chong, J. Amer. Chem. Soc., 91, 7775 (1969).

85. K. W. Turnbull, S. J. Gould and D. Arigoni, Chem. Commun., 597 (1972).

86. D. H. Bowen and J. Macmillan, Tetrahedron Lett., 4111 (1972).

87. A. Nickon, D. F. Covey, F.-C. Huang and Y.-N. Kuo, J. Amer. Chem. Soc., 97, 904 (1975).

88. S. F. Campbell, R. Stephens and J. C. Tatlow, Tetrahedron, 21, 2997 (1965).

89. R. Keese and E. P. Krebs, Angew. Chem. Int. Ed. Engl., 10, 262 (1971).

90. R. Keese and E. P. Krebs, Angew. Chem. Int. Ed. Engl., 11, 518 (1972).

91. D. Grant, M. A. McKervey, J. J. Rooney, N. G. Samman and G. Step, Chem. Commun., 1186 (1972).

92. D. Lenoir, Tetrahedron Lett., 4049 (1972).

93. W. Burns and M. A. McKervey, Chem. Commun., 858 (1974).

94. A. H. Alberts, J. Strating and H. Wynberg, Tetrahedron Lett., 3047 (1973).

95. B. L. Adams and P. Kovacic, J. Amer. Chem. Soc., 95, 8206 (1973).

96. M. Farcasiu, D. Farcasiu, R. T. Conlin, M. Jones, Jr. and P. v. R. Schleyer, J. Amer. Chem. Soc., 95, 8207 (1973).

97. H. H. Grootveld, C. Blomberg and F. Bickelhaupt, Chem. Commun., 542 (1973).

98. A. D. Wolf and M. Jones, Jr., J. Amer. Chem. Soc., 95, 8209 (1973).

99. D. B. Ledlie, J. Org. Chem., 37, 1439 (1972).

100. D. B. Ledlie and J. Knetzer, Tetrahedron Lett., 5021 (1973).

101. D. B. Ledlie, J. Knetzer and A. Gitterman, J. Org. Chem., 39, 708 (1974).

102. P. M. Warner, R. C. Larose, C.-M. Lee and J. C. Clardy, J. Amer. Chem. Soc., 94, 7607 (1972).

103. P. M. Warner, R. C. LaRose, R. F. Palmer, C.-M. Lee, D. O. Ross and J. C. Clardy, J. Amer. Chem. Soc., 97, 5507 (1975).

104. C. B. Reese and M. R. D. Stebles, Tetrahedron Lett., 4427 (1972).

105. C. B. Reese and M. R. D. Stebles, Chem. Commun., 1231 (1972).

106. P. M. Warner, J. Fayos and J. C. Clardy, Tetrahedron Lett., 4473 (1973).

107. C. B. Reese, private communication.

108. D. B. Ledlie and L. Bowers, J. Org. Chem., 40, 792 (1975).

109. W. E. Parham, D. R. Johnson, C. T. Hughes, M. K. Meilahn and J. K. Rinehart, J. Org. Chem., 35, 1048 (1970).

110. W. E. Parham, D. C. Egberg and W. C. Montgomery, J. Org. Chem., 38, 1207 (1973).

111. P. Warner, R. LaRose and T. Schleis, Tetrahedron Lett., 1409 (1974).

112. D. Seyferth, H. Yamazaki and D. L. Alleston, J. Org. Chem., 28, 703 (1963).

113. J. T. Groves and K. W. Ma, Tetrahedron Lett., 909 (1974).

114. P. W. DeHaven and R. A. Jacobson, Ames Laboratory, U.S.E.R.D.A., Iowa State University, unpublished results.

115. P. M. Warner, S-L. Lu, E. Meyers, P. W. DeHaven and R. A. Jacobson, Tetrahedron Lett., 4449 (1975).

116. P. G. Gassman, R. N. Steppel and E. A. Armour, Tetrahedron Lett., 3287 (1973).

117. R. L. Kronenthal and E. I. Becker, J. Amer. Chem. Soc., 79, 1095 (1957).

118. P. D. Bartlett, W. D. Closson and T. J. Cogdell, J. Amer. Chem. Soc., 87, 1308 (1965).

119. G. LeNy, Compt. Rend., 251, 1526 (1960).

120. J. A. Berson, D. S. Donald and W. J. Libbey, J. Amer. Chem. Soc., 91, 5580 (1969).

121. A. V. Kemp-Jones, N. Nakamura and S. Masamune, Chem. Commun., 109 (1974), and earlier references cited therein.

122. X. Creary, J. Org. Chem., 40, 3326 (1975).

123. (a) S. Winstein and J. Sonnenberg, J. Amer. Chem. Soc., 83, 3235 (1961); (b) P. D. Bartlett and M. R. Rice, J. Org. Chem., 28, 3351 (1963).

124. S. Winstein, E. C. Friedrich, R. Baker and Y. Lin, Tetrahedron Suppl., 8, Part II, 621 (1966).

125. P. Warner and S-L. Lu, J. Amer. Chem. Soc., 97, 2356 (1975).

126. (a) S. Kabuss, H. Friebolin and H. Schmid, Tetrahedron Lett., 469 (1965); (b) W. R. Moore, E. Marcus, S. E. Fenton and R. T. Arnold, Tetrahedron, 5, 179 (1959).

127. A. C. Cope and E. S. Graham, J. Amer. Chem. Soc., 73, 4702 (1951).

128. We thank Professor Groves (see ref. 14 of ref. 115) for the ir spectra of cis and trans carboxylic acids.

129. J. W. Emsley, J. Feeney and L. H. Sutcliffe, "High Resolution Nuclear Magnetic Resonance Spectroscopy," Pergamon Press, New York, N.Y., 1965, pp 580-

130. J. K. Crandall and W. H. Machleder, J. Amer. Chem. Soc., 90, 7347 (1968).

131. J. F. Pazos, J. G. Pacifici, G. O. Pierson, D. B. Sclover and F. D. Greene, J. Org. Chem., 39, 1990 (1974).

132. For a leading reference, see N. J. Turro, Accounts Chem. Res., 2, 25 (1968).

133. L. F. Fieser, "Organic Experiments" D. C. Heath and Company, Boston, Mass. 1964, p96.

134. R. O. Hutchins, C. Milewski and B. Maryanoff, J. Amer. Chem. Soc., 95, 3662 (1973).

135. P. D. Bartlett, R. E. Pincock, J. H. Rolston, W. G. Schindel and L. A. Singer, J. Amer. Chem. Soc., 87, 2590 (1965).

136. von V. Prelog, K. Schenker and W. Küng, Helv. Chem. Acta Acta., 36, 471 (1953).

137. G. W. Kabalka and J. D. Baker, Jr., J. Org. Chem., 40, 1834 (1975).

138. M. S. Kharasch and C. Reinmuth, "Grignard Reactions of Nonmetallic Substances" Prentice-Hall Inc., N.Y., 1954, p 56.

139. E. C. Ashby, Quart. Rev., 21, 259 (1967).

140. H. H. Grootvelt, C. Blomberg and F. Bickelhaupt, Tetrahedron Lett., 1999 (1971).

141. H. M. Walborsky and A. E. Young, J. Amer. Chem. Soc., 83, 2595 (1961); 86, 3288 (1964).

142. H. M. Walborsky and M. S. Aronoff, J. Organometal. Chem., 51, 31 (1973).

143. J. Smid, Angew. Chem. Int. Ed. Engl., 11, 112 (1972).

144. G. M. Whitesides, R. J. Rogers, H. L. Mitchell and Y. Fujiwara, J. Org. Chem., 39, 857 (1974).

145. J. L. Webb, C. K. Mann and H. M. Walborsky, J. Amer. Chem. Soc., 92, 2042 (1970).

146. (a) H. W. H. J. Bodewitz, C. Blomberg and F. Bickelhaupt, Tetrahedron Lett., 281 (1972); (b) H. W. H. J. Bodewitz, C. Blomberg and F. Bickelhaupt, Tetrahedron, 29, 719 (1973).

147. W. T. Ford and G. Buske, J. Amer. Chem. Soc., 96, 621 (1974).

148. S. J. Cristol and A. L. Noreen, J. Amer. Chem. Soc., 91, 3969 (1969).

149. D. E. Applequist and A. H. Peterson, J. Amer. Chem. Soc., 82, 2372 (1960).

150. H. M. Walborsky, C. Chen and J. L. Webb, Tetrahedron Lett., 3551 (1964).

151. K. Sisido, S. Kozima and K. Takizawa, Tetrahedron Lett., 33 (1967).

152. T. Ando, F. Namigata, H. Yamanaka and W. Funasaka, J. Amer. Chem. Soc., 89, 5719 (1967).

153. (a) H. G. Kuivila, L. W. Menapace and C. R. Warner, J. Amer. Chem. Soc., 84, 3584 (1962); (b) L. W. Menapace, H. G. Kuivila, J. Amer. Chem. Soc., 86, 3047 (1964).

154. E. J. Kupchik and R. J. Kiesel J. Org. Chem., 29, 764 (1964); 29, 3960 (1964).

155. F. D. Greene and N. N. Lowry, J. Org. Chem., 32, 882 (1967).

156. (a) H. G. Kuivila, Accounts Chem. Res., 1, 299 (1968); (b) F. R. Jensen and D. E. Patterson, Tetrahedron Lett., 3837 (1966); (c) H. G. Kuivila, Synthesis, 499 (1970); (d) D. J. Carlsson and K. U. Ingold, J. Amer. Chem. Soc., 90, 1055, 7047 (1968).

157. T. Ishihara, K. Hayashi and T. Ando, J. Org. Chem., 40, 3264 (1975).

158. L. A. Singer and J. Chen, Tetrahedron Lett., 939 (1971).

159. R. W. Fessenden and R. H. Schuler, J. Chem. Phys., 39, 2147 (1963).

160. L. J. Altman and R. C. Baldwin, Tetrahedron Lett., 2531 (1971).

161. T. Ando, K. Wakabayashi, H. Yamanaka and W. Funasaka, Bull Chem. Soc. Jap., 45, 1576 (1972).

162. L. J. Altman and J. C. Vederas, Chem. Commun., 895 (1969).

163. (a) L. Pauling, J. Chem. Phys., 51, 2767 (1969); (b) A. J. Dobbs, B. C. Gilbert and R. O. C. Norman, J. Chem. Soc., A, 124 (1971).

164. R. C. Bingham and M. J. S. Dewar, J. Amer. Chem. Soc., 95, 7180, 7182 (1973).

165. L. Kaplan, J. Amer. Chem. Soc., 88, 4531 (1966).

166. L. J. Altman and B. W. Nelson, J. Amer. Chem. Soc., 91, 5163 (1969).

167. J. Jacobus and D. Pensak, Chem. Commun., 400 (1969).

168. L. J. Altman and T. R. Erdman, Tetrahedron Lett., 4891 (1970).

169. C. L. Osborn, T. C. Shields, B. A. Shoulders, C. G. Cardenas and P. D. Gardner, Chem. & Ind., 766 (1965).

170. J. Hatem and B. Waegell, Tetrahedron Lett., 2019 (1973).

171. J. Hatem and B. Waegell, Tetrahedron Lett., 2023 (1973).

172. T. Ando, H. Yamanaka, F. Namigata and W. Funasaka, J. Org. Chem., 35, 33 (1970).

173. T. Ishihara, E. Ohtani and T. Ando, Chem. Commun, 367 (1975).

174. H. M. Walborsky, F. J. Impastato and A. E. Young, J. Amer. Chem. Soc., 86, 3283 (1964).

175. R. L. Letsinger, J. Amer. Chem. Soc., 72, 4842 (1950).

176. D. Y. Curtin and J. W. Crump, J. Amer. Chem. Soc., 80, 1922 (1958).

177. P. K. Freeman, L. L. Hutchinson and J. N. Blazevich, J. Org. Chem., 39, 3606 (1974).

178. M. J. S. Dewar and J. M. Harris, J. Amer. Chem. Soc., 91, 3652 (1969).

179. C. P. Lewis and M. Brookhart, J. Amer. Chem. Soc., 97, 651 (1975).

180. D. T. Longone and W. D. Wright, Tetrahedron Lett., 2859 (1969).

181. A. G. Bemis, Ph. D. Dissertation, Iowa State University, Ames, Iowa (1966).

182. (a) J. San Filippo, Jr., C-I. Chern and J. S. Valentine, J. Org. Chem., 40, 1678 (1975); (b) R. A. Johnson and E. G. Nidy, J. Org. Chem., 40, 1680 (1975); (c) E. J. Corey, K. C. Nicolaou, M. Snibasaki, Y. Machida and C. S. Shiner, Tetrahedron Lett., 3183 (1975).

183. (a) R. C. Lamb, P. W. Ayers, M. K. Toney and J. F. Garst, J. Amer. Chem. Soc., 88, 4261 (1966); (b) E. Müller and T. Töpel, Chem. Ber. 72, 273 (1939).

184. G. Van Der Kerk, J. Noltes and J. Luijten, J. Appl. Chem., 7, 366 (1957).

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