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Synthesis, reactivity, and spectroscopic properties of substituted bicyclo(n.1.0) alkanes

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Synthesis, reactivity, and spectroscopic properties of substituted bicyclo[n.1.0]alkanes

by

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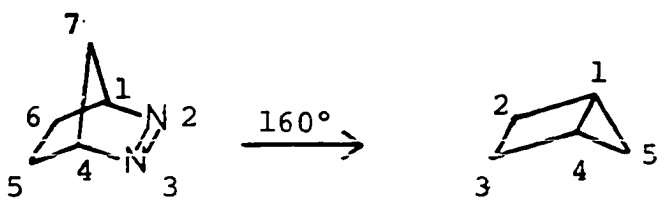
HISTORICAL

Methylene Transfers to Cyclobutenes

Unlike many highly strained ring systems which are known only in substituted forms, the first authenticated (1) example of a bicyclo[2.1.0]pentane was the parent hydrocarbon (1) which Criegee and Rimmelin (2) prepared from the previously known (3) azo compound 2. Although several important contributions to the understanding of this unusual ring system were (and continue to be) made through studies on the parent compound, further progress was dependent on the synthesis of appropriately substituted functional derivatives. The original synthesis has been applied to a few substituted bicyclopentanes



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(4,5,6,7), but the difficulty in preparing suitably substituted azo precursors (particularly those with substituents on positions 1,(4) or 7) has been a serious limitation on this method.

The need for specifically substituted bicyclopentanes has been met by the development of several new synthetic approaches, two of which have been particularly important because of their

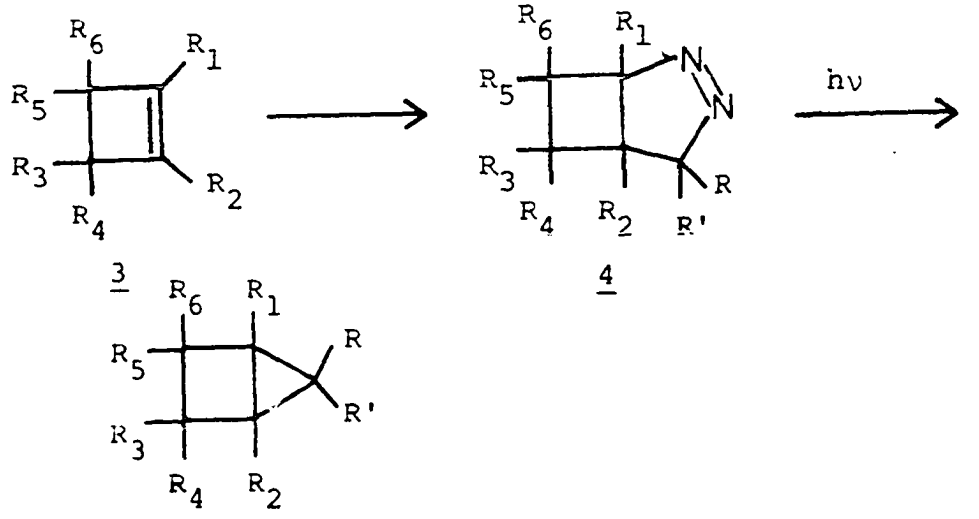
wide applicability. These methods, which complement each other, each involve a methylene transfer to a cyclobutene, one in a direct and the other in an indirect transfer reaction.

Indirect transfer

The indirect approach (Scheme 1) developed in 1967, by three independent groups of investigators (8,9,10) involves two steps, the first of which is the 1,3-dipolar cycloaddition of a diazoalkane to an electron-deficient cyclobutene 3 to give a pyrazoline 4. Photolysis of the pyrazoline as a solution in acetone or in an inert solvent (ether or pentane) in the presence of a sensitizer like benzophenone produces good to excellent (40%-90%) yields of bicyclopentanes 5 with only minor contamination from other products (10,11,12,13). Direct irradiation on the other hand generally leads to complex product mixtures with drastic reduction in bicyclopentane yields (8,9,10,11). Alternatively, the pyrazolines can be thermally decomposed, but yields are lower and undesired side reactions predominate. Representative examples of bicyclopentanes which have been prepared by the pyrazoline route are listed in Table 1. The scope of the pyrazoline method is defined primarily by the types and positions of substituents on the cyclobutene. For example diazomethane readily forms a pyrazoline with 1-carbomethoxyclobutene (8,9,10,11) but does not react with cis-3,4-dicabomethoxycyclobutene (13).

Table 1. Substituted bicyclo[2.1.0] pentanes (5) prepared via the pyrazoline route (Scheme 1)

R_1	R_2	R_3	R_4	R_5	R_6	R	R'	Ref.
CO_2CH_3	H	H	H	H	H	H	H	(8,9,10,11)
CO_2CH_3	H	CH_3	H	H	H	H	H	(10,11)
CO_2CH_3	H	CH_3	CH_3	H	H	H	H	(10,11)
CO_2CH_3	H	CH_3	CH_3	H	H	CH_3	H	(10,11)
CO_2CH_3	H	CH_3	CH_3	H	H	CH_3	CH_3	(10,11)
CO_2CH_3	CO_2CH_3	H	H	H	H	CH_3	CH_3	(12)
$COCH_3$	H	CH_3	CH_3	H	H	H	H	(10,11)
COØ	H	CH_3	CH_3	H	H	H	H	(10)
CN	H	CH_3	CH_3	H	H	H	H	(10,11)
H	H	Cl	H	Cl	H	CH_3	CH_3	(12a,12b)
H	H	Cl	H	Cl	H	CH_3	H	(12b)
H	H	CO_2CH_3	H	CO_2CH_3	H	CH_3	CH_3	(12b)
H	H	H	H	H	H	H	H	(13)



3 4

5

Scheme 1

Likewise, pyrazoline formation was not observed with diazomethane and either cyclobutenyl acetate or 1-phenylcyclobutene (11). Although White et al. (13) have recently reported a 76% yield of pyrazoline from cyclobutene and diazomethane (unspecified amounts) in pentane at room temperature, the reaction time was long. Thus pyrazoline formation is favored by a strongly electron deficient cyclobutene and proceeds most efficiently when electron withdrawing substituents are attached directly to olefinic carbon. Consequently, the synthesis is especially useful for bridgehead substituted compounds. Furthermore, these same substituents, once incorporated into the bicyclopentane nucleus can be transformed into a wide variety of new functionalities adding tremendous versatility to the method.

Little is known about possible limitations on the diazoalkane since nearly all the reported examples have involved only diazomethane, diazoethane, or 2-diazopropane. However, Welch (11) noted that the pyrazolines formed from 1-carbomethoxy-3,3-dimethylcyclobutene and either phenyldiazomethane or diphenyldiazomethane failed to evolve nitrogen on irridation.

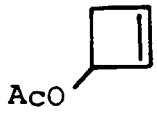
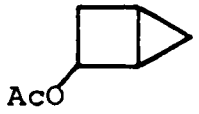
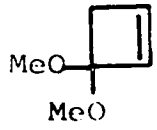
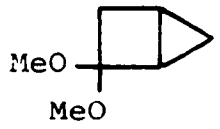
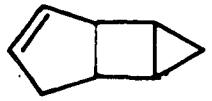
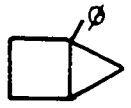
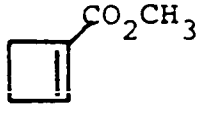
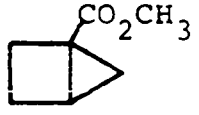
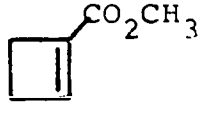
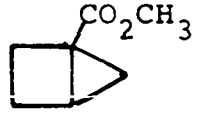
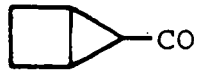
Direct transfer

The direct approach involves simply a direct, one-step addition of a methylene to a cyclobutene via a carbene or carbenoid transfer reagent. However, of the wide variety of methylene transfer reagents that have become available

following renewed interest in divalent carbon species in the early 1950's, relatively few have been employed in bicyclopentane synthesis. Nearly all the known examples involve either unsubstituted methylene from a Simmons-Smith reagent or cuprous salt catalyzed decomposition of diazomethane, or carbethoxy carbene from ethyl diazoacetate. Nevertheless, direct transfer has provided several useful bicyclopentanes not readily accessible by other methods (see Table 2).

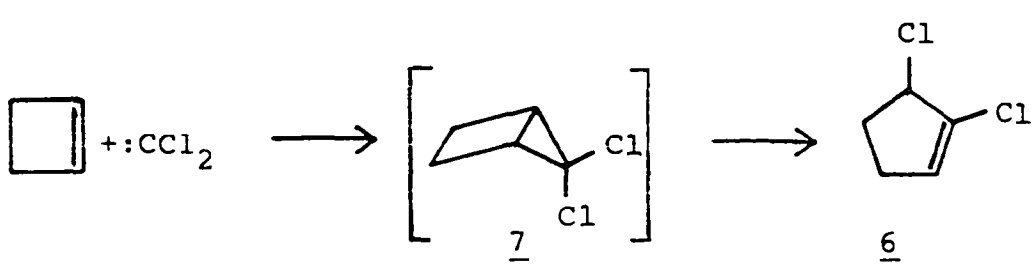
Although the few reported examples by no means define the potential of this useful procedure, a few generalizations seem safe. Carbene additions to electron-deficient olefins generally proceed very poorly, and electron-deficient cyclobutenes are not exceptions. For example 1-carbomethoxycyclobutene in the presence of diazomethane and cuprous chloride gives no reaction, and in the presence of methylene iodide and a zinc-copper couple gives only a 5% yield of the bicyclopentane (8). Similar results were obtained with the same transfer reagents and 1-carbomethoxy-3,3-dimethylcyclobutene (11). Yields of bicyclopentanes from similar transfer reagents and cyclobutenes lacking strong deactivating groups range from 30-50%. Although the data available for comparison is quite limited, it appears that cyclobutenes undergo direct methylene addition less readily than the corresponding cyclopentenes and larger ring olefins. For example Simmons-Smith reactions on 1-phenylcyclobutene and the correspondingly

Table 2. Carbene and carbenoid additions to cyclobutenes

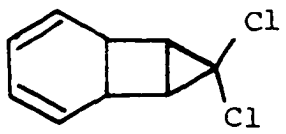
Cyclobutene	Methylene transfer agent	Product	Yield	Ref
	CH_2N_2/Cu_2Cl_2		(-)	(14)
	CH_2N_2/Cu_2Cl_2		54%	(15,16)
	CH_2N_2/Cu_2Br_2		(-)	(16)
	CH_2N_2/Cu_2Cl_2		23%	(17)
	$CH_2I_2/Zn\text{-}Cu$		43%	(18)
	$(ICH_2)_2ZnI$		47%	(19)
	$CH_2I_2/Zn\text{-}Cu$		5%	(8)
	CH_2N_2/Cu_2Cl_2		0%	(8)
	$N_2CHCO_2C_2H_5/Cu$		< 30%	(20,21)
	$N_2CHCO_2C_2H_5/h\nu$		< 37%	(21)

substituted cyclopentene and cyclohexene give the corresponding cyclopropanes in yields of 43%, 56%, and 66% respectively (18). The reaction of bis-(iodomethyl)zinc iodide with cyclobutene, cyclopentene, and cyclohexene produces the corresponding bicyclo[n.1.0]alkanes in yields of 47%, 65%, and 73% respectively (19). The monotonic decrease in yields with decreasing ring size may be a reflection of increasing strain in the products.

Although the first example of a cyclopropane synthesis via direct methylene transfer to an olefin involved a dihalocarbene (22), and although the halomethylenes have subsequently received more attention from both theoretical and synthetic points of view than any other class of methylene, only two reports of halomethylene additions to cyclobutenes can be found in the literature prior to 1969. E. Vogel, in reference to some unpublished results obtained with H. Kiefer, reported that the addition of dichlorocarbene to cyclobutene produced 2,3-dichlorocyclopentene (6). The latter was presumed to arise from the rearrangement of 5,5-dichlorobicyclo[2.1.0]pentane (7) in its nascent state (23). No experimental details were given, however. An earlier report of a compound incorporating



a 5,5-dichlorobicyclo[2.1.0]pentyl moiety appeared in a 1958 German patent (24), in which it was claimed that the addition of dichlorocarbene to cyclooctatetraene produces the tricyclic compound 8. However, Vogel (23) later established the structure of the product as the bicyclic compound 9. Yang (25) reported a very unusual reaction between 1,2-dimethyl-



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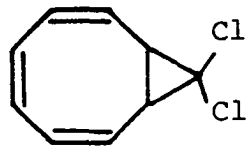

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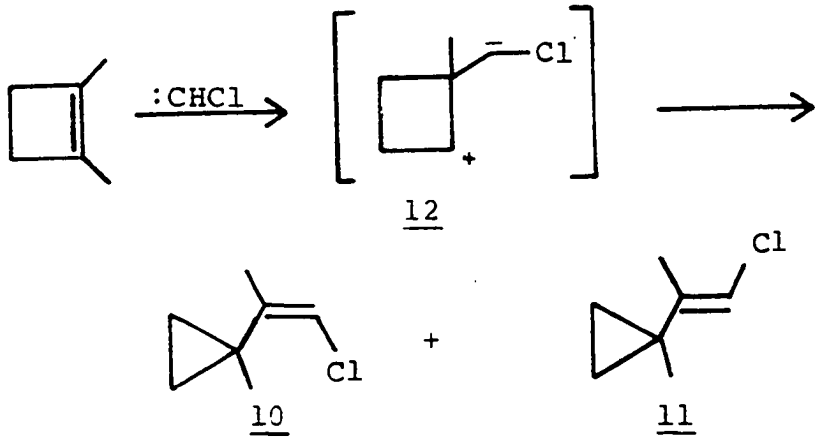
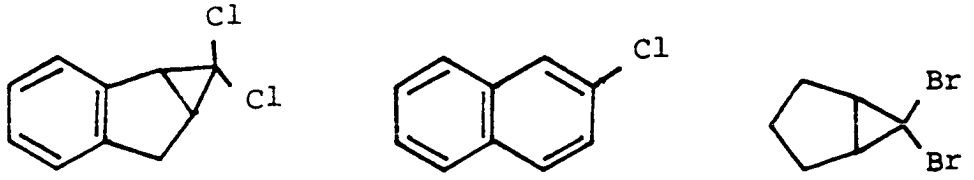
cyclobutene and chlorocarbene photochemically generated from chloroform. The only products isolated corresponding to a 1:1 addition were the isomeric vinylcyclopropanes 10 and 11. Analogous results were obtained with photochemically generated iodocarbene. The products could not be explained in terms of a vibrationally excited bicyclopentane intermediate since biocyclopentanes give cyclopentenes on thermolysis. It was proposed that a photochemically generated halocarbene adds in its singlet state to the strained olefin in a stepwise fashion to initially give the dipolar intermediate 12 which then undergoes a cyclobutyl-cyclopropylcarbinyl rearrangement to the observed products. The photochemically generated halocarbenes behaved normally with other olefins, giving 7-halonorcaranes with cyclohexene and stereospecific cis-addition to cis- and trans-2-butene.

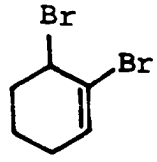


Thermal Rearrangements of Halocarbene-Cyclic Olefin Adducts

Soon after they became readily accessible (22) it was apparent that certain halocarbene-cyclic olefin adducts were thermally unstable. Parham et al. (26) isolated the dichlorocarbene-indene adduct 13 and found that it readily rearranged to 2-chloronapthalene (14). Sonnenberg and Winstein (27) reported a similar rearrangement of the dibromocarbene adduct of cyclopentene (15) to 2,3-dibromocyclohexene (16) during distillation. On the other hand, 8,8-dichlorobicyclo[5.1.0]octane (17), was reported (28) to be very stable to heat. The synthetic importance of these ring



13 14 15



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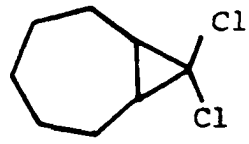

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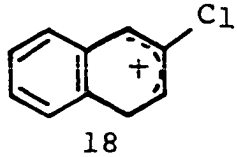
expansion reactions was soon recognized (29,30) although mechanistic details remained a matter for speculation. Parham et al. (26) had found that the rearrangement of 13 followed first order kinetics in 80% aqueous ethanol and in the presence of sodium hydroxide. This, combined with a primary positive salt effect observed with added sodium perchlorate led the authors to propose a mechanism involving as the initial and rate determining step chloride ionization to give either the rearranged cation 18 directly or the cyclopropyl cation 19, which would rapidly rearrange to 18.



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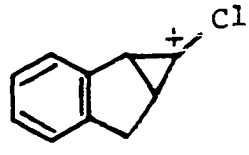

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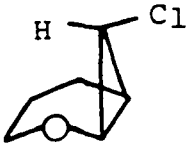
Although the conversion of cyclopropyl to allyl derivatives under solvolytic conditions had been known for some time, it was not known whether discrete cyclopropyl cations or concerted ionizations to allyl cations were involved. Roberts and Chambers (31), who were the first to study the solvolysis of a cyclopropane derivative in detail, found that the

acetolysis of cyclopropyl tosylate proceeded some 10^5 times slower than the acetolysis of cyclohexyl tosylate and gave allyl acetate as the only isolable product. Based on the slow rate of acetolysis 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 carbonium ion center, followed by fast ring opening to the allyl cation. This conclusion was later questioned by Schleyer and Nicholas (32) who noted that the acetolysis rate of cyclopropyl tosylate was 100 times faster than that of 7-norbornyl tosylate despite larger bond angles at the carbonium ion center of the latter. The mechanism of ring opening in reactions involving cyclopropyl cations as potential intermediates has subsequently received widespread attention. It has gradually become clear that the purely thermal rearrangements of halocarbene adducts of cyclic olefins, like the solvolytic reactions, are carbonium ion processes subject to control by stereochemical and electronic factors and also ring size.

Stereochemistry

Schweizer and Parham (33) isolated the epimeric 7-chloro-2-oxabicyclo[4.1.0]heptanes 20 and 21 and found that one isomer was thermally unstable, being converted to 2,3-dihydrooxepin (22) on distillation from quinoline, while the other isomer was stable at its boiling point. The authors incorrectly (34) assigned structure 20 to the thermally labile

isomer, primarily on the basis of possible backside assistance by oxygen to chloride ionization. Stereospecificity in the rearrangement of a dihalocyclopropane had been demonstrated



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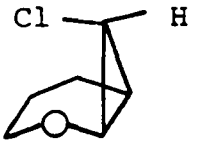

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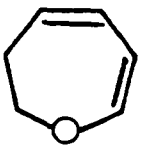
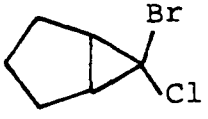


22

earlier by Skell and Sandler (35) in the silver ion assisted hydrolysis of epimeric 6-bromo-6-chlorobicyclo[3.1.0]hexanes 23. Although specific structural assignments could not be made, the "α isomer" of 23 gave 2-bromo-2-cyclohexanol (24a) as the sole product, while the only product obtained from the "β isomer" of 23 was the corresponding chloro derivative 24b. It therefore became apparent that the stereochemical disposition of the leaving group was a critical factor in determining the course of the rearrangement. The first experimental



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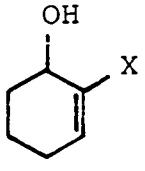
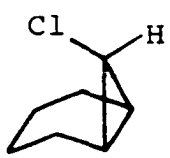


24 A X = Br
B X = Cl

determination of the stereochemistry of the reaction was reported by Cristol et al. (36) in 1965. Acetolysis of endo-7-chlorobicyclo[4.1.0]heptane (25) proceeded readily at

125° ($k = 1.4 \times 10^{-6}$ sec^{-1}), whereas the exo-isomer (26) was recovered unchanged after prolonged treatment at 210°. The dichloro derivative 27 showed consistent behavior, being slightly less reactive ($k = 4.5 \times 10^{-7}$ sec^{-1}) than the endo-isomer (25). Thus it was shown that an endo-leaving group is



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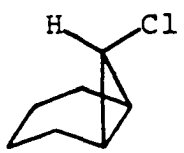

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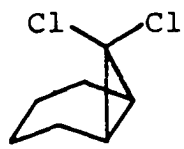
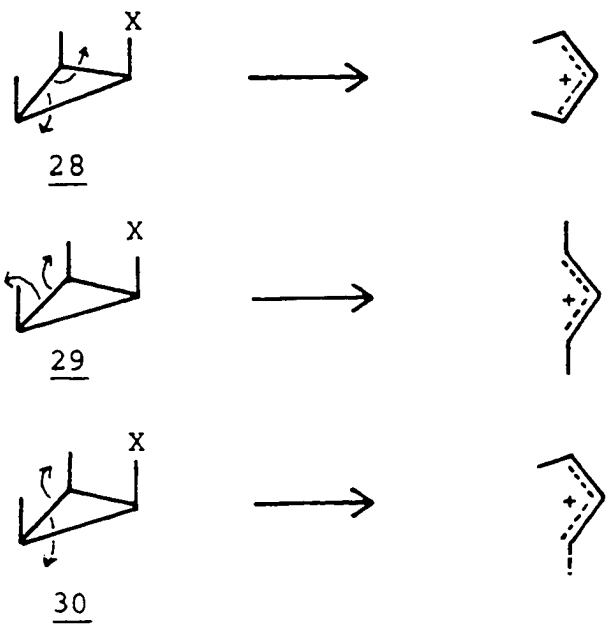


27

required for the reaction to proceed at a reasonable rate.

These observations amounted to the first experimental confirmation of theoretical predictions made slightly earlier first by Woodward and Hoffman (37) and later by Longuet-Higgins and Abrahamson (38). Based on the principle of orbital symmetry conservation it was predicted that the concerted thermal ring opening of a cyclopropyl cation to an allyl cation (Scheme 2) should be stereospecific, disrotary process as shown in 28 or 29 as opposed to a conrotatory process shown in 30. Following a question by DePuy (39) (40) concerning a possible difference in the two disrotatory modes with respect to the leaving group, Woodward and Hoffman (37) carried out extended Huckel calculations which favored the mode (28) in which substituents cis to the leaving group rotate toward each other and substituents trans to the leaving group rotate apart

when ring opening is concerted with ionization. It has been pointed out (40,41) that such a process can be intuitively appreciated by considering the ionization to proceed through backside displacement of the leaving group by the electrons in the breaking σ bond. These predictions have subsequently received numerous other confirmations based on the extensive

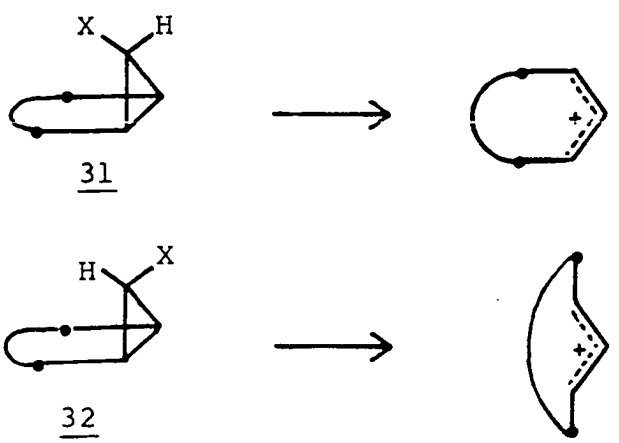


Scheme 2

kinetic investigations of cyclopropyl tosylate solvolyses by DePuy et al. (39,42), Schleyer et al. (43), Schollkopf et al. (44) and also the direct observation of stereoisomeric allylic cations derived from isomeric 2,3-dimethylcyclopropyl chlorides in strong acid media (45). However, it should be noted that there are a few rare examples where discrete cyclopropyl

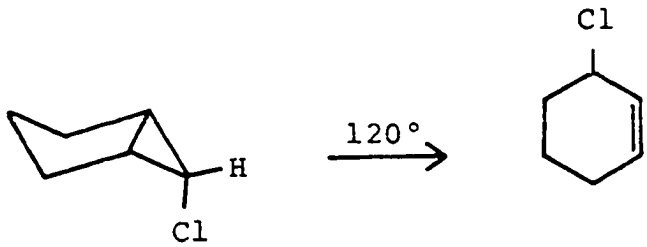
cations may be generated and do not rearrange. These include several amine deaminations (46,47,48,49,50) and solvolyses of 1-bicyclopropyl derivatives (51,52,53).

The stereochemical consequences of the predicted mode of ring opening for halocarbene cyclic olefin adducts (or the corresponding structures with other leaving groups are shown in Scheme 3. When C-2 and C-3 of the cyclopropyl derivative

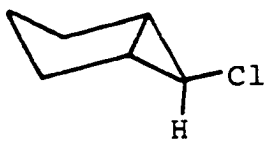


Scheme 3

are joined by a short methylene bridge, endo-leaving groups (31) lead to relatively strain free cis,cis allylic cations while exo-leaving groups (32) give highly strained trans,trans-allyic cations. It should therefore be expected that exo-leaving groups would be extremely resistant to ionization. Consequently, thermal rearrangements of bicyclic halocyclopropanes involving a concerted heterolytic process should be subject to the same stereoelectronic control. This is precisely what has been observed in numerous instances, several examples of which follow.



Ref. (54,55)



N.R.

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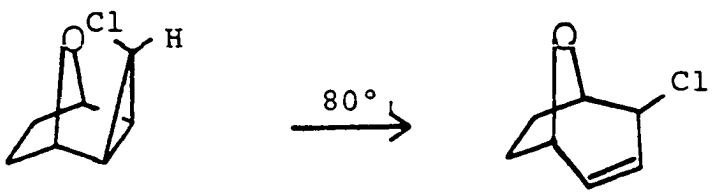

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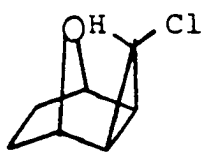

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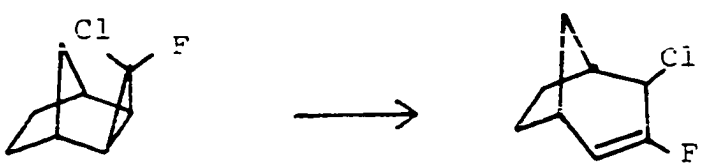

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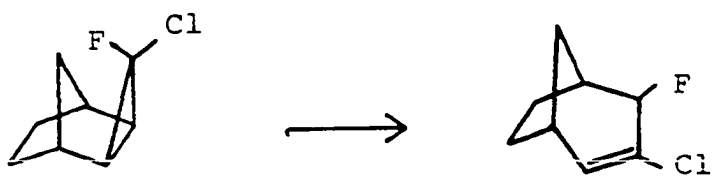

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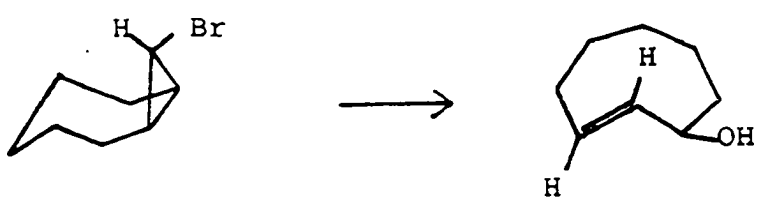
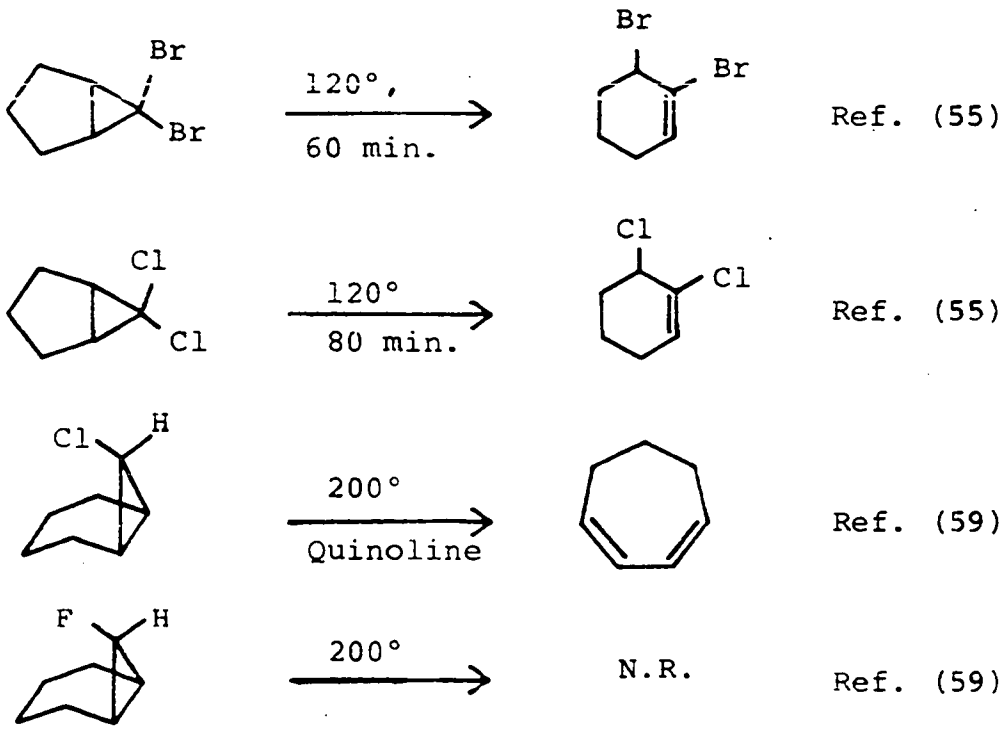


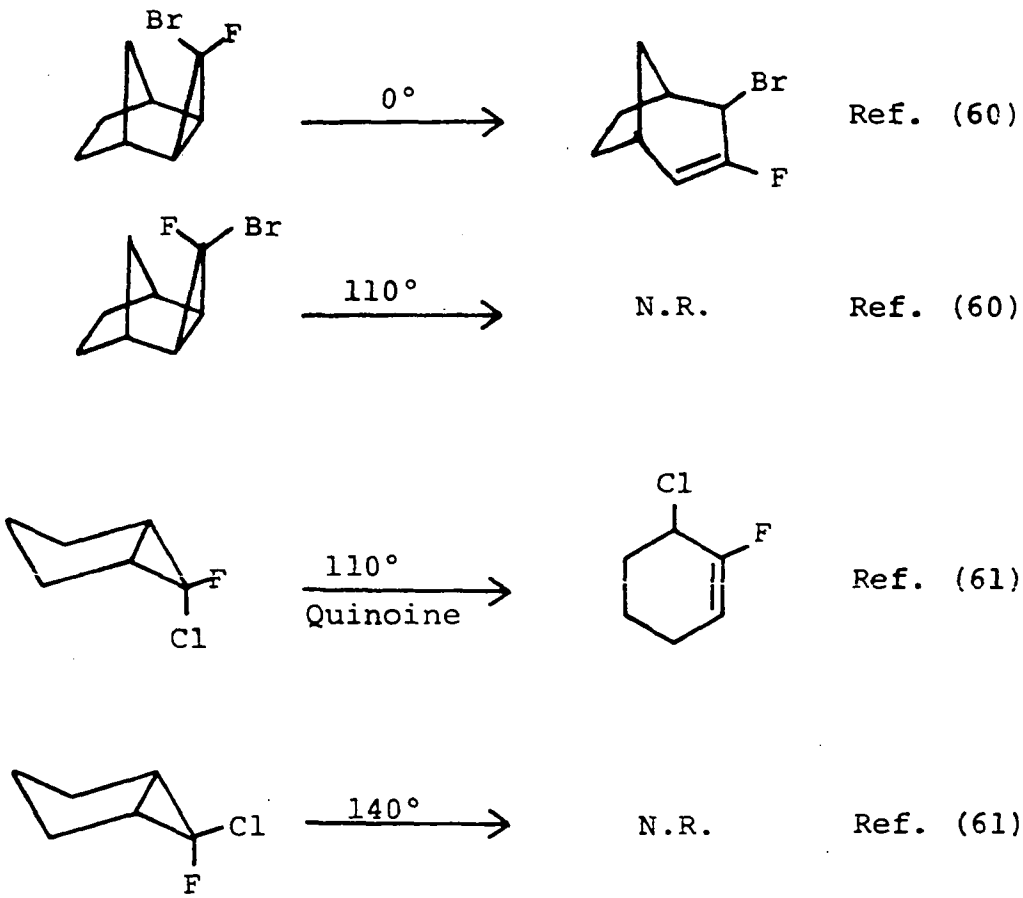
Ref. (58)

Electronic factors

Since the thermal rearrangements under consideration presumably do involve a concerted heterolytic fission to give a halide ion and an allylic cation, it should be expected that the nature of the leaving group and the stability of the intermediate allylic cation would have a substantial effect on the rate.

Thermal stabilities of adducts do indeed show a marked dependence on the halogen substituent decreasing in the order F > Cl > Br as expected, with fluoride ion being a particularly poor leaving group. Most of the evidence for this, as illustrated by the relative thermal stabilities of the following pairs of compounds, is semiquantitative, but the trend is unmistakably clear.

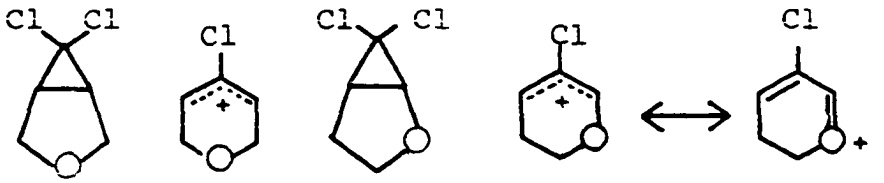




There are many examples of stability differences in cyclopropane derivatives which can only be attributed to electronically controlled stability differences in the intermediate allylic cations (which the transition states resemble). Indeed the observation by DePuy (39,41,42) that 2-arylcyclopropyl tosylates are solvolyzed more readily than the parent tosylate was among the first evidence for concerted ring opening since the results implied some charge delocalization onto the benzylic carbon in the rate determining step. Related behavior has been observed in both solvolytic and

thermal rearrangements of bicyclic halocyclopropanes. For example the slower acetolysis rate of 27 relative to 25 and also the slower thermolysis rates of 6,6-dichlorobicyclo[3.1.0]-hexane (1.5 hr at 70°) relative to endo-6-chlorobicyclo[3.1.0]-hexane (3 hr at 126°) (55) can be attributed to the inductive destabilization of the intermediate cations derived from the dihalogenated compounds by the chlorine substituent.

Another pair of compounds which exhibit differences in thermal stability attributable to electronic differences in the intermediate allylic cations are 6,6-dichloro-3-oxa- (33) and 6,6,dichloro 2-oxalicyclo[3.1.0] hexane (34) (55). Compound 33 is more stable (2.7 hr at 235° for complete rearrangement) than its homocyclic analog discussed above as a result of inductive destabilization by oxygen in the intermediate carbonium ion 35. The isomeric compound 34, on the other hand, can give rise to the resonance stabilized intermediate 36 resulting in much more facile rearrangement (15 min at 60°).



33 35 34 36

Similar arguments have been invoked to explain the greater thermal lability of 7,7-dibromobicyclo[4.1.0]hept-2-ene (62) and 6,6-dichlorobicyclo[3.1.0]hex-2-ene (55) relative to

their saturated analogs.

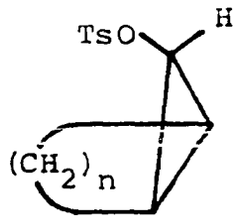
There are also several rearrangements, many of preparative importance, where the intermediate cations are stabilized by extra-annular substituents (63).

Ring-size effects

The qualitative effect of ring size on the thermal stability of halocarbene adducts of cyclic olefins has been observed in several instances, though the phenomenon has not been investigated in detail or fully explained. 6,6-Dibromobicyclo[3.1.0]hexane, for example, is completely rearranged after 60 minutes at 120° (55) while the next higher homolog, 7,7-dibromobicyclo[4.1.0]heptane is stable below 200° (62). The next member in the series, 8,8-dibromobicyclo[5.1.0]octane is even more stable requiring temperatures greater than 240° for rearrangement (64). Bergman (28), who had reported similar observations for the corresponding dichloro-derivatives, also observed that of the three, only dichlorobicyclohexane rearranged in ethanolic silver nitrate at 25°. On the questionable assumption that cyclic allylic cations should follow the same order of stability as their saturated analogs, Bergman argued that the opposite order of reactivity should be observed if stability of the intermediate carbonium ions was the controlling factor. Strain energy differences in the bicyclic cyclopropanes was suggested as the most important factor in controlling the relative ease of rearrangement. This argument

was supported by the observation (28) that relatively unstrained compounds such as 1,1-dichloro-2-phenylcyclopropane and 1,1-dichloro-2,2-diphenylcyclopropane fail to rearrange in ethanolic silver nitrate despite the fact that stable carbonim ions would be formed.

Ring size dependence on the stability of bicyclic cyclopropane derivatives has been studied more quantitatively by Schollkopf, Schleyer, and coworkers (44) in their investigations into solvolyses of bicyclic tosylates. A series of endo- and exo-bicyclo[n.1.0]alkyl tosylates, 37 and 38, gave the relative acetolysis rates (100°) shown below. The authors suggested that the monotonic rate decrease with increasing



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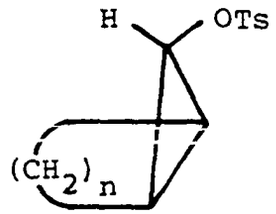


38

n	Rel Rate
3	25,000
4	62
5	3.1
6	3.5

n	Rel Rate
3	<0.01
4	1.7
5	2,500
6	10,000

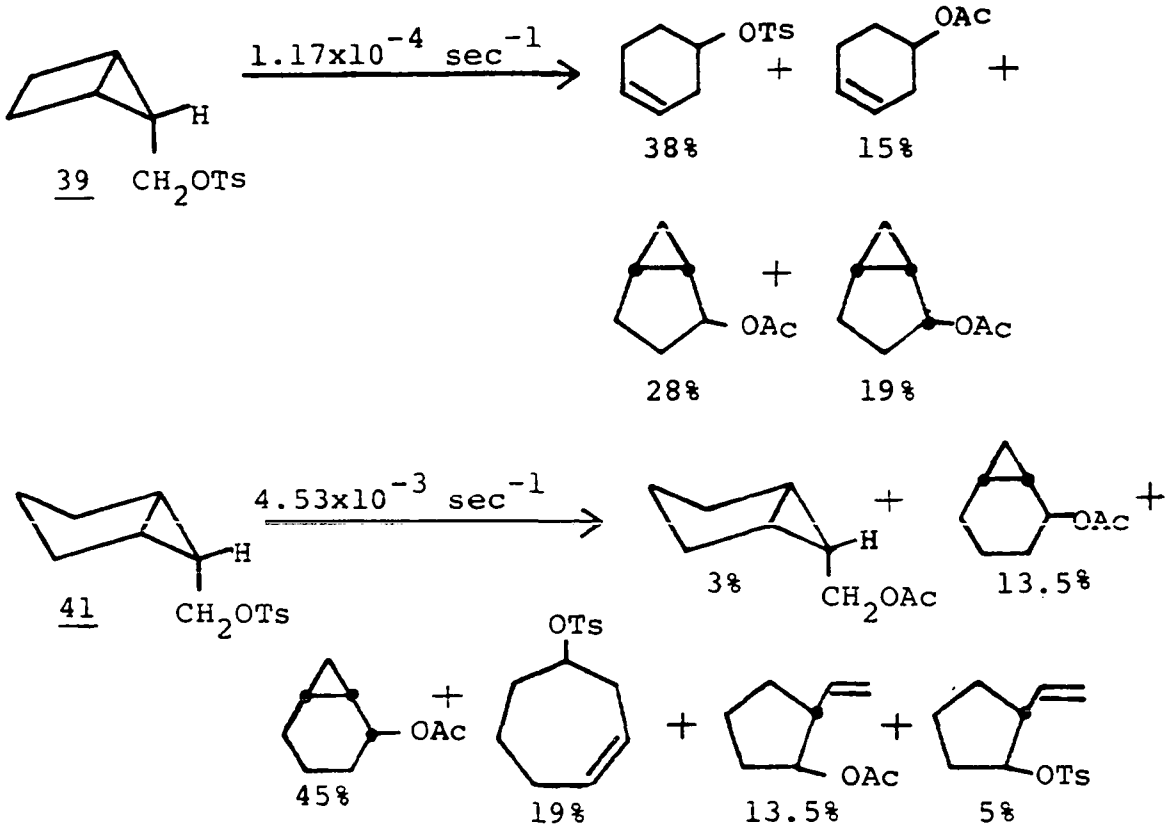
ring size in the endo series might indeed be a result of decreasing stability of the cyclic allylic cation intermediates; strain energy was not mentioned. The opposite order of reactivity in the exo series was attributed to the increasing ease in forming the trans, trans-allylic cations as the ring size increases.

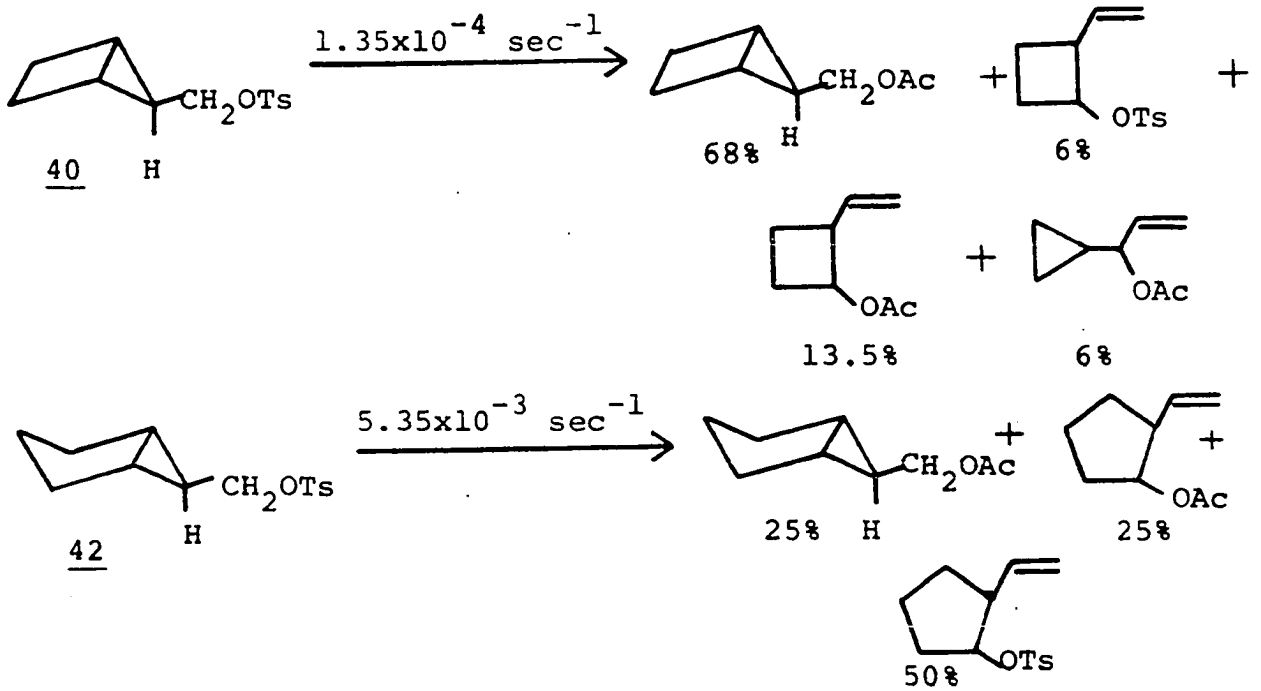
Bicyclo[2.1.0]pentyl and Related Cationic Intermediates

Cyclopropylcarbinyl and cyclobutyl derivatives have long been of interest because of their high solvolytic reactivity and the possibility that their solvolysis reactions might proceed through a common intermediate. In the first modern investigation of these systems Roberts and Mazur (65a) observed that the nitrous acid induced deamination of cyclopropylcarbinylamine and cyclobutylamine and also the solvolysis of the corresponding chlorides led to product mixtures consisting of similar proportions of cyclopropylcarbinyl, cyclobutyl and allylcarbinyl alcohols. An unusually high solvolytic reactivity was also noted for cyclopropylcarbinyl and cyclobutyl chloride which reacted 40 and 2 times as fast, respectively, as β-methallyl chloride. Subsequently, numerous investigations of these systems have been undertaken in an effort to determine the structures of the intermediate cations and the various factors which affect their stability and

control their rearrangements. Cyclopropylcarbinyl and cyclobutyl cations have recently been reviewed (65b). Several studies on bicyclo[2.1.0]pentanes and related compounds have provided important contributions to the understanding of cyclopropylcarbinyl and cyclobutyl derivatives in general and at the same time have revealed some interesting properties associated with strained σ bonds.

Wiberg and Ashe have studied the acetolysis and ethanolysis of endo- (39) and exo- (40) bicyclo[2.1.0]pentane-5-methyl tosylate (20,21) and endo- (41) and exo- (42) bicyclo-[3.1.0]hexyl-6-methyl tosylate (21,66). Product distributions and rates for the acetolysis at 17° are summarized below. The

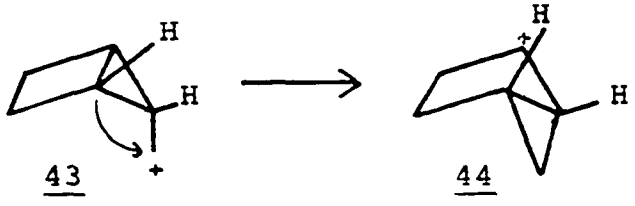




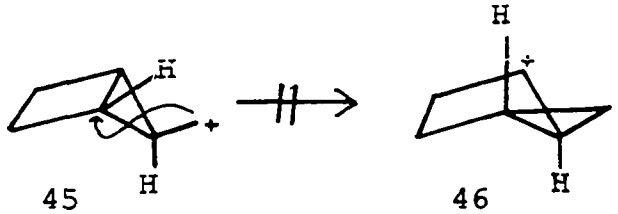
rates for the bicyclohexyl tosylates 41 and 42 were nearly independent of their stereochemistry and showed a normal rate enhancement (67) for 2,3-dialkylsubstitution in cyclopropylcarbinyl tosylates. The rates of the bicyclopentyl tosylates 39 and 40, though also independent of stereochemistry, were slower than the bicyclohexyl compounds by a factor of 40. Solvolysis in aqueous ethanol, a more nucleophilic solvent, led in each case to an increase in the parent alcohol at the expense of rearrangement products. These results were interpreted to mean that solvolysis proceeds in each case to initially give an ion which is structurally similar to the parent tosylate and which can then either be trapped by solvent to give parent alcohol or rearrange to a more stable ion. The decreased rates of solvolysis of 39 and 40 relative to 41 and 42 were consistent with earlier CNDO calculations

on the parent cyclopropylcarbinyl cation which predicted a decrease in the 1,2 and 1,3 bond orders and an increase in the 2,3 bond order relative to the hydrocarbon (68). Ionization of the bicyclopentanes and bicyclohexanes would lead to a shortening of and a strain increase in the 1,4 and 1,5 bonds respectively. The strain increase is less easily accommodated in the already highly strained 1,4 bond of the bicyclopentanes, and slower rates of ionization result. The pair of exo-tosylates, 41 and 43 gave analogous sets of products, consisting chiefly of parent acetates and cyclopropylcarbinyl-allylcarbinyl rearrangement products. The pair of endo-tosylates also gave analogous sets of products, but these differed significantly from the exo derived products by the presence of 2-northuganyl and 2-norcaranyl acetates from 40 and 42 respectively. Since these are (at least formally) cyclopropylcarbinyl-cyclopropylcarbinyl rearrangement products, the results might have an important bearing on the stereochemistry of the rearrangement. If it is assumed that 43, the ion initially formed from 39, rearranges to the 2-northuganyl ion 44 by attack of the positively changed carbon on the 1,4 bond, then attack must occur from the backside since the product contains cis-fused cyclopropane ring. The analogous process in 45, the ion initially formed from 40, would produce 46 which has a highly strained trans-fused cyclopropane ring

and is consequently not formed. More recently Wiberg and Szeimies (69) have argued that cyclopropylcarbinyl-cyclopropyl-



43 44

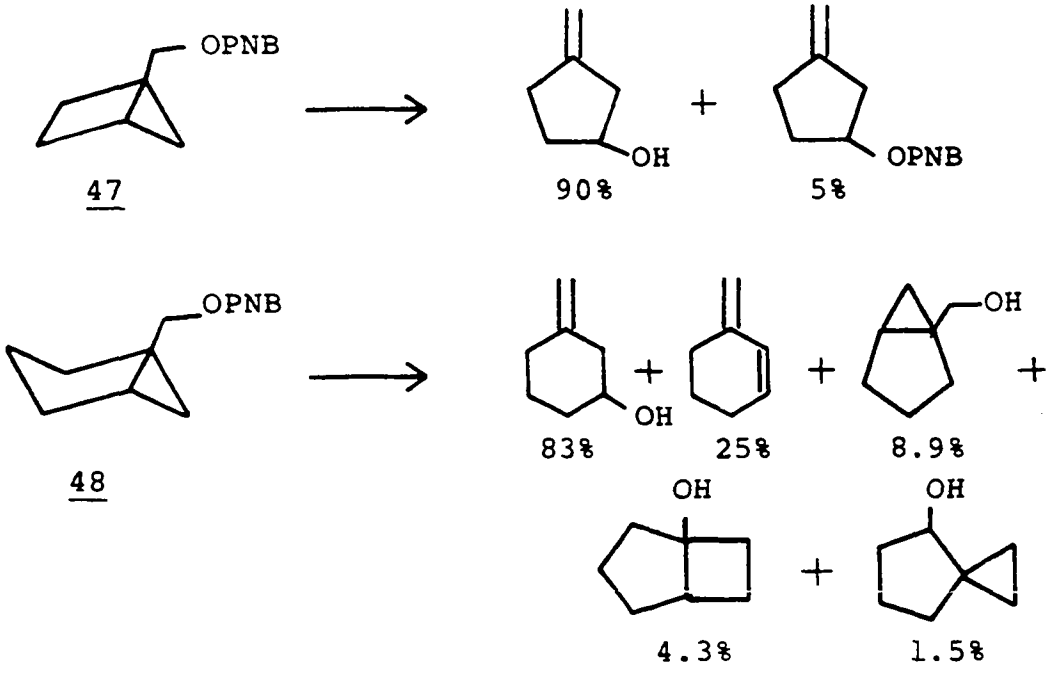


45 46

carbinyl rearrangements proceeding through intermediate puckered cyclobutyl cations should produce the same stereochemical results. Indeed CNDO calculations (69) on the parent cyclopropylcarbinyl cation indicate that this mode may be preferred to the direct pathway.

The solvolytic behavior of 40, 41, 42, and 43 stands in strong contrast to that of isomeric bicyclo[n.1.0]alkane-1-methanol derivatives. Dauben and Wiseman (9) have prepared bicyclo[2.1.0]pentane-1-methanol by lithium aluminum hydride reduction of 1-carbomethoxybicyclo[2.1.0]pentane which they had synthesized via the pyrazoline route. Attempted

preparation of the methanesulfonate ester gave chiefly 3-methylenecyclopentyl methanesulfonate and none of the bicyclic ester. The p-nitrobenzoate ester 47 was more stable and could be studied solvolytically. The solvolysis of 47 in 60% aqueous acetone at 100° proceeded at a rate some 400,000 times faster than that of cyclopropylmethyl p-nitrobenzoate and some 570 times as fast as the next higher homolog, bicyclo[3.1.0]-hexane-1-methyl p-nitrobenzoate (48) (70). The major products from 47 were 3-methylene-cyclopentanol and 3-methylenecyclopentyl p-nitrobenzoate. Small amounts of 2-methylenecyclopentanol and 1-hydroxymethylcyclopentene were also produced, but apparently were not primary products. Thus solvolysis of 48 proceeds exclusively through fragmentation of the 1,4 bond. Analogous behavior in a bicyclopentane bridgehead carbinyl cation has been observed by Kinstle et al. (10) in the acid catalyzed rearrangement of 3,3-dimethylbicyclo[2.1.0]pentane-1-methanol to 2,2-dimethyl-4-methylenecyclopentanol. By comparison, bridgehead bond fragmentation is the major but not the exclusive reaction pathway in the solvolysis of 48. Significant amounts of parent alcohol, cyclopropylcarbinyl-cyclobutyl and cyclopropylcarbinyl-cyclopropylcarbinyl rearrangement products are formed in addition to the major (81%) product, 3-methylenecyclohexanol.

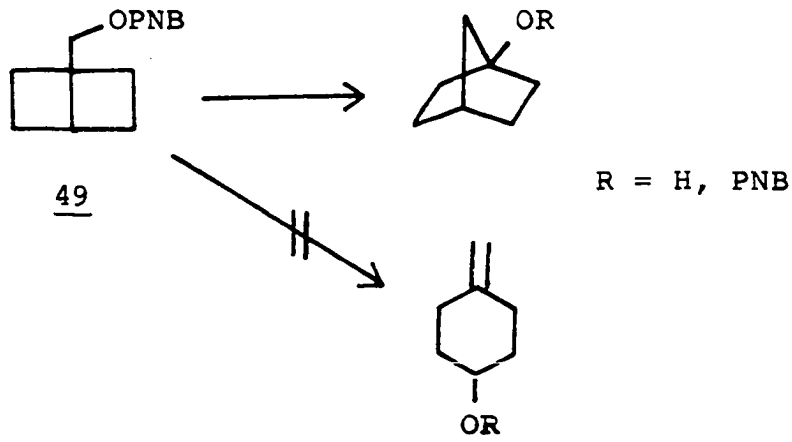


It seems clear that the differences in reactivity between 47 and 48 result almost entirely from the differences in their strain energies. Bicyclo[2.1.0]pentane has a strain energy of 53.6 kcal/mole (71) and methylenecyclopentane a strain energy of 6.3 kcal/mole (72). A reaction involving conversion of a bicyclo[2.1.0]pentane to a methylenecyclopentane would therefore release some 47 kcal/mole of strain energy. Alkyl-oxygen cleavage in 47 would be accompanied by an increase in length of the 1,4 and 1,5 bonds according to the CNDO model of the cyclopropylcarbinyl cation (68) discussed previously. A portion of the 47 kcal/mole of strain energy in the 1,4 bond would be released in the transition state and be available to assist ionization. By comparison, bicyclo[3.1.0]hexane has a strain energy of 33.9 kcal/mole and methylenecyclohexane a

strain energy of 1.9 kcal/mole, so that a reaction involving conversion of a bicyclohexane to a methlenecyclohexane would release only 32 kcal/mole of energy. Thus the smaller amount of potential strain release in 49 is reflected in a slower rates of ionization and rearrangement through other pathways in addition to bridgehead bond fragmentation. Bicyclo[1.1.0]-butane with a strain energy of 64 kcal/mole (67) is more highly strained than bicyclo[2.1.0]pentane, but conversion to a methylenecyclobutane would release only 38 kcal/mole (9). The solvolysis rate of bicyclo[1.1.0]butane-1-methyl p-nitro-benzoate (73) is intermediate between that of 47 and 48 and further supports the concept of strain assisted ionization.

An interesting comparison can be made between the solvolytic behavior of bicyclo[n.1.0]alkane-1-methyl deriva-tives, exemplified by 47 and 48, and that of bicyclo[n.m.o]-alkane-1-methyl derivatives where n≠m≠1 (no cyclopropane ring). The most striking example is that of bicyclo[2.2.0]hexane-1-methyl p-nitrobenzoate (49) (74), the most highly strained member of the series. Solvolysis of 49 (60% acetone, 100°) proceeds at about the same rate as bicyclo[1.1.0]butane-1-methyl p-nitrobenzoate or about 7×10^6 times as fast as the extrapolated rate for neopentyl p-nitrobenzoate and gives norbornanol derivatives as the only products. A mechanism involving ionization with assistance from the strained zero bridge bond was proposed. Conversion of 49 to norbornanol

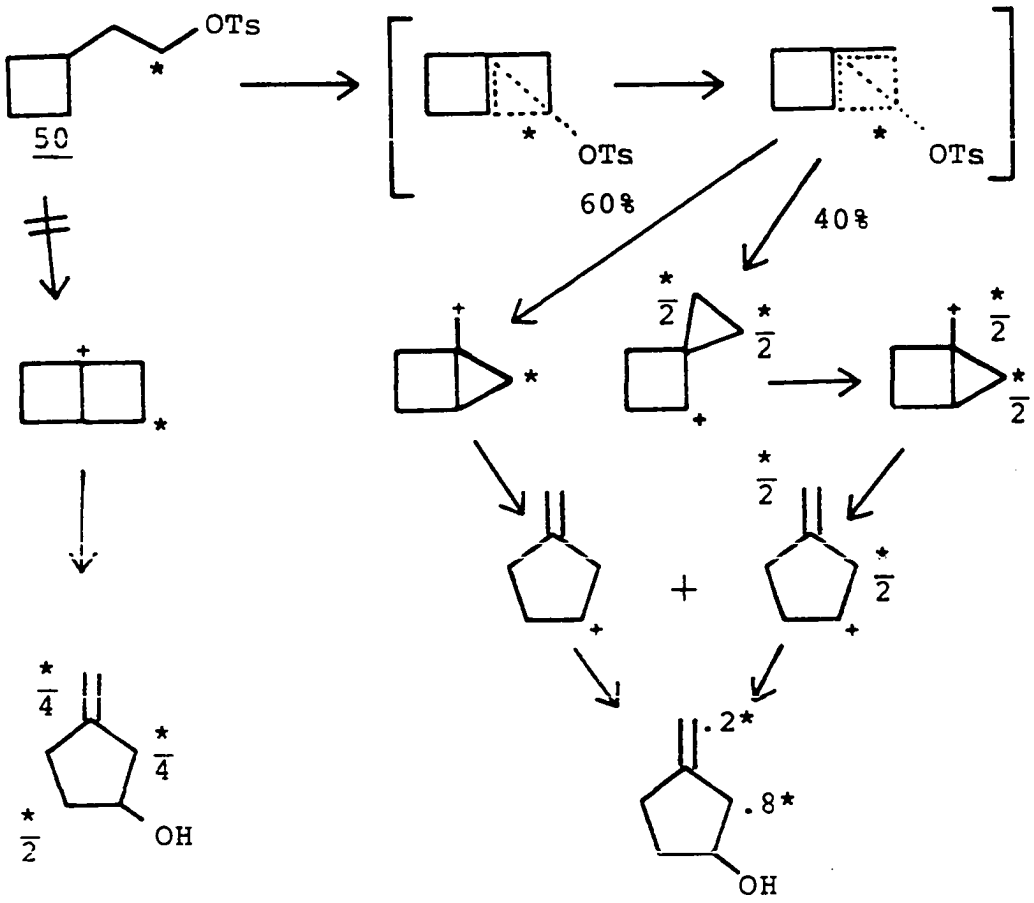
involves a strain release of ca-34 kcal/mole a portion of which would be available to assist ionization. Perhaps more interesting is the fact that 50 is not converted to 4-methylene-cyclohexanol via fragmentation of the zero bridge bond, despite the fact that such a process would release approximately 50 kcal/mole or 16 kcal/mole more than is available from rearrangement to the norbornane ring system. Apparently fragmentation is an exclusive property of cyclopropane rings which results from their unique electronic properties.



49

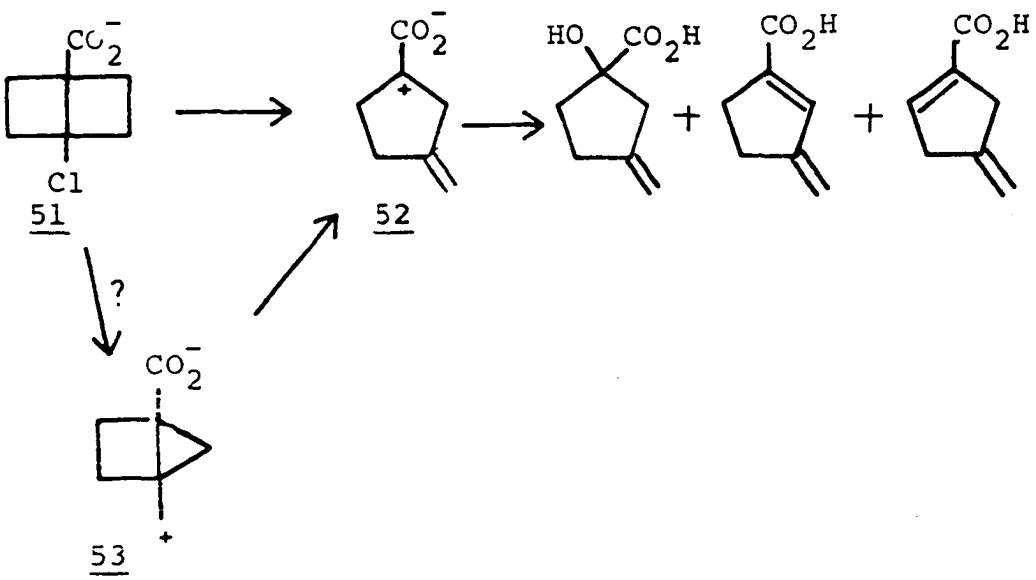
Bicyclo[2.1.0]pentane-1-methyl cations (or nonclassical analogs) may be involved in two rearrangement reactions. Wiberg and Hiatt (75) have found that the solvolysis of 2-(Δ^1cyclobutenyl)ethyl tosylate (50) gives a product mixture very similar to that obtained from 47. Under certain conditions small amounts of spiro[2.3]hexyl-4 derivatives were also found among the solvolysis products. The solvolysis of

deuterium labeled 50 gave 3-methylenecyclopentanol with a deuterium distribution consistent with 60% of the reactant going directly to the bicyclo[2.1.0]-pentane-1-methyl cation and 40% going to the spiro[2.3]hexyl-4 cation, which then gives the other ion. The results of the deuterium labeling



experiment completely ruled out any involvement of a classical bicyclo[2.2.0]hexyl-1-cation which might have been expected by

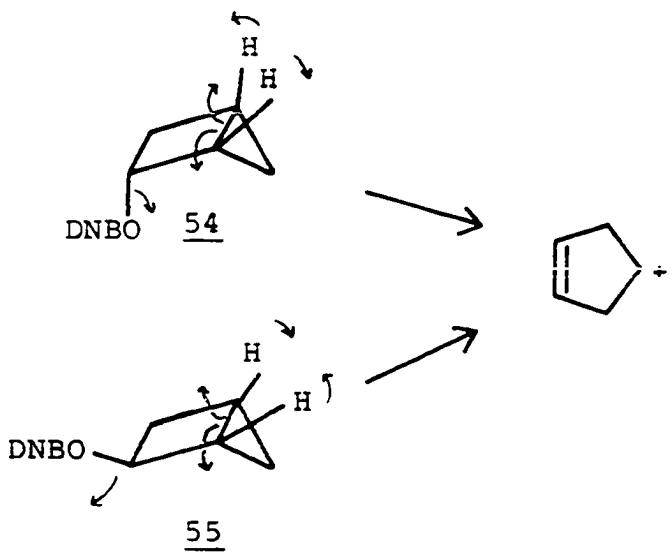
analogy with 2-(Δ^1-cyclopentenyl) ethyl tosylate. The latter gives bicyclo[3.2.0]heptan-1-ol as a major solvolysis product (67). However, evidence exists that at least one bicyclo-[2.2.0]hexyl-1-cation may rearrange via a bicyclo[2.1.0]pentane-1-methyl cation intermediate. Scherer and Katsumoto (76) have reported that the solvolysis of 51 gives products formally derived from the 3-methylene cyclopentyl cation 52 which in turn suggests the possible intermediary of the bicyclopentane cation 53. The authors favored a delocalized intermediate



over the classical ion 53 since a bicyclo[2.1.0]pentane was not among the observed products. The high reactivity observed for 48, however, makes it now seem likely that 53, if formed, would rearrange to 52 before trapping could occur.

Wiberg et al. (15,16) have generated the bicyclo[2.1.0]-pentyl 2-cation from the solvolysis of endo- (54) and exo- (55)

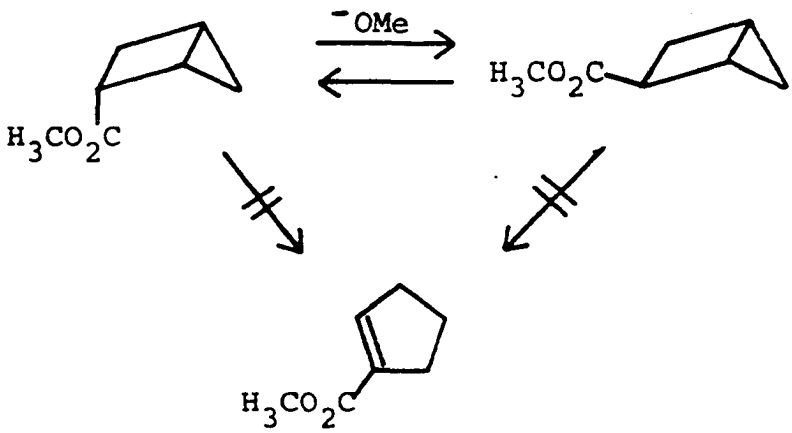
bicyclo[2.1.0]pentyl 2-dinitrobenzoate. These systems are rather unusual since alkyl oxygen cleavage leads to an intermediate which is simultaneously a cyclobutyl and a cyclopropylcarbinyl cation. Both 54 and 55 gave 3-cyclopenten-1-ol derivatives as the only solvolysis products, but the solvolysis rates showed a marked dependence on stereochemistry. The exo-isomer had a reactivity typical of a secondary cyclopropylcarbinyl derivative, but the endo-isomer was more reactive by a factor of 10^7. These results were particularly intriguing since the overall strain release in each reaction would be essentially the same. The suggestion that ring opening in cyclobutyl cations might require a specific mode of orbital motion similar to that required by cyclopropanes had been made earlier by DePuy (41). In explaining the behavior of 54 and 55, Wiberg proposed that maximum overlap between the



developing empty p orbital and the orbitals of the bond being broken is required for a concerted accelerated solvolysis of a cyclobutyl derivative. The required orbital motion in 54 leads to a decrease in strain resulting in an accelerated rate, while the opposite motion required of 55 leads to a small strain increase resulting from increased nonbonded interactions of the bridgehead hydrogens, and no acceleration occurs. That the cyclobutane bond which is broken in 54 and 55 is also common to a cyclopropane ring is incidental since large endo/exo rate ratios are also observed for the corresponding bicyclo[m.2.0]alkyl derivatives (m>2) (16). In these systems the endo/exo rate ratio falls off rapidly as m increases resulting in decreased strain and decreased repulsion of bridgehead protons in the transition states derived from the exo-isomers.

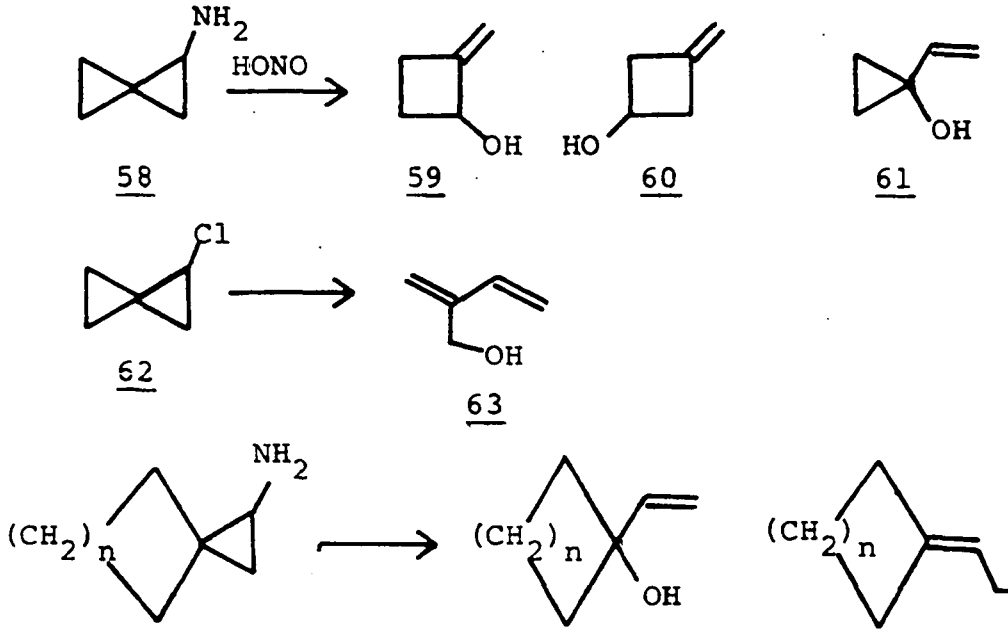
In contrast to the facile ring opening of the bicyclo-[2.1.0]pentyl 2-cation, the anions generated from isomeric 2-carbomethoxybicyclo[2.1.0]pentanes show no tendency to rearrange. Brook and Brophy (77,78) attributed this to the stabilization of the anion by the carbomethoxyl and to the fact that the transition state for the rearrangement would resemble the antiaromatic bishomocyclopropenyl anion.

The bicyclo[2.1.0]pentyl 1-cation (56) has recently received much attention in connection with its possible intermediacy in the rearrangement of the spiropentyl cation

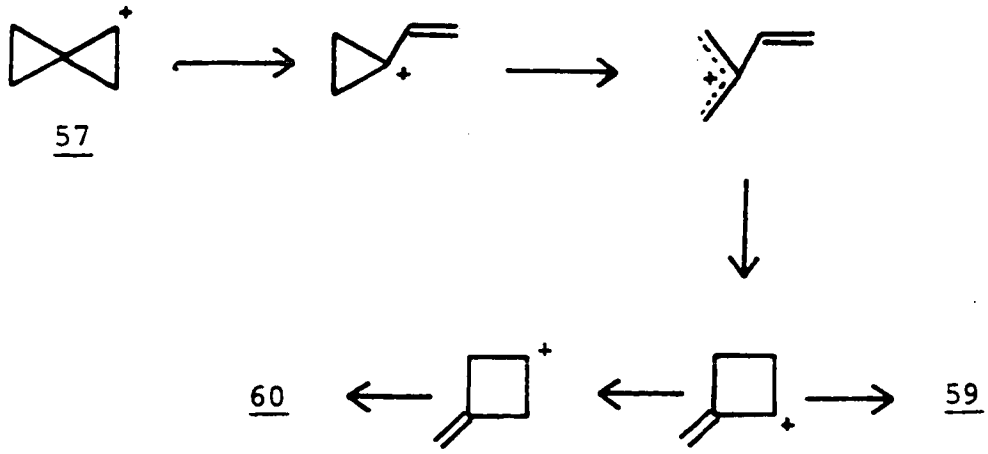


(57). The latter ion is of interest because it is both a cyclopropyl and a cyclopropylcarbinyl cation and because the geometrical constraints imposed by the spiropentane ring system should provide information about the geometrical requirements for cyclopropylcarbinyl interactions. The deamination of spiropentyl amine (58) was reported by Applequist and Fanta (79) in 1960 to give 2- and 3-methylene-cyclobutanol, 59 and 60 as the major products. The reaction was later reinvestigated by Konzelman and Conley (80) who also detected small amounts of the cyclopropyl ring opening compound, 1-vinylcyclopropanol (61) among the reaction products. The hydrolysis of spiropentyl chloride (62) on the other hand, gave only 2-hydroxymethylbutadiene (63), which could easily be accounted for by a mechanism involving two successive or simultaneous ring openings of cyclopropyl cations (81). Likewise, the deamination of spirocyclopropyl

amines in which the adjacent spiro ring was larger than cyclopropyl gave chiefly cyclopropyl ring opening products (80).

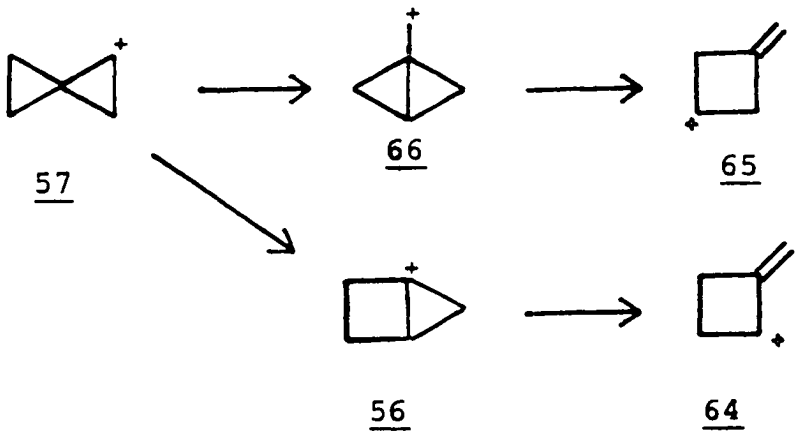


Two fundamentally different mechanisms were proposed to account for the methylenecyclobutanols from 58. One possibility suggested by Applequist and Fanta (79) amounted to an extension of the solvolysis mechanism for 62 with an added ring closure of the isopropenyl cation to the allylic cation 64 to account for 59 and a rearrangement of 64 to 65 to account for 60 (Scheme 2). The unusual measure of stability implied by this mechanism for 65 relative to 64 is in disagreement with the kinetic data of Kiefer and Roberts (82) and also with recent observations of Applequist et al. (83) who generated 64 solvolytically from 2-methylenecyclobutyl chloride and found no products derived from 65.



Scheme 4

The second mechanism, shown in Scheme 5, was proposed by Konzelman and Conley (80) and embodied parts of alternative mechanisms suggested by Applequist and Fanta (79) and Kiefer and Roberts (82). This mechanism differs from the first in that the initial rearrangements of the spiropentyl cation (57) to the bicyclo[2.1.0]pentane-1-cation (56) and the bicyclo-[1.1.0]butane bridgehead carbinyl cation (66) are rearrangements typical of cyclopropylcarbinyl cations and not cyclopropyl cations. However, the solvolysis rate of 62 (84) was only slightly faster than that of cyclopropyl chloride, suggesting little cyclopropylcarbinyl interaction in 57. In order to distinguish the two possibilities Applequist and co-workers (83) prepared and deaminated a deuterium labeled spiropentyl amine. The deuterium distribution in the methylene cyclobutanols was completely inconsistent with Scheme 4 but

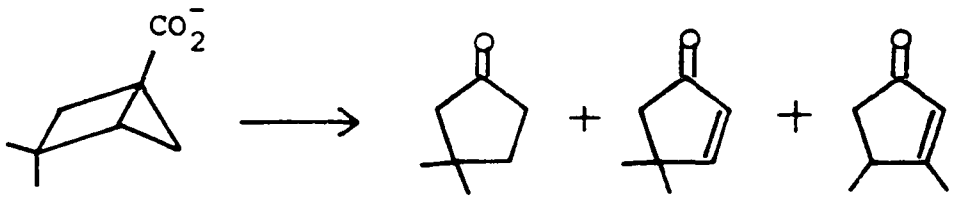


Scheme 5

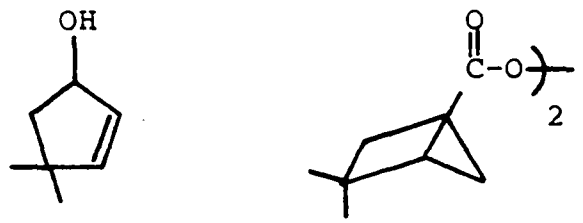
was consistent with Scheme 5 if rearrangement of the spiropentyl cation occurred before symmetrical solvation was achieved.

Kinstle et al. (85) and Welch (11) approached the question of an intermediate bicyclopentane bridgehead cation in the reaction by attempting to generate the 3,3-dimethylbicyclo-[2.1.0]pentyl 1-cation (67) directly. Electrolysis of the bridgehead carboxylate anion 68 at a carbon anode, a condition known to produce carbonium ion rather than radical intermediates (86,87,88,89,90,91,92), gave ketones 69, 70, and 71 and no products analogous to those obtained from the deamination of spiropentyl amine. Although it was not detected among the electrolysis products, alcohol 72 was postulated as the primary product and in an independent experiment was shown to give ketones 69, 70, and 71 under the

electrolysis conditions. The possibility that the ketones might be arising from a bridgehead radical intermediate was considered unlikely since no rearranged products were detected in the pyrolysis of diacylperoxide 73. Although the formation of 72 from the bridgehead cation 67 could not be rationalized



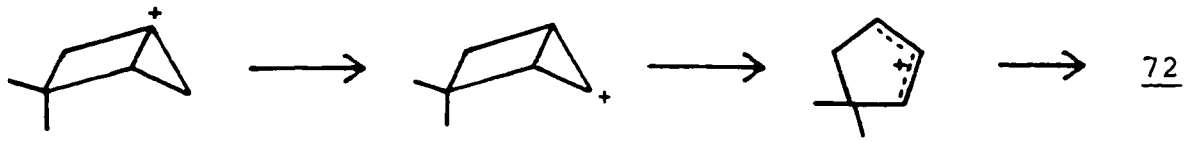
68 69 70 71



72 73

in terms of any initial rearrangement of 67 known to be characteristic of either a cyclopropyl or a cyclobutyl cation, the high degree of strain in the system might result in exceptional behavior. One mechanism which was considered (but not proven) involved a C-5 to C-1 hydride shift in 67 followed by or in concert with cyclopropyl cation ring opening and then solvent trapping (Scheme 6). The failure to observe methylenecyclolutanols (or products derived from them) in the electrolysis of 68 was interpreted (11) to mean that 56 is

probably not an intermediate in the rearrangement of 57, although this conclusion was somewhat weakened by the fact that the method of generating the cations had not been the same.



67 72

Scheme 6

RESULTS AND DISCUSSION

Halocarbene Additions to Cyclobutenes

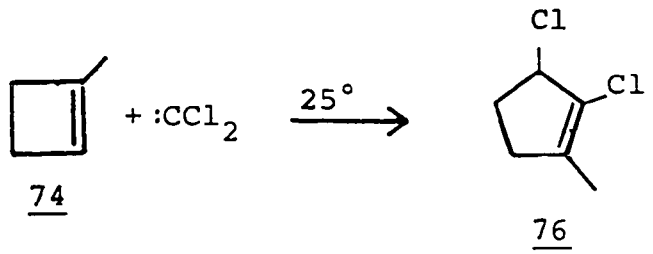
Dihalocyclopropanes are exceedingly versatile compounds which have been found to undergo a variety of reactions of both synthetic and theoretical importance. Several examples of these including reduction to cyclopropanes, dehydrohalogenation to (intermediate) cyclopropenes, and reductive elimination to cyclopropylidine-like intermediates have been recently reviewed (93). Several bicyclic dihalocyclopropanes, have proven especially interesting and useful, as for example in conversions to novel bicyclic olefins, cyclic allenes, and tricyclic alkanes. Compounds in this series, of which the lowest known members are bicyclo[3.1.0]hexanes, generally exhibit a strong behavioral dependence on ring size under a given set of reaction conditions. We became interested in extending the series to include the 5,5-dihalobicyclo[2.1.0]pentanes in order to explore the synthetic potential of these compounds in conversions to other bicyclopentanes and to generally compare their reactivity with less strained members of the series. Of special interest was the gas phase thermolysis of a 5,5-diflurobicyclopentane. Pyrolysis of bicyclopentane at temperatures near 300° gives cyclopentenes as the major product (94). This reaction is generally believed to proceed through homolysis of the bicyclopentane 1,4-bond to give a

1,3-diradical followed by a hydrogen atom migration to one of the radical sites, probably a 1,2-shift from C-5. Consistent with this view is the more recent observation that other substituents on C-5, notably ethoxylcarbonyl (94) and acetyl (95) can also migrate. We wondered whether a fluorine atom migration, a rarely observed phenomenon, would be observed during the pyrolysis of a 5,5-diflurobicyclopentane.

The rapid progress in the area of dihalocyclopropane chemistry has paralleled the development of dihalomethylene transfer agents, and the addition of halocarbene or carbenoid species to olefins remains by far the method of choice for preparing these compounds. Despite a multitude of reports over the last 17 years concerning the addition of halocarbenes to cyclic olefins of all descriptions and the obvious potential of the method for synthesis of the potentially useful and interesting 5-halobicyclopentanes, the addition of halogenated carbenes to cyclobutenes had been almost completely ignored until this work was initiated in 1967. The brief mention by Vogel (23) in 1963 that the addition of dichlorocarbene to cyclobutene produces the ring expansion product 2,3-dichlorocyclopentene had not been accompanied by experimental details and did not rule out the possibility that a 5,5-dichlorobicyclo[2.1.0]pentane might be isolable under suitable conditions. Our own study was initiated with the reaction of dichlorocarbene and 1-methylcyclobutene (74). 1-Methylcyclobutene, in addition to being more easily prepared (96) and

handled than the parent olefin, offered the methyl substituent as a useful spectral label. The methyl group of 1-methyl-5,5-dichlorobicyclo[2.1.0]pentane (75), the product hoped for, would be expected to appear in the nmr spectrum as a singlet between δ1.0 and δ1.5 and be the highest field resonance in spectra of potential mixtures containing 75, thereby offering nmr as a method of detecting the bicyclopentane in early stages of the reaction or workup. Methyltrichloroacetate and sodium methoxide generated in situ from sodium hydride and methanol was employed as the source of dichlorocarbene (59). In a typical experiment, a suspension of sodium hydride (1 equiv) in a solution of the olefin (2 equiv) and methyltrichloroacetate (1 equiv) was treated with a 10% excess of methanol gradually introduced over 4 hr at temperatures near 25°. Spectra (nmr) of the crude reaction mixture recorded at intervals over the reaction period, though heavily dominated by absorptions of the reactants and by-products of the carbene precursor (chloroform and dimethylcarbonate), clearly did not contain the expected methyl singlet above δ1.5. Thus the dichlorobicyclopentane could not be detected as a stable entity during even the early stages of the reaction. Major product absorptions were visible at δ1.8 (broadened or perturbed singlet) and at δ4.7 (complex multiplet) along with some very minor resonances between δ5.0 and δ6.3.

The volatile components of the reaction mixture were removed and trapped by low temperature (Ca. 35°) bulb to bulb distillation leaving a substantial tary residue. After removal of starting materials and by-products from the volatile fraction there remained less than 19% of the theoretical quantity (1/1 addition) of a very labile material which appeared by nmr analysis to be a mixture with one major component and an undetermined number of minor components. All attempts to separate and analyze this mixture by vpc techniques resulted in complete destruction of the major and most of the minor components as indicated by comparing the nmr spectrum of the collected effluent with that of the mixture before chromatography. These results were not unexpected since samples of this material had undergone complete decomposition to tar within a few days at room temperature and within a few minutes at 80°. Likewise, contact of this material with silica gel resulted in an almost instantaneous conversion to tar accompanied by evolution of a pungent, fuming gas, apparently hydrogen chloride. Although its lability made it impossible to obtain an analytically pure specimen, the major product was eventually isolated in a reasonably pure state by low temperature fractionation techniques. Fractionation was continued until no appreciable changes were observed in nmr spectra of successive fractions. The compound so isolated was assigned the structure 1-methyl-2,3-dichlorocyclopentene (76)



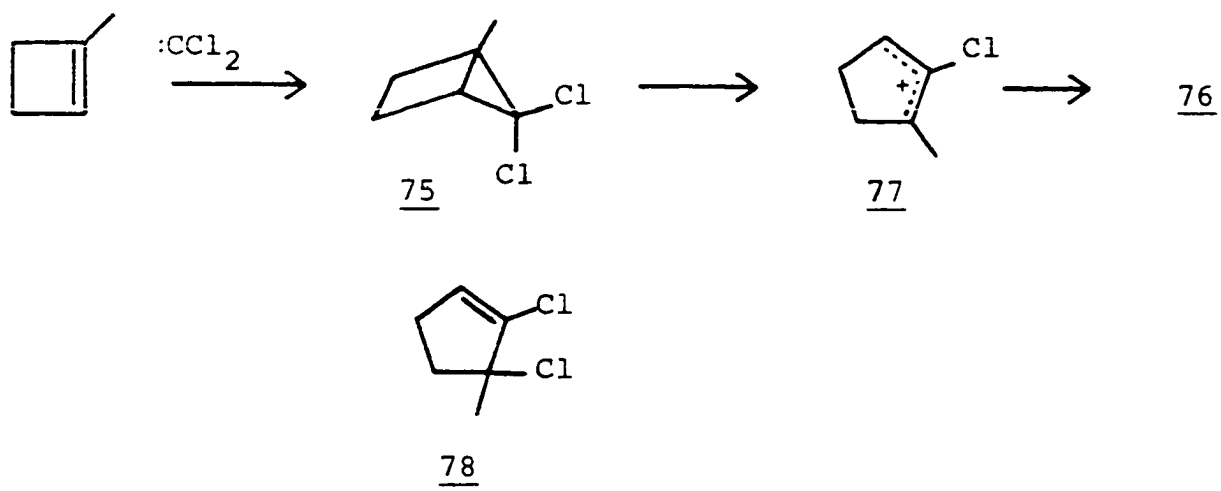
74 76

on the basis of its spectral data. The mass spectrum of 76 contains weak molecular ions at m/e 150, 152, and 154 in the required abundance ratio and a base peak at m/e 79 corresponding to the loss of one hydrogen and two chlorine atoms from the molecular ion. The nmr spectrum of 76 is shown in Figure 1 with assignments as follows: δ1.8, perturbed singlet, methyl; δ2.4, complex multiplet, ring methylenes; δ4.8, complex multiplet, allylic methine. Additional support for this assignment comes from comparisons with model compounds discussed below. The thermal instability of 76 is also consistent with its structure since the related compound, 3-chlorocyclopentene is itself very unstable, decomposing to tars within a few hours at room temperature (97). It seems likely that the tars formed in this reaction arise largely from the decomposition of 76, although the stability of 76 under the reaction conditions was not explicitly examined.

The nature and origin of the minor components characterized chiefly by complex absorptions extending from δ5.0 to δ6.3 in

the nmr spectrum of the crude mixture remains undetermined. However the amounts of these compounds appeared to increase during the isolation procedure suggesting that they are not primary products.

The formation of 76 in the reaction of dichlorocarbene with 74 is clearly analogous to the formation of 2,3-dichlorocyclopentene in the addition of dichlorocarbene to cyclobutene (23) and can best be explained in terms of an electrocyclic ring expansion of an intermediate bicyclopentane as shown in Scheme 7. It can be assumed that dichlorocarbene attacks the olefin to generate the bicyclopentane (75) which is thermally unstable and rapidly undergoes the type of ring expansion characteristic of bicyclic halocyclopropanes. Orbital symmetry and proven analogies in homologous compounds require



Scheme 7

that the endo-chlorine be the leaving group. Chloride ionization and synchronous disrotatory opening of the 1,4-bond presumably leads to the allylic ion pair 77, which collapses to the observed product 76. The overall strain release in the conversion of a bicyclopentane to a cyclopentene is approximately 47 kcal/mole making the 75→77 conversion very favorable thermodynamically. Nevertheless, pyrolytic transformations of bicyclopentanes to cyclopentenes usually require temperatures near 300°. That 75 readily rearranges at 25° and undoubtedly at much lower temperatures must be attributed almost entirely to the fact that chloride ionization and rupture of the highly strained 1,4 bond is a synchronous process leading to a transition state in which considerable strain has already been relieved. A secondary factor affecting the stability of 75 would be the stability of the intermediate cation 77 (which the transition state resembles). It is probable that the methyl substituent, by providing additional stabilization in the intermediate 77 would make 75 slightly less thermally stable than the parent dichlorocompound 7. However, the extent to which the structures of the intermediate carbonium ions contribute to the differences in stability between 75 and its higher homologues cannot easily be evaluated since stabilities of cyclic allylic cations as a function of ring size are not known.

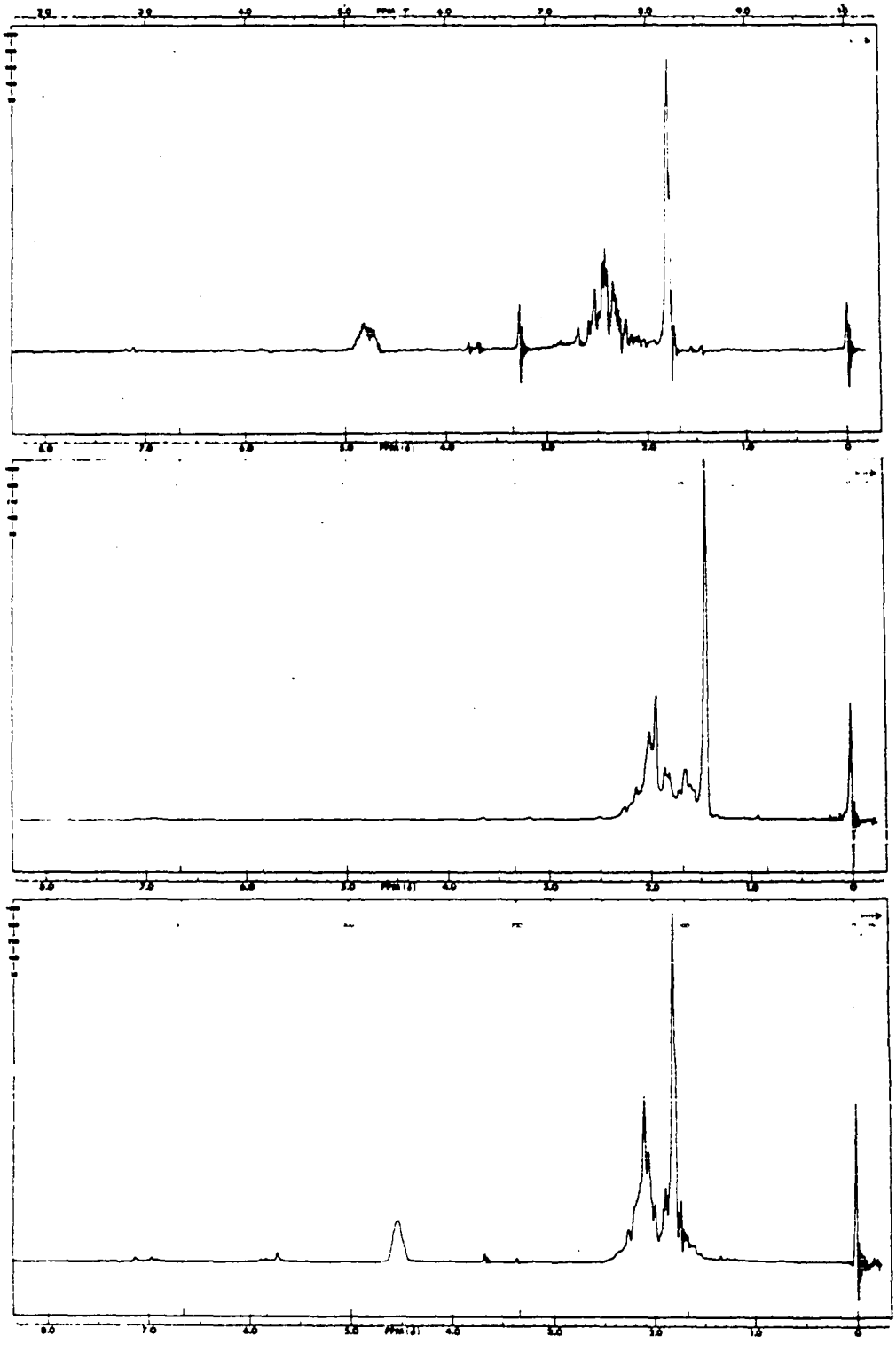
A result which has yet to be explained is the absence of the isomeric rearrangement product 78 as a major product of this reaction. Indeed 78 may have been completely absent, but its presence in the reaction mixture in quantities up to 10% that of 76 was not excluded by nmr data. It would be expected that collapse of the ion pair 77 would give a mixture of 76 and 78; moreover, the higher charge density at the allylic carbon bearing the methyl substituent might favor collapse to 78. Of the two isomers, 76 should be more stable thermodynamically since it contains the combination of a more highly alkylated double bond and a less reactive secondary allylic chlorine. If 78 is formed initially, it is possible that it isomerizes to 76 or is otherwise destroyed under the reaction conditions. The ease with which 76 decomposes to tar suggests the possibility of a similar and possibly more rapid fate for 78. On the other hand it is possible that unknown factors cause 75 to rearrange exclusively to 76.

In order to shed more light on this matter the homologous model compound 6,6-dichloro-1-methylbicyclo[3.1.0]hexane (79) was prepared and its thermal rearrangement studied. The synthesis of 79, whose nmr spectrum is shown in Figure 2, was readily accomplished by the addition of dichlorocarbene to 1-methylcyclopentene. It is known that 6,6-dichlorobicyclo-[3.1.0]hexane is completely rearranged to 2,3-dichlorocyclohexene after 90 minutes at 170° (55). As would be anticipated

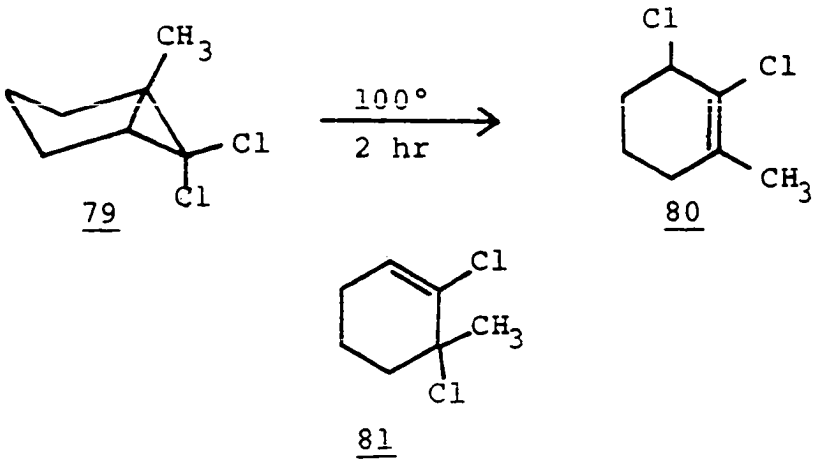
Figure 1. 60 MHz nmr spectrum of 1-methyl-2,3-dichlorocyclopentene (76)

Figure 2. 60 MHz nmr spectrum of 1-methyl-6,6-dichlorobicyclo[3.1.0]hexane (79)

Figure 3. 60 MHz nmr spectrum taken after heating 79 at 100° for 120 minutes; the major product is 1-methyl-2,3-dichlorocyclohexene (80)



with the potential stabilizing influence of the methyl substituent in an ionic transition state, 79 rearranges at a faster rate. A neat sample of 79 was heated at 100° in the probe of an nmr spectrometer. Over a period of 120 minutes the spectrum of 79 was gradually replaced by the spectrum shown in Figure 3. Analysis of the pyrolysate by vpc gave ambiguous results because of partial decomposition of the product in the chromatograph. However, the nmr spectrum of the pyrolysate could not be appreciably altered by low temperature fractionation. The integration of the spectrum is consistent with the pyrolysate being at least 90% of a single component assigned the structure 1-methyl-2,3-dichlorocyclohexene (80). The mass spectrum of 80 contains a base peak at m/e 93 corresponding to the loss one hydrogen and two chlorines from the molecular ion which is not observed. The chemical shifts of 80 agree closely with the analogous shift reported for 2,3-dichlorocyclohexene (55). The position of the allylic methine resonance at δ4.53 clearly distinguishes 80 from the



79 80 81

alternative rearrangement product 81. However, minor resonances at δ1.7 and 5.75 in the nmr spectrum of the pyrolysate may arise from the methyl and olefinic protons of 81 respectively. Alternatively, these signals may arise from a small amount of a cyclohexadiene formed in an elimination reaction. Thus the results of this experiment are consistent with but do not demand a high degree of specificity in the initial ring expansion isomerization of 79. The possibility that 81 is formed initially and then suffers a rapid and virtually irreversible rearrangement to 80, the thermodynamically more stable isomer, cannot be ruled out. Whatever the details may be, the thermal behavior of 79 suggests that the apparent specificity in the rearrangement of 75 is not exceptional.

It has been demonstrated repeatedly that bicyclic halocyclopropanes with endo-fluorine substituents are appreciably more stable thermally than the corresponding chlorides or bromides. An endo-fluorine substituent would therefore be expected to provide maximum stabilization for a 5,5-dihalobicyclopentane. We were especially interested in a 5,5-difluorobicyclopentane for some pyrolysis studies mentioned above and therefore turned our attention to potential sources of difluorocarbene. There are few synthetically useful difluorocarbene precursors and practically none of these can be employed at low temperatures. The thermal decomposition of

difluorodiazerine in the presence of olefins gives good yields of cyclopropanes, but only at temperatures near 160° (98). The photolytic decomposition of the same reagent at 25° also gives cyclopropanes, but yields are low even for activated olefins (98). Furthermore this precursor is not commercially available and its synthesis (99) is both difficult and hazardous without special equipment. Perhaps the most generally useful difluorocarbene transfer reagent presently available is trimethyl(trifluoromethyl)tin developed by Seyferth and co-workers (100). Difluoronorcarane for example is obtained in 89% yield upon heating equimolar quantities of the tin reagent and sodium iodide in the presence of a slight excess of cyclohexene in dimethoxyethane at 80° for 20 hr.

We have investigated the reaction of difluorocarbene prepared from trimethyl(trifluoromethyl)tin with 1,2-dimethylcyclobutene (82) (101) at somewhat lower temperatures than are normally employed in order to minimize the chance for thermal rearrangements. The reaction was followed by nmr spectroscopy in an effort to detect the potentially unstable difluorobicyclopentane and at the same time determine the extent of reaction by observing the conversion of trimethyl-(trifluoromethyl)tin (singlet, δ0.4) to trimethyltin iodide (singlet, δ0.9). Decomposition of trimethyl(trifluoromethyl)-tin was 60% complete after 21 hr at 50° and 85% complete after an additional 12 hr at 62-68°. Essentially all of the

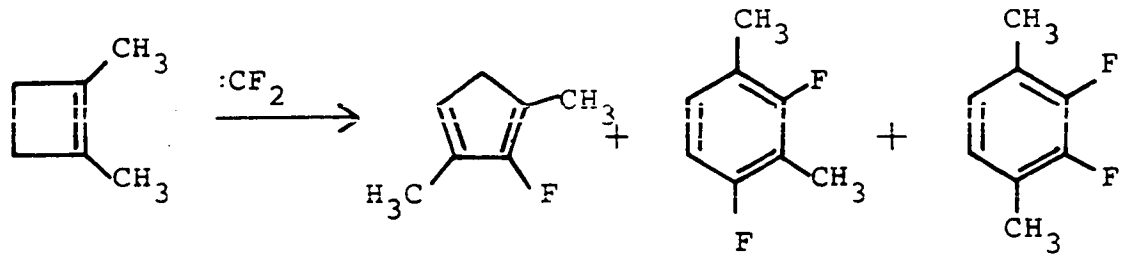
resonances in the nmr spectra of the crude mixture could be assigned to starting materials or products which were later identified. No signals assignable to a bicyclopentane were observed at any time during the reaction period.

After passing gaseous ammonia through the reaction mixture to convert trimethyltin iodide to its nonvolatile ammoniate, the volatile components of the mixture were removed under reduced pressure and then subjected to vpc analysis. Five products A, B, C, D, and E in order of increasing retention time and in respective area ratios of 106 : 54.5 : 10 : 16.8 : 2.9 were detected. The three major components A, B, and D were collected for spectral analysis.

Component A had a mass spectral molecular weight of 112 and an nmr spectrum (Figure 4) consisting of a six proton doublet at δ 1.9, a two proton multiplet at δ 2.6 and a one proton multiplet at δ 5.7. The compound was reasonably stable as a dilute solution in carbon tetrachloride but rapidly dimerized when collected as a neat liquid at room temperature. The data permit a resonable assignment of A as a cyclopentadiene with a fluorine and two methyl substituents on the olefinic carbons. Although the nmr spectrum does not clearly establish the specific substitution pattern, structure 83 is the most likely choice for reasons which will become apparent.

Components B and D were identified as isomeric difluoroxylenes on the basis of their nmr and mass spectra. Each had

a mass spectral molecular weight of 142. The pmr spectrum of B shown in Figure 5 indicated a completely unsymmetrical substitution pattern as did its fmr spectrum which revealed two nonequivalent fluorines. A highly symmetrical substitution pattern for D on the other hand was indicated by the chemical shift equivalence of the six methyl protons and both ring protons (comparison of 50 and 100 MHz pmr spectra) as well as both fluorines. The 60 MHz pmr spectrum of D is shown in Figure 6. A more detailed analysis of the nmr spectra of B and D along with consideration of the most probable pathway for their formation suggested structures 84 and 85 for B and D respectively. These assignments were confirmed by comparing



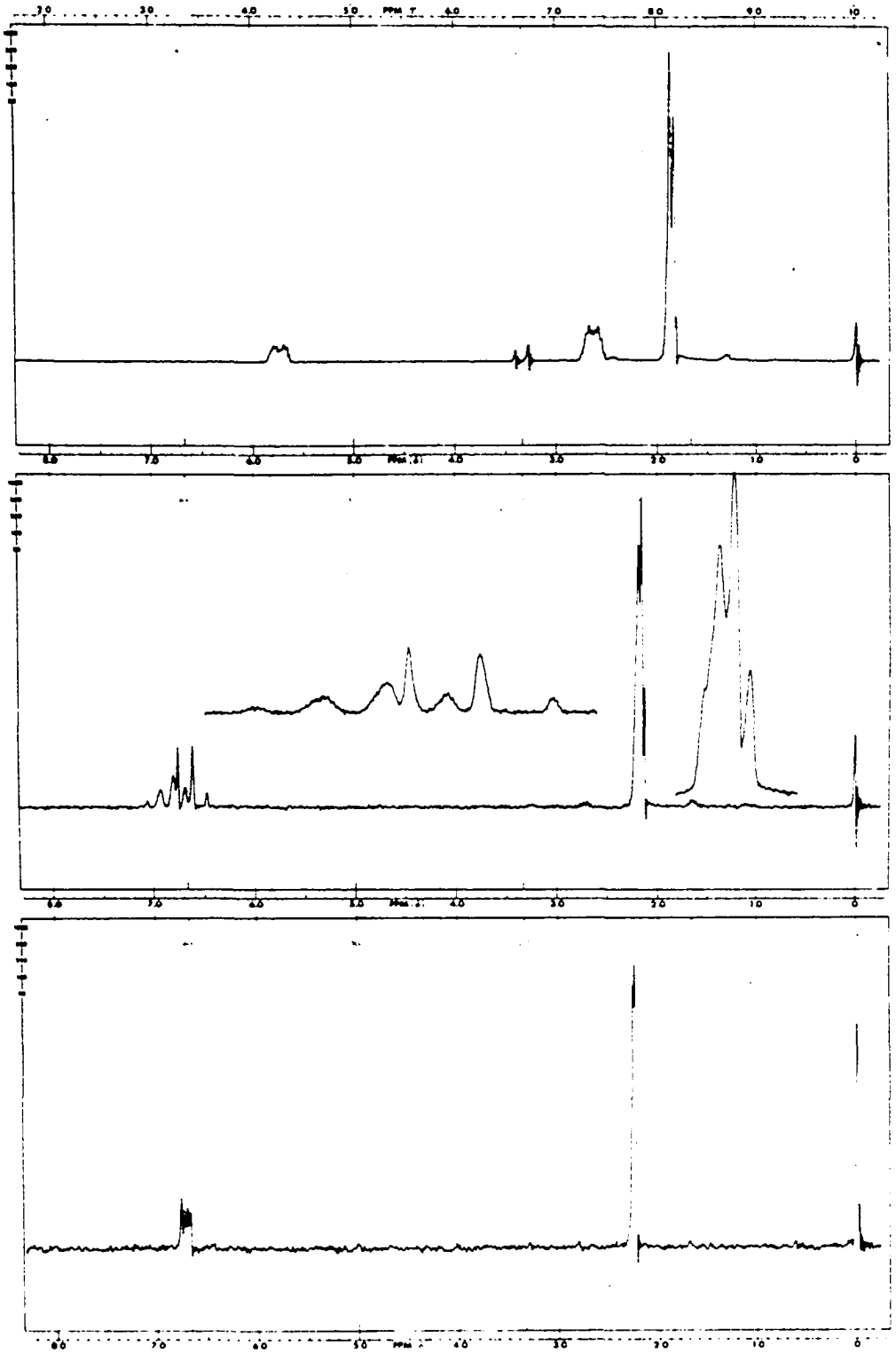
82 83 84 85

the spectral properties of B and D with those of authentic specimens of 84 and 85 prepared by unambiguous independent routes.

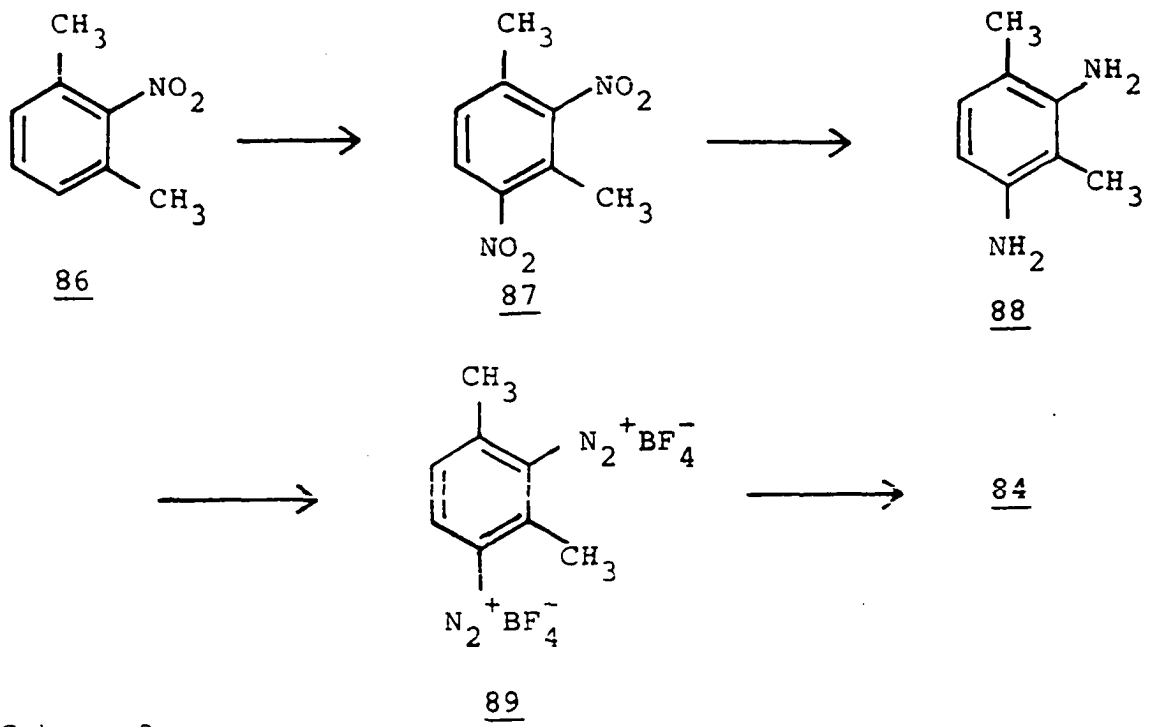
Figure 4. 60 MHz pmr spectrum of 1,3-dimethyl-2-fluoro-1,3-cyclopentadiene (83)

Figure 5. 60 MHz pmr spectrum of 2,4-difluoro-m-xylene (84)

Figure 6. 60 MHz pmr spectrum of 2,3-difluoro-p-xylene (85)



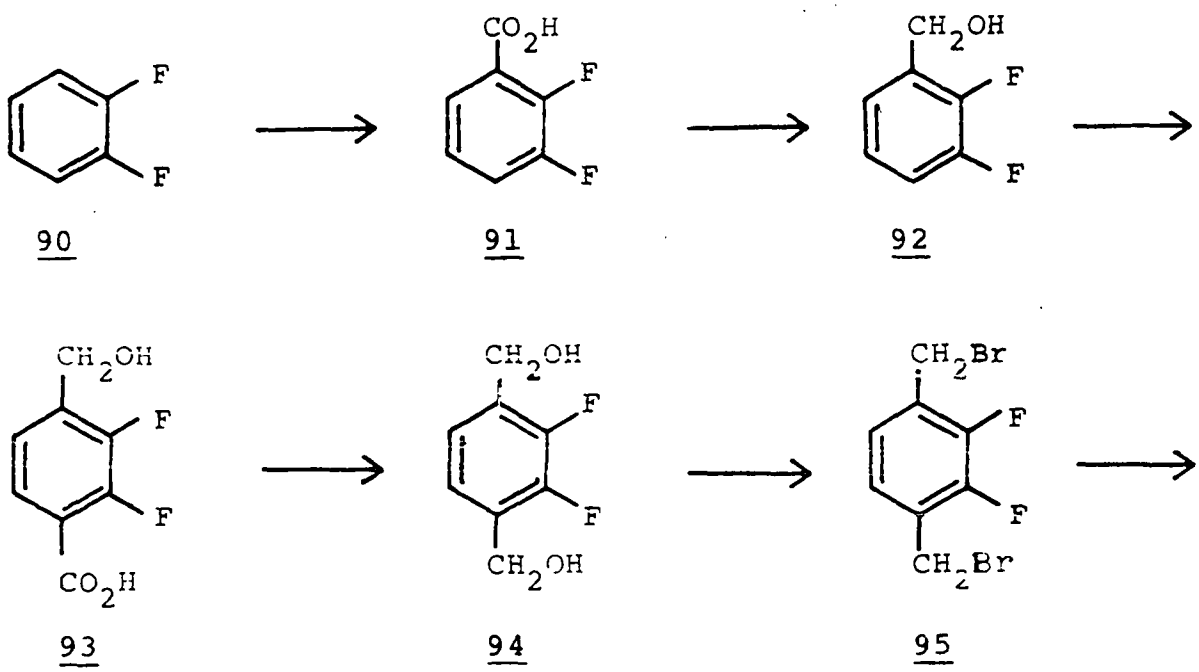
The synthesis of 84 (Scheme 8) was accomplished in four steps starting with commercially available 2-nitro-m-xylene (86). Mononitration of 86 (102) gave 2,4-dinitro-m-xylene (87) which was reduced to the previously known (103) diamine 88; the structure of 88 was confirmed by its nmr spectrum. Diazotization of 88 produced the bis-diazonium fluoroborate 89 which on pyrolysis afforded authentic 84.



Scheme 8

An attempted synthesis of 85 by an analogous route involving 2,3-diamino-p-xylene was unsuccessful, apparently failing at the diazotization step. A synthesis which did provide an authentic specimen of 85 is outlined in Scheme 9.

Gilman and Soddy (104) have shown that metalation of fluorobenzenes with n-butyl lithium followed by carbonation produces only the o-fluorobenzoic acids. Advantage of this specificity was taken in converting o-difluorobenzene (90) to 2,3-diflurobenzoic acid 91. Reduction of 91 to 2,3-diflurobenzyl alcohol (92), followed by a second metalation and carbonation gave 93, which was reduced to the dialcohol 94. Conversion of 94 to the corresponding dibromide 95 followed by reduction with lithum aluminum hydride gave authentic 85.

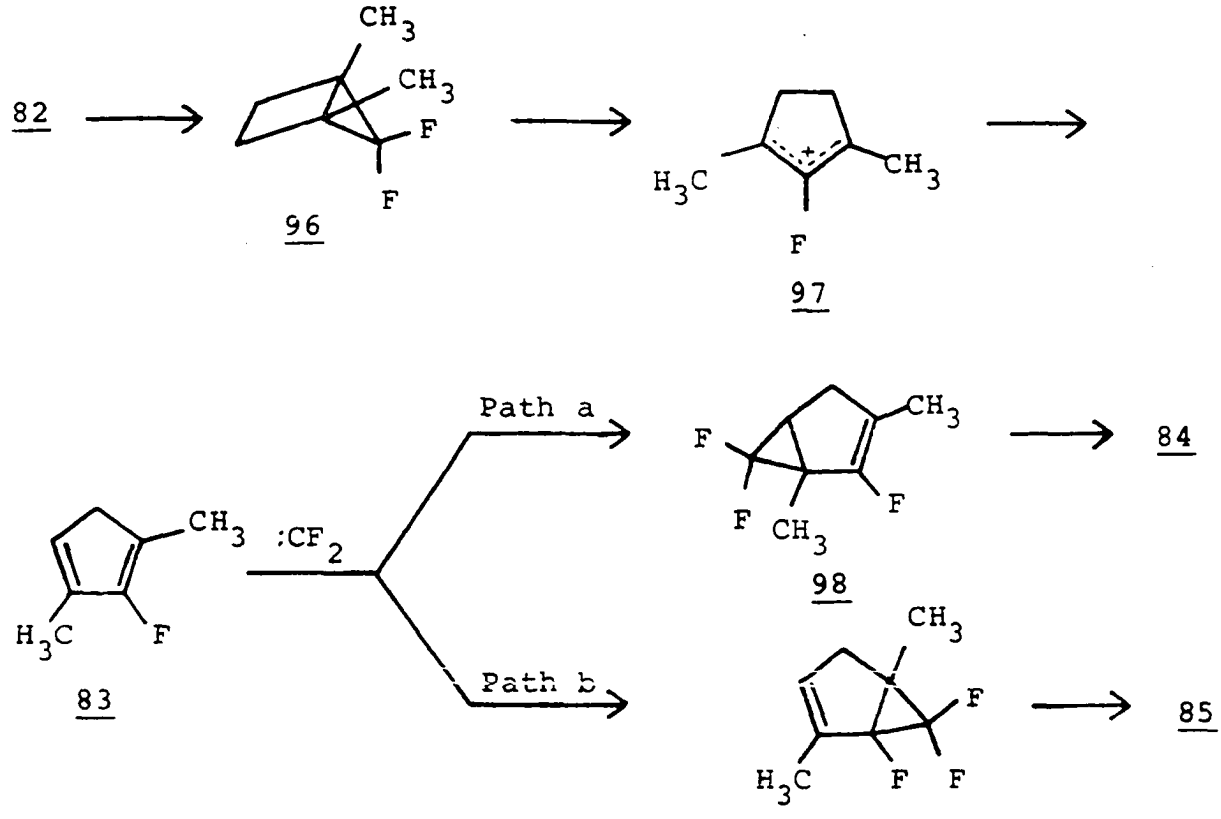


90 91 92 93 94 95

85

Scheme 9

The formation of 83, 84, and 85 in the reaction of difluorocarbene with 1,2-dimethylcyclobutene must be explained once again in terms of an initial generation and facile rearrangement of an intermediate bicyclopentane (Scheme 10). It is assumed that difluorocarbene adds to the olefin to give

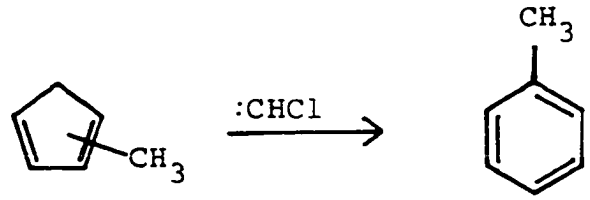


Scheme 10

transient 5,5-difluoro-1,4-dimethylbicyclo[2.1.0]pentane (96). Relief of strain in the latter compound provides a sufficient driving force for heterolysis of the endo-fluorine carbon bond giving the ion pair 97. Loss of proton from 97 gives a cyclopentadiene which because of symmetry must be 83. Addition of difluorocarbene to 83 along the paths a and b

would produce the 6,6-difluorobicyclo[3.1.0]hex-2-enes 98 and 99 which upon eliminative ring expansion would give the observed difluoroxylenes 84 and 85 respectively. That 83 is indeed the precursor of 84 and 85 is supported by the fact that the relative amounts of 84 and 85 increase at the expense of 83 as the reaction progresses. Furthermore, attack of difluorocarbene on 83 should occur preferentially at the more nucleophilic double bond (path a) giving a predominance of 84 over 85 as observed.

The formation of benzene derivatives in reactions of halocarbenes with cyclopentadienes is not unprecedented. In 1961 terBorg and Bickel (105) obtained only chlorobenzene from the reaction of cyclopentadienyl sodium with chloroform at 40°. More recently Baird and co-workers (55) were able to isolate 6,6-dichlorobicyclo[3.1.0]hex-2-ene and show that it is completely rearranged to chlorobenzene after 25 minutes at 55°. We have further found that the reaction of chlorocarbene (106) with a mixture of monomethylcyclopentadienes at room temperature produces toluene as the major (70%) product. The thermal lability of halocarbene adducts of cyclopentadienes can be attributed in part to the stabilizing influence of the double bond in the intermediate allylic cation. It also seems probable that aromatization provides a significant driving force in these rearrangements.

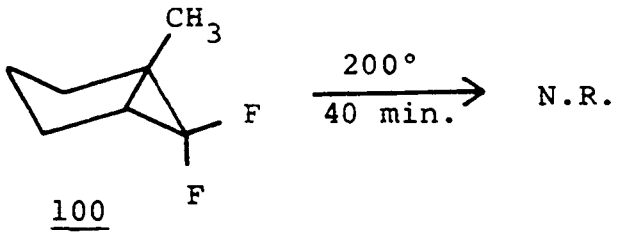


The instability of bicyclopentane 96 at 50° was unexpected. In an attempt to further determine the limits of stability of an endo-5-flourobicyclo[2.1.0]pentane the reaction of chlorofluorocarbene with 1-methylcyclobutene at room temperature was examined. Chlorofluorocarbene derived from the reaction of methyl chlorodifluoroacetate and in situ generated sodium methoxide adds to cyclohexene to give similar amounts of epimeric chlorofluoronorcaranes (59). Thus it could be expected that a mixture of 5-chloro-5-fluorobicyclo[2.1.0]-pentanes would be produced initially in the reaction of chlorofluorocarbene with 1-methylcyclobutene and that the epimer having the endo-fluorine would be produced in sufficient amounts to be detected if it were stable.

The reaction of chlorofluorocarbene with 1-methylcyclobutene was carried out in the same manner as the dichlorocarbene addition discussed previously. No evidence for a bicyclopentane could be observed in the nmr spectrum of the crude reaction mixture. The products from this reaction were thermally labile and were not characterized. Presumably they

are rearranged cyclopentenes.

The experiments involving additions of fluorinated carbenes to cyclobutenes provide impressive testimony to the importance of strain relief in rearrangements of halocarbene adducts of cyclic olefins. The difference in thermal stability between the bicyclopentanes and their next higher homologs is particularly striking. Thus, while an endo-5-fluorobicyclo-[2.1.0]pentane could not be detected as a stable entity even at temperatures as low as 25°, we have found that 6,6-difluoro-1-methylbicyclo[3.1.0]hexane (100) is stable at 200°. A solution of 100 in tetraglyme was heated at 160° for 15 min



100

and then at 200° for 40 min with no detectable change in its nmr spectrum. After 1 hour at 230°-250° 100 was completely destroyed. The primary thermolysis products were observed to undergo further change at this temperature and were not investigated.

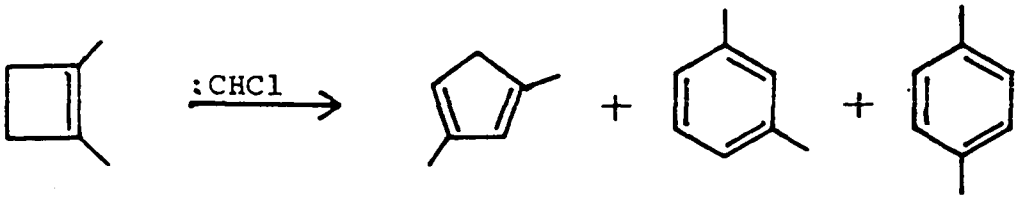
In the course of this work there appeared a report by Yang and Marolewski (25) that chlorocarbene generated photochemically from chloroform adds to 1,2-dimethylcyclobutene (82) to give vinylcyclopropanes 10 and 11 as the only 1:1 addition

products. Moreover, these products could not be explained in terms of a bicyclopentane intermediate. It seemed of interest therefore to examine the addition of chlorocarbene derived from another source to 82.

The standard combination of methyl lithium and methylene chloride employed as the source of chlorocarbene (106) in our investigation is known to produce predominantly endo-adducts with cyclic olefins. Cyclopentene, for example gives the 6-chlorobicyclo[3.1.0]hexanes in a 3/1 endo/exo ratio (55). A "normal" addition of chlorocarbene to 82 should then proceed initially to give a mixture of endo- and exo-5-chloro-1,4-dimethylbicyclo[2.1.0]pentanes. Only the exo isomer should be stable though it might be a minor product.

The reaction of methylene chloride and methyl lithium in the presence of a three-fold excess of 82 at room temperature produced a crude reaction mixture whose nmr spectrum contained no evidence for the vinyl cyclopropanes obtained by Yang. The volatile products which were removed and trapped at low temperatures corresponded to less than 8% of the theoretical quantity for 1:1 addition, and only two of these products could be isolated in sufficient quantity for characterization. These appeared as a single peak on vpc analysis and were identified as m- and p-xylene in a 3/1 ratio by comparison (nmr) with an authentic mixture. Although none of the other major products of this reaction were stable under the vpc

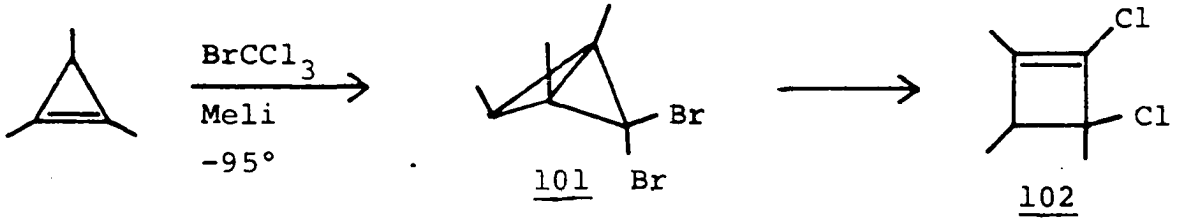
conditions, resonances at δ 1.88 (doublet), (1.98 doublet), 2.7 (multiplet), 5.65 (multiplet), and 5.9 (multiplet) readily assignable to methyl, methylene, and olefinic protons of 1,3-dimethylcyclopentadiene, the supposed precursor of the xylenes, were visible in the crude nmr spectrum. Thus chlorocarbene



from at least one source adds to 82 in a normal fashion with the products clearly implying an intermediate bicyclopentane.

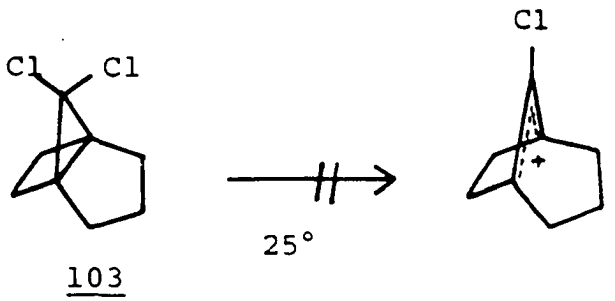
Our results can be summarized at this point by noting that dihalocarbene additions to cyclobutenes give without exception rearranged products derived from intermediate 5,5-dihalobicyclo[2.1.0]pentanes. Even endo-fluorine substitution does not prevent rearrangement at temperature above 50° and apparently not even at 25°. One is naturally led to inquire about the stability limits for these compounds and suitable low temperature experiments, if they could be devised, might provide the answers. However, some very recent results of Trost and Atkins (107) suggest that sufficiently low temperatures may be difficult to attain at least for the chloro-derivatives. 1,2,3-Trimethylcyclopropene was treated with dichlorocarbenoid derived from methyl lithium and bromotrichloromethane. The expected dichlorobicyclobutane 101 could

not be observed in the nmr spectrum of the reaction mixture at -73° within one hour after mixing the reagents at -95°. The only product detected at low temperatures and eventually isolated was the ring expansion isomer 102. The authors attributed the instability of the bicyclobutane to a release of



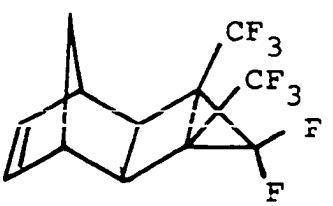
101 102

some 25 kcal/mole of strain energy which accompanies a concerted endo chlorine ionization and 1-3 bond fragmentation with eventual rearrangement to 102. As noted above, rearrangements of bicyclo[2.1.0]pentanes to cyclopentenes release some 47 kcal/mole of strain energy or 22 kcal/mole more than a bicyclobutane to cyclobutene conversion. It seems very likely therefore that halobicyclopentanes would be appreciably less stable than their bicyclobutane analogs. Judging from the experiment of Trost and Atkins, temperatures well below -100° might be required for endo-5-chlorobicyclopentanes (Eq. 75) to be stable. An interesting exception is the novel tricyclic compound 103 prepared by Wiberg and Burgmaier (108). Despite an estimated strain energy of 60 kcal/mole for the corresponding hydrocarbon (109), 103 is stable at room temperature. That stability should not be surprising, however, since



103

rearrangement would involve a transition state having appreciable double bond character at the bridgeheads. On the only other occasion that a stable molecule containing a 5,5-dihalobicyclo[2.1.0]pentane moiety has been prepared, special circumstances were also involved. Sargeant (110) has found that the cycloaddition of 1,2-bis(trifluoromethyl)-3,3-difluorocyclopropene and quadricyclane produces 104, which is stable at 61°. The main factors which contribute to the



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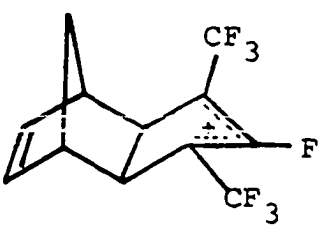


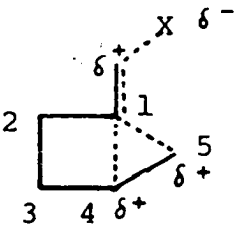
105

stability of this molecule are the strength of the carbon fluorine bond but probably more importantly the inductive destabilization of a transition state resembling 105 by the trifluoromethyl substituents.

Solvolysis of 3,3-Difluorobicyclo[2.1.0]pentane-1-methanol Esters

The propensity for 1,4 bond cleavage and maximum strain relief pervades the chemistry of bicyclo[2.1.0]pentanes to the extent that important but more subtle properties of this ring system may often be obscured. The introduction of appropriate substituents or other structural modifications designed to encourage alternate modes of reaction by making the most direct pathways for 1,4 bond fragmentation energetically unfavorable is a valuable means of gaining further insight into this highly strained system.

One of the most dramatic effects of strain in a reaction of a bicyclopentane has been demonstrated by Dauben and Wiseman (9) in their solvolysis study of bicyclo[2.1.0]pentane-1-methyl p-nitrobenzoate (47). Solvolysis of 47 in 60% aqueous acetone at 100° proceeds at a rate some 4×10^5 times that of cyclopropylmethyl p-nitrobenzoate and gives only products formally derived from the 3-methylenecyclopentyl cation. It was postulated that ionization of 47 leads to the bicyclic cyclopropylcarbinyl cation 106. Since the rate data clearly imply a substantial release of strain energy in attaining the transition state, the electrons of the 1,4 bond would be delocalized to a greater extent than those of the 1,5 bond. Consequently a greater portion of the incipient positive charge would be localized on C_4 as ionization proceeds.



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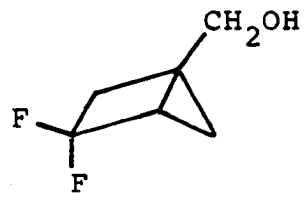
The introduction of a strong electron withdrawing substituent at C_3 should modify this system in two important ways: Such substitution should result in decreased electron density in the 1,4 bond in the ground state thereby reducing the ability of that bond to participate in the ionization step. A second consequence would be to destabilize any incipient positive charge on C_4 in proceeding to the transition state. Both effects should result in an appreciably lower solvolysis rate, but a more interesting consequence of charge destabilization at C_4 might be to force the system to seek alternate modes of rearrangement such as those involving more extensive charge delocalization to carbon-5.

With the above considerations in mind we have examined the solvolysis of esters of 3,3-difluorobicyclo[2.1.0]pentane-1-methanol (107). The ability of β-fluoro substituents to strongly destabilize carbonun ions has been convincingly demonstrated by Olah and Pittman (111). Thus 1,1,1-trifluoro-2-propanol and related alcohols, though quantitatively



107

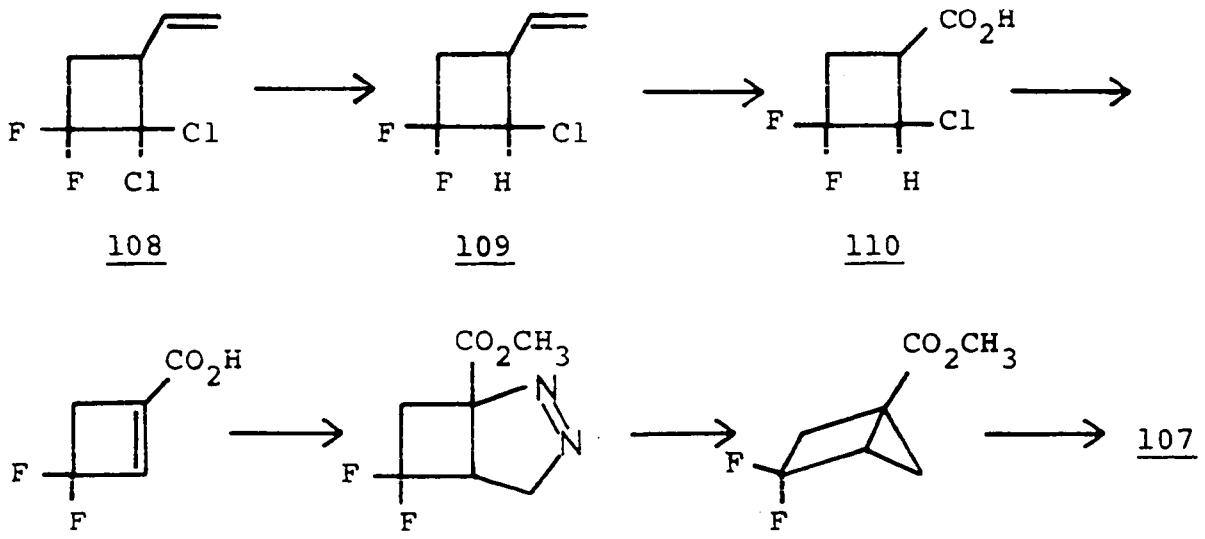
protonated in fluorosulfonic acid media, do not eliminate water to give carbonium ions. Although other substituents could provide the desired inductive effect, fluorine offers several advantages. Among these are a relatively small steric requirement, the relative inertness of the carbon fluorine bond, and the availability of ^{19}F nmr (fmr) as a supplementary analytical tool.

Synthesis

3,3-difluorobicyclo[2.1.0]pentane-1-methanol was synthesized in a six-step reaction sequence starting with commercially available 1-vinyl-2,2-dichloro-3,3-difluorocyclobutane (108) (Scheme 11). Reduction of 108 with triphenyl or tri-n-butyltin hydride gave the corresponding nomochloro derivative 109 as approximately a 1/1 mixture of cis-trans isomers. Oxidation of 109 with either potassium permanganate or ozone-hydrogen peroxide produced the β-chloroacid 110, which upon mild treatment with aqueous potassium hydroxide was converted to 3,3-difluorocyclobutenecarboxylic acid (111). The structure of 111 is confirmed by its spectra. Acid 111

absorbs in the infrared at 3050 cm^{-1} and 1728 cm^{-1} (carboxyl) and at 1626 cm^{-1} and 1616 cm^{-1} (c=c). The pmr spectrum consists of triplets at δ 3.18 (3.7 Hz, 2H) and δ 6.70 (1.3 Hz, 1H) for the ring methylene and vinyl proton respectively, and a singlet at δ 13.48 (1H) for the acid proton. The fmr spectrum of 111 consists of a triplet of doublets corresponding within experimental error to the splittings in the proton spectrum. A molecular ion peak at m/e 134 is observed in its mass spectrum.

Reaction of 111 with ethereal diazomethane at room temperature gave within seconds a quantitative conversion to the pyrazoline ester 112 which exhibited characteristic absorptions in the infrared at 1750, 1550, and 1444 cm^{-1}. The pmr spectrum of 111 contained a perturbed (fluorine) AB portion of an ABX system at δ 4.3-5.3 characteristic of a Δ^1-pyrazoline.



Scheme 11

The facility with which diazomethane reacts with 111 is a noteworthy indication of the strong inductive effect of fluorine since pyrazoline formation with other cyclobutene-1-carboxylic acids requires from 20 hours at room temperature to several days at -30°.

The benzophenone sensitized photolysis of 112 (benzene solution, pyrex immersion well) proceeded smoothly to give 1-carbomethoxy-3,3-difluorobicyclo[2.1.0]pentane 113 in 70% isolated yield. The structure of 113 was confirmed by its spectra and microanalysis. Ester 113 gives a molecular ion at m/e 162 in its mass spectrum and absorbs in the infrared region at 3085 cm^{-1} (cyclopropane C-H stretch) and 1730 cm^{-1} (cyclopropanecarboxylic ester). The 100 MHz pmr spectrum of 113 shows the usual absence of high field resonances for cyclopropyl hydrogens exhibited by other bicyclopentane-1-carboxylic acid derivatives. Only one of the cyclopropyl hydrogen (5-endo) is clearly visible, and it appears as a multiplet at δ 1.47-1.62. The other cyclopropyl hydrogen on C_5 overlaps with one of the cyclobutane methylene protons to give a complex absorption at δ 1.47-1.62. Overlapping resonances are also seen for the remaining cyclobutane methylene proton and bridgehead proton at δ 2.65-3.12. The methyl hydrogens appear as a singlet at δ 3.65, the lowest field resonance in the spectrum. The fmr spectrum of 113 is basically of the AB type with J_{FF} = 196 Hz, typical of geminal F-F coupling. The basis

for these assignments is explained in a later section dealing with the detailed analysis of nmr spectra of 113 and related compounds.

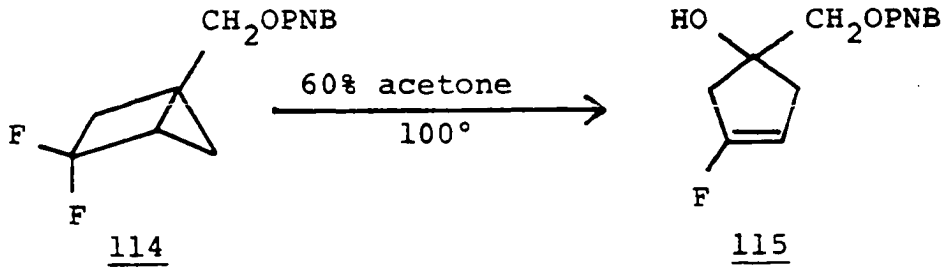
Reduction of 113 with the theoretical amount of lithum aluminum hydride at 0° gave the desired alcohol 107 in greater than 90% yield. The 100 MHz pmr spectrum of 107 contained an AB pattern (J_{AB} = 13 Hz) centered at δ 3.80 characteristic of bridgehead carbinyl methylenes in bicyclopentane-1-methanols. Both of the cyclopropyl hydrogens at C_5 were moved upfield giving rise to a single complex absorption at δ 1.05-1.40 while other features of the spectrum were similar to those of 113. When a large excess of lithium aluminum hydride was employed in the reduction of 113, relatively little of the desired bicyclic alcohol was obtained, and a different compound of undetermined composition containing a prominent multiplet, at δ 4.9 in its pmr spectrum was the major product. Likewise, alcohol 107 upon passage through a variety of vpc columns was converted to a new compound whose structure was not immediately determined but which was characterized by an almost identical multiplet at δ 4.9. An explanation for this unusual behavior was eventually provided through the solvolysis studies which followed.

Preparation of 3,3-difluorobicyclo[2.1.0]pentane-1-methyl p-nitrobenzoate (114) by reaction of alcohol 107 with p-nitrobenzoyl chloride in pyridine proceeded smoothly and in

good yield. The crystalline ester 114 was easily purified by recrystallization, and material of near analytical purity was used in the solvolysis studies.

Solvolytic studies

By the standards of the parent p-nitrobenzoate (47), the fluorinated derivative 114 was extremely unreactive. When a solution of 114 in 60% aqueous acetone was heated at 100° for 2.5 hours there remained greater than 86% unreacted ester. By comparison, 47 is reported to be completely destroyed after 2 hours at 100° in 80% aqueous acetone. After heating a solution of 114 in 60% aqueous acetone at 100° for 72 hours no starting material was found, and a new p-nitrobenzoate ester 115 was isolated in 90% yield. No other products could be detected in the pmr spectrum of the crude products. The



114 115

structure of 115 rests on a combination of spectral and chemical evidence. The mass spectrum of 115 contains a molecular ion at m/e 281, and exhibits pertinent absorptions in

its infrared spectrum at 3610 cm^{-1} and 3450 cm^{-1} (OH), 1732 cm^{-1} (carbonyl) and 1688 cm^{-1} [C=CF, (57,112)]. The 60 MHz pmr spectrum of 115 is shown in Figure 7 with assignments as follows: multiplet, δ 2.6-2.9 (4H), ring methylenes; broad singlet, (disappears upon washing with D_2O) δ 3.2 (1H), hydroxyl; singlet δ 4.4 (2H), OCH_2; multiplet, δ 5.0 (1H), vinyl proton; singlet, δ 8.2 (4H), aromatic protons. The fmr spectrum consists of a single unresolved multiplet at 119 ppm. Treatment of 115 with α-napthylisocyanate produced a sharply melting α-napthylurethane whose pmr spectrum was similar to that of 115 but having the hydroxyl resonance replaced by resonances due to the α-napthylurethyl group. The urethane had a mass spectral molecular weight of 450 which along with the nmr data confirms the formulation of the solvolysis product as C_5H_5F (CH_2)(OH)(OPNB). The chemical shift of the singlet methylene at δ 4.4 in 115 is more consistent with a CH_2OPNB moiety than a CH_2OH moiety. Moreover, the hydroxyl resonance of the solvolysis product remains a singlet when the nmr spectrum is taken in dimethylsulfoxide solution requiring that the hydroxyl be attached to a quaternary carbon (113). A somewhat disturbing feature of the pmr spectrum of 115 was the vinyl proton multiplet at δ 5.0 in which no large coupling to fluorine is observed. Although cis proton-fluorine coupling across a carbon carbon double bond has been reported to range from 3-20 Hz values of 10 Hz are more typical (114). Very

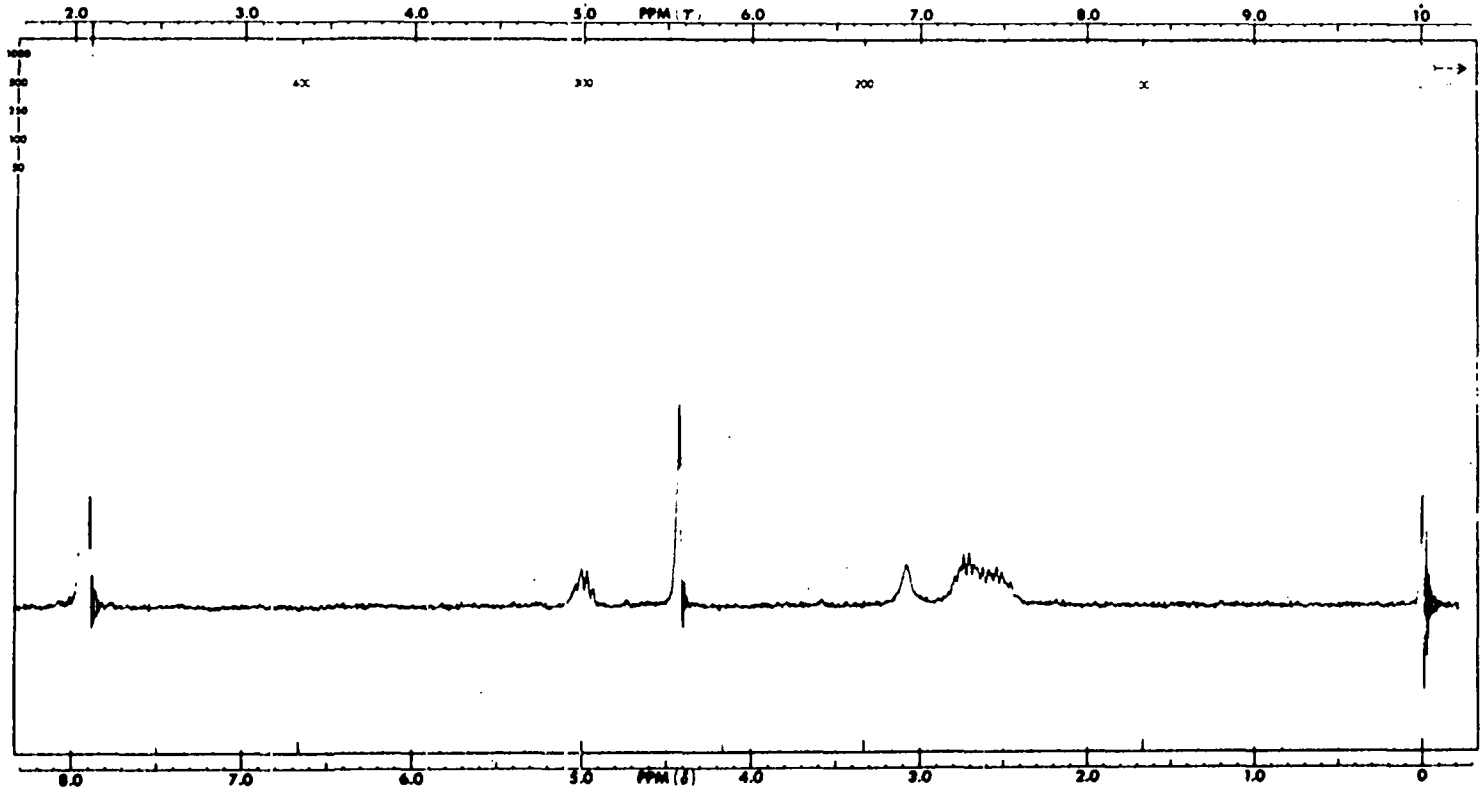
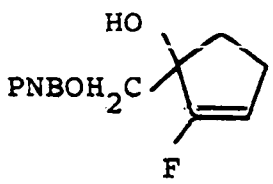


Figure 7. 60 MHz pmr spectrum of 115

recently, however, Strobach and Boswell (112) have reported nmr spectral parameters of several 1-fluorocycloalkenes. Although vinyl proton-fluorine coupling was observed to range from 17-37 Hz for six-membered and larger rings, the coupling in 1-fluorocyclopentene was too small to be easily measured. Furthermore, the chemical shift of the vinyl proton at δ 4.92 reported for 1-fluorocyclopentene is in excellent agreement with the shift at δ 5.0 in 115. Although the chemical shift of the ring methylene protons at δ 2.6-2.9 strongly implies that they are allylic, the data does not rigorously exclude isomers 116 and 117 as possible alternatives to 115. Final confirmation of structure 115 was obtained by converting the solvolysis product to dibromide 118. The pmr and fmr spectra



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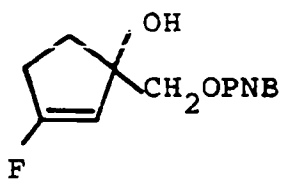

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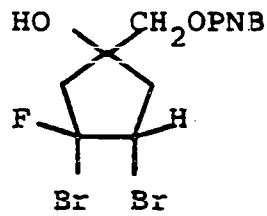
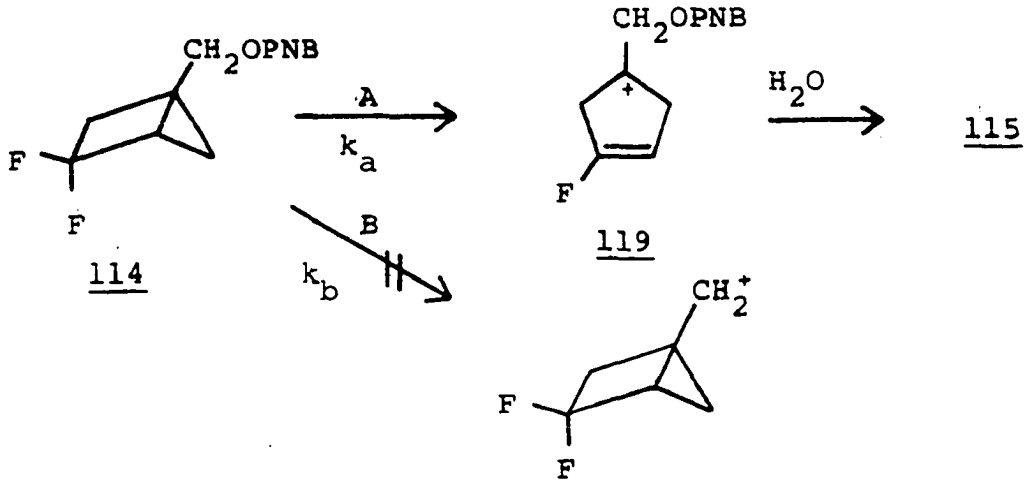


118

of 118 clearly showed vicinal coupling of three protons to fluorine and vicinal coupling of one fluorine (J_{HF} = 27 Hz) and two protons (J = 9 Hz) to the hydrogen α to bromine which would be inconsistent with dibromides derived from 116 or 117.

The rearrangement of 114 to 115 is formally analogous to the solvolytic rearrangement of bicyclo[2.1.0]pentyl-2-dinitrobenzoates to 3-cyclopenten-1-ol derivatives (15,16) suggesting that the mechanistic details of the rearrangements are also analogous. The high endo/exo rate ratios observed for the dinitrobenzoates has led Wiberg et al. (15,16) to propose that solvolysis of the endo isomer proceeds via concerted cleavage of the alkyl-oxygen bond and the 1,4 bond thereby utilizing a portion of the bicyclopentene strain energy in attaining the transition state. Orbital symmetry considerations support that argument since maximum overlap of the developing empty p orbital and an appropriate orbital in the fragmenting 1,4 bond is maintained.

It seems likely then that solvolysis of 114 proceeds as shown in Scheme 12, path A: concerted fragmentation of the endo fluorine-carbon and 1,4 bonds with rate constant k_a leading to intermediate ion 119 which collapses with solvent to give 115. Heterolysis of the alkyl-oxygen bond with rate constant k_b (Scheme 12, path 6) the process originally intended for study is completely excluded at the expense of the more facile carbon-fluorine heterolysis. A corollary to the concerted bond fragmentations proposed here and elsewhere by Wiberg et al. (15,16) is that substituents at C-1 should have an appreciable effect on the solvolysis rate of bicyclopentanes with leaving groups at C-3 depending on the stabilizing

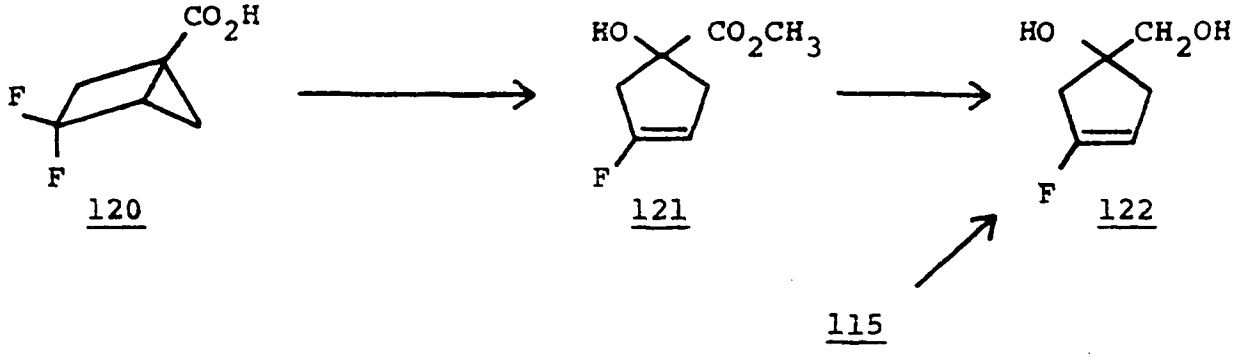


Scheme 12

influence of the substituent on the incipient positive charge at C-1. The synthetic scheme employed here makes it particulary convenient to vary the C-1 substituent of 3,3-difluorobicyclopentene so that this hypothesis could readily be tested.

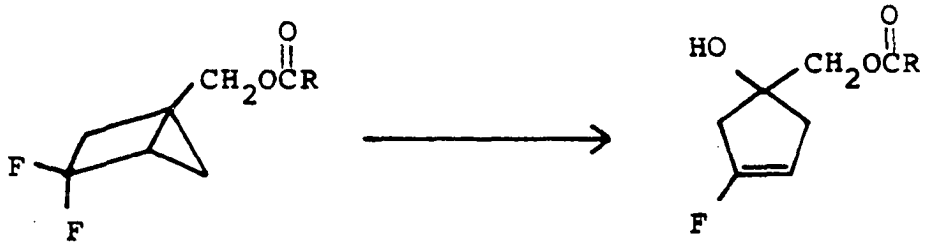
When in the course of studying the solvolysis of 114 it became apparent that p-nitrobenzoate moiety was not directly involved we examined the solvolysis of 3,3-difluorobicyclo-[2.1.0]pentane-1-carboxylic acid 120 which bears no potential leaving group on the carbinyl carbon. Solvolysis of 120 in 1 M aqueous sodium hydroxide was rapid, being at least 93% complete after only 4 hours at 55°. Gas chromotographic analysis of the crude solvolysis product after esterification with diazomethane revealed two components in a 93:7 ratio. The major component gave spectral data consist with the α-hydroxyester 121. Ester 121 was reduced with lithium

aluminum hydride to glycol 122 which gave a positive periodate



test and an nmr spectrum identical to that of the hydrolysis product of p-nitrobenzate 115. Since the solvolysis was conducted in basic media, the actual species in solution would be the carboxylate anion derived from 120. The negatively charged moiety at C-1 would have a particularly strong stabilizing influence on any incipient positive character at C-1 which would readily account for the rapidity of the reaction if concerted C-F and 1,4-bond fragmentations are involved.

A more quantitative determination of the effect of the C-1 substituent on the solvolysis rates of 3,3-difluorobicyclopentanes was made by determining the solvolytic rate constants for p-nitrobenzoate 114 and the corresponding benzoate and acetate esters 123 and 124. Solvolyses were carried out in 60% aqueous acetone with 2,6-lutidine added to prevent hydrolysis of the esters. The ampoule technique in conjunction with nmr spectroscopy was used to monitor the extent of reaction. In each case the integrated 100 MHz spectrum of the



114 R = p-$NO_2C_6H_4$

123 R = C_6H_5 124 R = CH_3

isolated crude mixture was obtained. The molar ratio of product (as determined from the area of the vinyl multiplet at δ 4.9-5) to initial starting material (as determined by the combined area of the OCH_2 singlets near δ 4.5 in both starting material and product) showed a first order increase with time. The half-life of each bicyclic ester was graphically determined and used to calculate the first order rate constants shown in Table 3. The relative solvolysis rates of 114, 123, and 124

Table 3. First order rate constants in 60% acetone at 100°

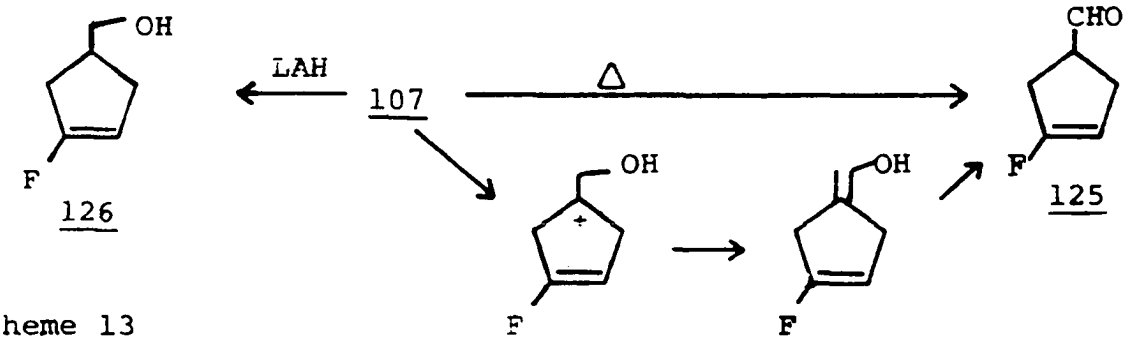
Compound	$k_1 \times 10^5$, sec^{-1}	Relative rate
114	1.39	1.00
123	1.96	1.40
124	4.00	2.88

clearly increase in the same direction as the ability of the C-1 substituent to stabilize a positive charge. Although the rate differences are not large it must be remembered that the

actual substituent changes in this series occur at a site four-bonds removed from C-1. However, the rate differences would seem to be too large to be caused purely by substituent influence on a cationic site at C-3, which would be the case if C-F and 1,4-bond cleavages were stepwise. Thus it is felt that the data in Table 3 strongly support the concerted pathway proposed above.

It was mentioned previously that certain difficulties were encountered during attempts to obtain 3,3-difluorobicyclo-[2.1.0]pentane-1-methanol 107 by reduction of the corresponding ester 113 with a large excess of lithium aluminum hydride and in obtaining an analytical specimen of 107 by preparative gas chromatography. A sample of 107 which was pure by nmr analysis gave three peaks (83.6:6:11 ratio) when injected onto a DEGS column at 115°. None of the bicyclic alcohol could be detected in the nmr spectrum of the collected mixture. The only component investigated was the major one which on the basis of its spectra and comparisons with previously encountered fluorocyclopentenes was identified as aldehyde 125. A mechanism for the 107→125 conversion can be written as in Scheme 13 involving concerted C-F and 1,4 bond heterolyses followed by loss of a proton and tautomerization to the observed product. Yet another instance where a facile C-F bond cleavage in a 3,3-difluorobicyclopentane derivative apparently occurs is in the lithium aluminum hydride reduction of ester 113. If an excess

of the reducing agent is employed varying amounts of a product characterized by a fluorocyclopentene-like multiplet at δ 4.9 are formed along with alcohol 107. This product was not fully characterized but nmr spectra of mixtures strongly suggest alcohol 126 as the most likely structure. This in turn



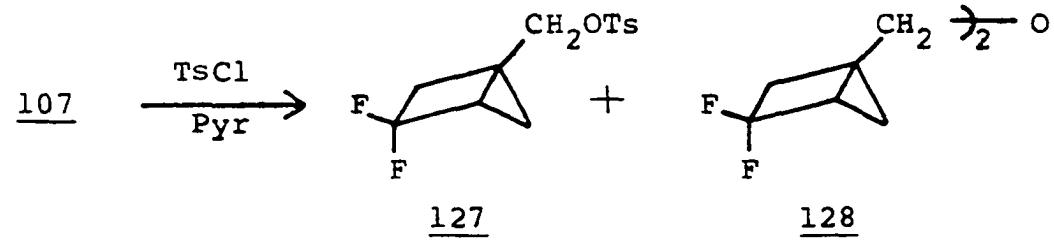
Scheme 13

suggests the possibility of an unprecedented hydride attack on C-1 of a bicyclopentane nucleus with concomitant fragmentation of the 1,4 and C-F bonds. Further investigation would be required to verify this interpretation, however.

That the solvolysis of p-nitrobenzoate 114 proceeds without giving detectable products of alkyl-oxygen cleavage is clearly attributable to destabilization of the transition state for that process by the fluorine substituents. An upper limit for the rate of alkyl-oxygen cleavage in 114 (Scheme 12, k_b) may be calculated from the rate data in Table 3 by assuming that products from that process amounting to no more than 5% of the total product could have gone undetected. That assumption leads to a calculated upper limit value of k_b (Scheme 12)= $5/95(1.39 \times 10^{-5}\ sec^{-1}) = .07 \times 10^{-5}\ sec^{-1}$. Comparison of

that value with the solvolysis rate constant of 1200×10^{-5} sec^{-1} for bicyclo[2.1.0]pentane-1-methyl-p-nitrobenzoate 47 under the same solvent/temperature conditions leads to the conclusion that fluorine substitution has inhibited the alkyl-oxygen cleavage process in 114 by a factor of at least 10^4.

In order to study the details of the alkyl-oxygen cleavage process the more reactive tosylate 127 was prepared. Preparation of 127 proceeded less smoothly than that of the p-nitrobenzoate owing to the formation large amounts of ether 128 even in the presence of a six-fold excess of p-toluene-sulfonyl chloride. Nevertheless, a clean separation of the



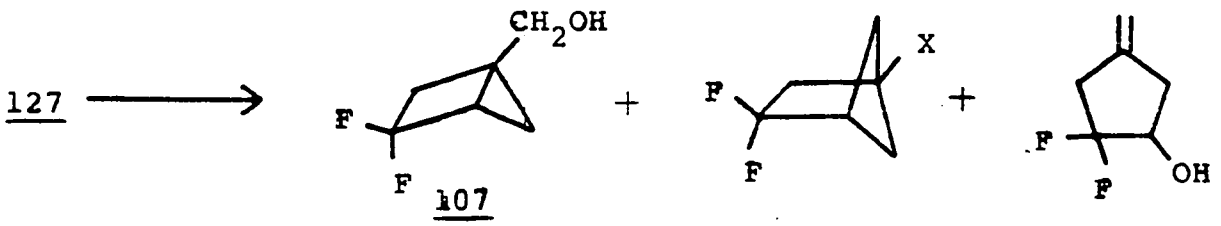
127 128

two products was readily achieved by partitioning in petroleum ether giving analytically pure 127 for use in kinetic studies. Solvolysis of 127 in 80% aqueous acetone at 40-55° produced a mixture of 64% solvolysis products and 36% unreactive internal return products (Scheme 14), the relative amounts of which were determined from product studies and from the experimental acid infinity titer obtained in the kinetic runs. The experimental infinity titer (64% of theory) did not change significantly over twenty half-lives of 127 demonstrating that the internal return products were stable under the solvolysis

conditions for 127.

Product studies The mixture of products obtained upon heating 127 in 80% aqueous acetone for a time corresponding to eleven half-lives was separated into alcoholic solvolysis product and less volatile internal return tosylate fractions by molecular distillation. The tosylate fraction consisted of approximately 90% of a single component which could be separated from minor components by chromatography following treatment of the mixture with bromine. The major internal return product has been assigned structure 129 on the basis of spectral data discussed below. The alcohol mixture was found by vpc analysis to consist of three components A, B, and C in a ratio of 10:45.5:44.5 respectively. Component A was identified as aldehyde 125 which was absent in the crude mixture but arises from pyrolysis of 107 in the gas chromatograph. The presence of 107 in the crude mixture before chromatography was established by nmr spectroscopy. Component C was identified as alcohol 130 while component B has been tentatively identified as alcohol 131.

The internal return product (129) was established as an isomer of 127 from high resolution mass measurement of the molecular ion at m/e 288. The ir spectrum of 129 is dominated by absorptions of the tosyl moiety and other than exhibiting no evidence for olefinic unsaturation is uninformative. The 100 MHz pmr spectrum of 129 (Figure 8) consists of a singlet



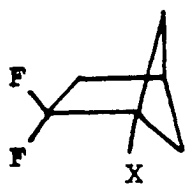
129 X = OTs 131

130 X = OH

Scheme 14

at δ 2.48 (tosyl methyl) superimposed on a series of overlapping multiplets at δ 1.95-2.65, total area 10H, and an AA'BB' pattern of the aromatic ring protons centered at δ 7.6, area 4H. The fmr spectrum of 129 consists of a single symmetrical triplet (J = 12 Hz). Similarities in the ir, pmr, and fmr spectra suggested a correspondence between component C of the alcohol fraction (130) and tosylate 129, which was indeed established by converting 130 on treatment with p-toluenesulfonyl chloride/pyridine to 129. Although the sole difference between the fmr spectra of 129 and 130 is a mere .5 ppm difference in chemical shifts, the pmr spectra of 129 and 130 (Figure 9) show appreciable differences in their high field regions which must be rationalized. In considering alternatives to 129 and 130, the absence of nonaromatic resonances below δ 2.65 in both spectra rule out those structures incorporating H-C-OR, H-C-F, or C=CH groupings, while the fmr spectra eliminate all structures with chemically

nonequivalent fluorines. The only alternatives to 129 and 130 which are compatible with the nmr spectra are the closely related compounds 132 and 133 respectively. Wiberg et al.



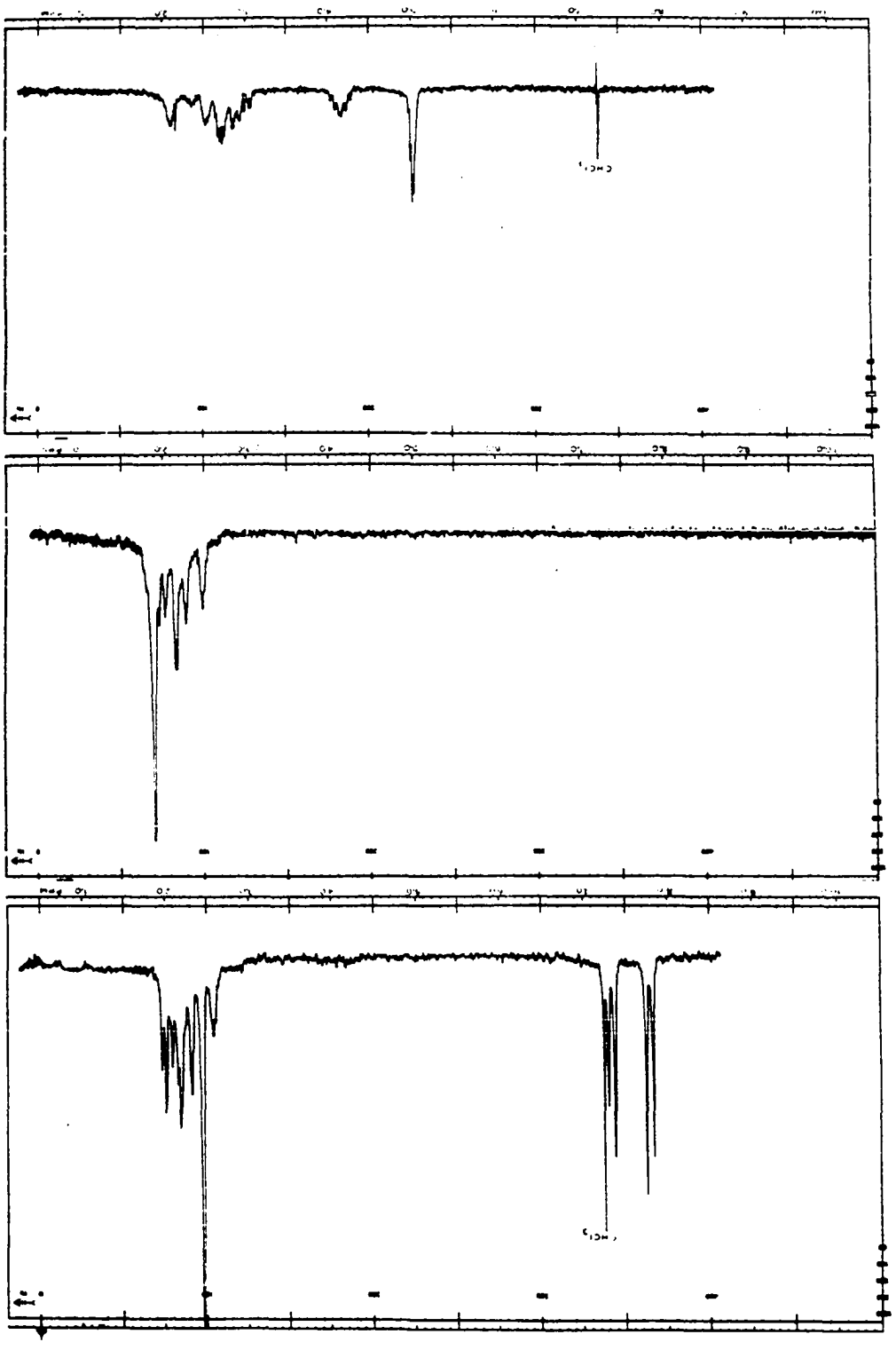
132 X = OTs
133 X = OH

(115) and Srinivasan and Sonntag (116) have published nmr data for several substituted bicyclo[2.1.1]hexanes which support the above assignments. In typical spectra the bridgehead protons of bicyclohexanes have chemical shifts very close to δ 2.5 and are the lowest field resonances. In 2,2-dichlorobicyclo[2.1.1]hexane the C-1 bridgehead hydrogen is shifted downfield to δ 3.0, while the other bridgehead hydrogen appears at δ 2.6 (116). The resonances at next higher field generally arise from protons on C-2 (or C-3) with typical values between δ 1.5 and δ 1.9, though the protons on C-3 of 2,2-dichlorobicyclohexane are shifted to δ 2.6 (116). The highest field resonances arise from the C-5 and C-6 methylenes appearing between δ 1.5 and δ 1.8. The spectra in Figures 8 and 9 each contain a multiplet near δ 2.5 assignable to the bridgehead proton. In Figure 9 a triplet at δ 2.17 (J_{HF} = 12 Hz) is

Figure 8. 100 MHz pmr spectrum of 129

Figure 9. 100 MHz pmr spectrum of 130

Figure 10. 100 MHz pmr spectrum of 131

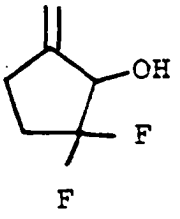


assignable to the methylene protons on C-2 of 130 or C-3 of 133; the corresponding triplet in Figure 8 is partially obscured on both sides by other resonances. The remaining resonances in each spectra then must be assigned to the C-5 and C-6 methylene hydrogens in 129 or 132 and 130 or 133. Although the appearance of resonances assigned to hydrogens on C-5 and C-6 varies from a complex pattern in Figure 8 to a broadened singlet in Figure 9, varying the bridgehead substituent can have an appreciable effect on the relative chemical shifts of the endo and exo protons on C-5 and C-6 of bicyclo[2.1.1]hexanes.

Although it has been shown that published nmr data is consistent overall with spectra assigned to 129 and 130 or 132 and 133, the spectra do not afford a ready means of distinguishing between the two sets of alternatives. The two most potentially useful criteria would be the magnitudes of the fluorine deshielding and coupling to the bridgehead proton. Using 2,2-dichlorobicyclo[2.1.1]hexane as a model and considering data from a survey of the literature which indicates that deshielding of protons by β-chlorine substituents is appreciably stronger than that of β-fluorine substituents leads one to predict that the chemical shift of the bridgehead proton in 129 or 130 should lie somewhere between δ 2.5 and δ 3.0, consistent with the observed values of δ 2.6 and δ 2.5. However, a value close to the nominal δ 2.5 would also be

predicted for 132 and 133. It might be expected that the long range coupling of fluorines to the bridgehead hydrogen in 132 and 133 would be almost absent while the vicinal coupling in 129 and 133 would be appreciable. Examination of molecular models indicates a dihedral angle of approximately 60° between the bridgehead hydrogen and each fluorine on 129. Studies on the dihedral angle dependence of vicinal H-F coupling are sparse. The data of Williamson et al. (117) though demonstrating general trends also illustrate that a wide range of coupling values may be observed for a given dihedral angle. In two cases where the dihedral angle was 60° coupling constants of 3.8 and 6.0 Hz were observed, though these values cannot necessarily be relied upon as representative. Thus the bridgehead hydrogen-fluorine coupling in 129 or 130 may be of approximately the same magnitude as the corresponding proton-proton coupling in 132 and 133-about 1 Hz based on model compounds (115). The fmr spectra are not resolved beyond the 12 Hz splitting mentioned above although the individual lines show shoulders and broadening which clearly indicate splitting in addition to that caused by the adjacent methylene. In summary the spectral data do not permit a clear choice between alternative pairs of structures above. Mechanistic considerations, however, leave structures 129 and 130 as the only reasonable possibilities.

Component B of the alcohol fraction has been tentatively assigned structure 131 on the basis of its pmr, fmr, and ir spectra. An unfortunate accident resulted in total loss of the limited sample before mass spectra or microanalytical data could be obtained. The ir spectrum of B contains hydroxyl bands at 3610 and 3420 cm^{-1} and vinylidine absorptions at 1675 and 895 cm^{-1}. The 100 MHz pmr spectrum of B (Figure 10) consists of a broad singlet at δ 2.1, 1H (concentration dependent), assigned to the hydroxyl; a complex absorption at δ 2.25-3.1, 4H, assigned to the protons on the ring; a symmetrical multiplet at δ 4.17, 1H, assigned to the methine α to the hydroxyl; and a multiplet at δ 5.03, 2H olefinic. The fmr spectrum shows fundamentally an AB pattern consisting of two doublets of multiplets with $J_{FF} = 240$ Hz, characteristic of nonequivalent geminal fluorines. The low S/N ratio in this spectrum resulted in only the more intense multiplet in the low field pair being sufficiently resolved to measure H-F coupling parameters. That multiplet consists of a triplet of doublets with J values of approximately 19 Hz and 9 Hz. On the basis of the above data the only reasonable formulation for B would be a methylenecyclopentanol with geminal fluorines on the ring. Of the six possible isomers only 131 and 134 incorporate a $CH-CF_2-CH_2$ moiety required by the fmr spectrum. A survey of literature nmr data for methylenecyclopentanes shows that a substituent, particularly a hydroxyl, α to the



134

exocyclic methylene induces an appreciable chemical shift non-equivalence of the olefinic hydrogens, while in compounds with only β substituents the olefinic protons have virtually identical chemical shifts (9,10,11,76,118). Thus the virtually identical shifts of the olefinic hydrogens in B makes 134 unlikely. The absence of splittings smaller than 6 Hz in the multiplet at δ 4.17 indicates an absence of allylic coupling to the methine proton which is also inconsistent with 134. The only feature of the nmr spectra of B which is difficult to rationalize with structure 131 is the somewhat small vicinal coupling between the methine hydrogen and each of the fluorines. As previously pointed out only one of these values can be measured from the fmr spectrum and is approximately 9 Hz though judging from the width of the other multiplets the other value is very similar. Considerable fortuitous overlap of lines in the δ 4.17 multiplet of the pmr spectrum precludes more accurate determination of J_{HF} values from that source. Literature values for vicinal HF coupling in five-membered

rings range from 14-21 Hz (112,119,120) though available data is sparse. This is in good agreement with the observed 19 Hz coupling between one of the fluorine and the two vicinal protons of the adjacent methylene. Final confirmation of the 131 structure assignment will require higher quality fmr and microanalytical data and quite possibly comparison with an independently synthesized authentic specimen.

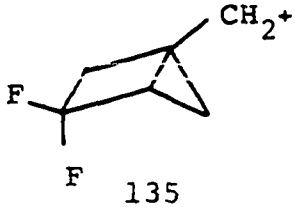
Kinetic studies The aliquot method was employed in determining the titrimetric rate constant for solvolysis of 127 in 80% acetone. Because of the large amount of internal return the experimental acid infinity titer was used in computations of rate constants. A plot of $\log|ml-ml_{\infty}|$ vs time (where ml = volume of base used at time t and ml_{∞} = ml base at $t = \infty$) was linear. The rate constant determined from such a plot corresponds to the sum of the rate constants for solvolysis and internal return and therefore refers to the apparent rate of ionization. Rate data for solvolyses of 127 and cyclopropylcarbinyl tosylate are summarized in Table 4. Activation parameters for solvolysis of 127, which are based on only two temperatures with a 10° difference (because of limitations in the constant temperature equipment employed), should be considered approximate only. Comparison of the rate constants in Table 4 for 127 and cyclopropylcarbinyl tosylate in 80% acetone at 20° shows that 127 is less reactive than cyclopropylcarbinyl tosylate by about one order of magnitude.

Table 4. Kinetic parameters for tosylate solvolyses

Tosylate	Temp, °C	Solvent	$k_1 \times 10^4$, sec^{-1}	$\Delta H^{\ddagger}$ kcal/mole	$\Delta S^{\ddagger}$, eu	Ref[a]
127	39.9	80% acetone	1.94	19	-16	(a)
	50.0	80% acetone	5.14			(a)
	20.0	80% acetone	.23			(a,b)
Cyclopropylcarbinyl	40.0	HoAc	17.8	21.8	- 2	(21)
	20.0	80% EtOH	11.3			
	20.0	80% acetone	3.4			(a,c)

[a](a) this work, (b) extrapolated from rates at higher temperatures, (c) extrapolated from data in 80% EtOH using the Grunwald-Winstein relationship $\log k/k_o = my$ (121a,b); for cyclopropylcarbinyl tosylate m = .75 (21); for 80% acetone y = 0.67 (122).

It can further be seen that the responsibility for the decreased reactivity of 127 lies in its large negative activation entropy rather than in the activation enthalpy. Indeed the magnitude of the entropy difference is probably minimized here since data for 127 was obtained in aqueous acetone which is significantly more polar than glacial acetic acid and would result in lower solvent contribution to the entropy change. This data suggests that orientational effects are more important in going to the activated complex from 127 than is the case with cyclopropylcarbinyl tosylate. It appears that neither the kinetic data nor the solvolysis products are completely consistent with an initial ionization to the classical bicyclopentylmethyl cation 135. Although that



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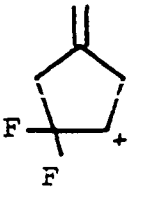

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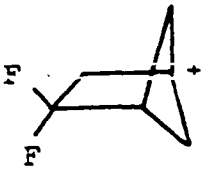

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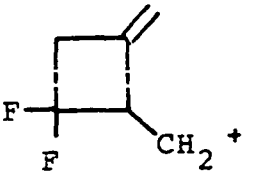


138

process would explain the formation of 107 through trapping of 135 and 129, 130, and 131 through rearrangement of 135 to ions resembling 136 and 137, it would not account for either the large negative activation entropy or the failure to observe significant amounts of products formally derived from 138. It is now generally accepted that cyclopropylcarbinyl cations

possess a "bisected" structure in which the empty p orbital is coplanar with the ring and that it is the overlap of the p orbital with the orbitals of the 1,2 and 1,3 bonds and the resulting delocalization of charge which is responsible for the unusually high stability of these species (65b). This type of overlap in 135 would ordinarily result in a lengthening of the 1,4 and 1,5 bonds with partial delocalization of the charge onto C-4 and C-5. While lengthening and eventual rupture of the 1,4 bond would provide maximum strain relief (47 kcal/mole) (9), destabilization of incipient positive character at C-4 by fluorine would strongly inhibit that process. Thus it might be anticipated that much of the burden of stabilizing the positive charge would fall on C-5. Rupture of the 1,5 bond leading to products formally derived from ion 138 would release approximately 28 kcal/mole based on the difference in strain energies of bicyclopentane (54 kcal/mole)(71) and cyclobutane (26 kcal/mole) (123). Although minor amounts of internal return products from the 1,5 bond fragmentation pathway cannot be discounted, it is clear that this is not an important rearrangement mode. While 129 and 130 comprise nearly 60% of the solvolysis products, there is little reason to believe that a rearrangement of 135 to 137 should be strongly favored over a rearrangement to 138. This conclusion is based on consideration of differences in strain relief, stereoelectronic factors, and stability of the product ions as potential

controlling factors in the rearrangement.

Although the strain energy of bicyclo[2.1.1]hexane has not been reported, the presence of a cyclobutane structural unit would demand a minimum value of 26 kcal/mole. Judging from a molecular model, the two carbon bridge does not increase strain appreciably. Thus the overall strain relief in the rearrangement of 135 to either 137 or 138 would be nearly the same and could not be responsible for a preference for the former.

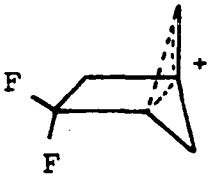
Estimates of the relative stability of ions 137 and 138 are more difficult to make though there is little reason to believe that the former is more stable. It may be assumed that the stability of the ethyl cation approximates and extreme lower limit to the stability of 138. The stability of the ethyl cation may be inferred from the acetolysis rate of ethyl tosylate, $k = 8.47 \times 10^{-6}$ sec^{-1} at 100° (75). Wiberg and Lowry (124) have reported that the solvolysis rate of 1-bromobicyclo[2.1.1]hexane in 40% aqueous ethanol ($k = 6.03 \times 10^{-5}$ sec^{-1}, 100°) exceeds that of 1-bromobicyclo[2.2.1]heptane by a factor 10^7 which is the opposite order of reactivity expected on the basis of I-strain in the corresponding bridgehead cations. However, the bicyclohexyl bromide gives completely rearranged products indicating that its high reactivity stems not from the inherently greater stability of the classical bicyclohexyl bridgehead cation but rather from a release of strain which accompanies ionization and simultaneous

rearrangement to a more stable ion. The leaving group in the bicyclohexyl bridgehead bromide occupies an equatorial position of the cyclobutane ring which permits a disrotatory opening of that ring concerted with ionization. That process could lead directly to the 3-methylenecyclopentyl cation which is presumably the precursor of methylcyclopentadiene, the product actually isolated. The analogous rearrangement of 138 would not readily occur since the resulting ion (136) is unstable. Thus I-strain should indeed be an important factor in the stability of 137 and leads to the prediction that 137 should be appreciably less stable than the 1-norbornyl cation. The stability of the latter can be inferred from the solvolysis rate of 1-bromobicyclo[2.2.1]heptane in 40% ethanol ($k = 6 \times 10^{-12}$, 100°). To the extent that these rate data reflect relative stabilities of 137 and 138 it may be concluded that the latter is probably the more stable ion.

One is also hard pressed to attribute a preferred rearrangement of 135 to 137 over 138 to more favorable stereoelectronic factors. If the bridgehead carbinyl carbon of 135 lies in the plane passing through C-1 and perpendicularly bisecting the cyclopropane ring (the geometry of the cyclopropylcarbinyl cation), it would be equidistant from C-1 and C-4. In that case the empty p orbital would be capable of interacting equally well with both the 1,4 and 1,5 bonds. Though, unlikely, any deviation from this geometry resulting

in an appreciably more efficient overlap of the p orbital with the 1,4 bond would indeed favor the rearrangement of 135 to 137. Critical evaluation of the importance of this point must await x-ray analysis of suitable bridgehead substituted bicyclopentanes, however.

The difficulties encountered in postulating 135 as the initial ionic species are removed if one assumes that ionization occurs with appreciable participation of the 1,4 bond to give a bridged ion such as 139 which shares characteristics of each of the classical ions 135, 136, and 137. Examination of a molecular model shows that the favored conformer of tosylate



139

127 has the leaving group trans to and coplanar with the 1,4 bond. To the extent that the favored ground-state conformation reflects the favored transition-state conformation, the 1,4 bond would be in the best orientation for participation of the developing p lobe during ionization.

It is interesting that rearrangements analogous to the 127 to 129 and 130 conversion have not been previously observed in bridgehead carbinyl esters of other bicyclo[n.1.0]alkanes

though they are common in other bicyclic systems. Bicyclo-[2.2.0]hexane-1-methyl p-nitrobenzoate; for example, gives exclusively 1-norbornanol derivatives (74). Dauben et al. (74) has summarized data for several bicyclo[n.m.o]alkane-1-methyl esters and has demonstrated a linear dependency of the log of the relative rate on the amount of strain energy released in the rearrangement. Thus the increasing difficulty in forming the planar carbonim ions is not reflected in the solvolysis rates. Rather the amount of strain available to assist ionization with participation by the zero-bridge bond is of overriding importance. If one attempts to predict a rate for the rearrangement of 127 to the bicyclo[2.1.1]hexane bridge-head alcohol derivative using Dauben's plot and a value of 26-28 kcal/mole for the change in skeletal strain one obtains a value which is between 10 and 100 times greater than the observed rate. Considering the approximation involved the calculated and observed values are surprisingly close and may be taken as further evidence for the participation of the 1,4 bond in the solvolysis of 127 as discussed above.

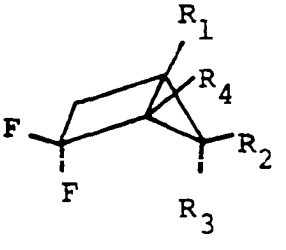
The NMR Spectra of 3,3-Difluorobicyclo[2.1.0]pentanes

Although nmr spectroscopy has proven to be a powerful tool in studies of organic fluorine compounds, correlation of spectral parameters with structure lags far behind that of most other classes of compounds. Reasons for this are the

comparitive rarity of organic fluorine compounds and the considerable variety found in fluorine chemical shifts and proton-fluorine spin-spin coupling. Improvements in synthetic techniques has resulted in the increasing use of fluorine as a controlling substituent or mechanistic probe and with it a growing need for diagnostic correlations between spectra and structure. One area where information is particularly sparse is the correlation of vicinal and long-range proton-fluorine coupling constants with molecular geometry. Ideal systems for these studies are rigid structures where the geometry is already known or can be estimated from molecular models. One such system is the 3,3-difluorobicyclo[2.1.0]pentane nucleus found in the previous section. Analysis of the spectra of these compounds would not only expand the limited knowledge of vicinal and long-range proton-fluorine coupling requirements, but also add to the limited information available on coupling parameters in bicyclo[2.1.0]pentanes. Although numerous bicyclopentanes are now known, only the spectrum of endo-bicyclo[2.1.0]pentan-2-ol has been analyzed in detail (125).

1-Carbomethoxy-3,3-difluorobicyclo[2.1.0]pentane 113, already available from previous work, gave spectra which looked potentially amenable to first-order analysis. Simplification of the spectra of 113 was accomplished by introducing deuteriums at C-4 and C-5. 1-Carbomethoxy-3,3-difluorobicyclo-[2.1.0]pentane-4-d (113-4-d) and 1-carbomethoxy-3,3-difluoro-bicyclo[2.1.0]pentane-5,5-d_2 were prepared as shown in Scheme

11 by substituting respectively triphenyltin deuteride and diazomethane-$\underline{d}_2$ for their nondeuterated analogs. Excessive overlap of multiplets in the spectrum of 113 precluded a complete analysis of that spectrum, and the final analysis was carried out on 1-cyano-3,3-difluorobicyclo[2.1.0]pentane (140), which was prepared by converting 113 to the corresponding amide followed by dehydration with phosphorus pentoxide. All spectra were to a close approximation first-order, and the coupling constants reported here were measured directly from the line spacings in the spectra. No attempt was made to determine the signs of coupling constants.



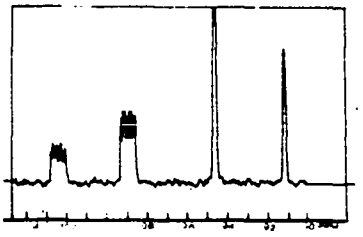
	R_1	R_2	R_3	R_4
113	CO_2CH_3	H	H	H
113-4-d	CO_2CH_3	H	H	D
113-5,5-$\underline{d}_2$	CO_2CH_3	D	D	H
140	CN	H	H	H

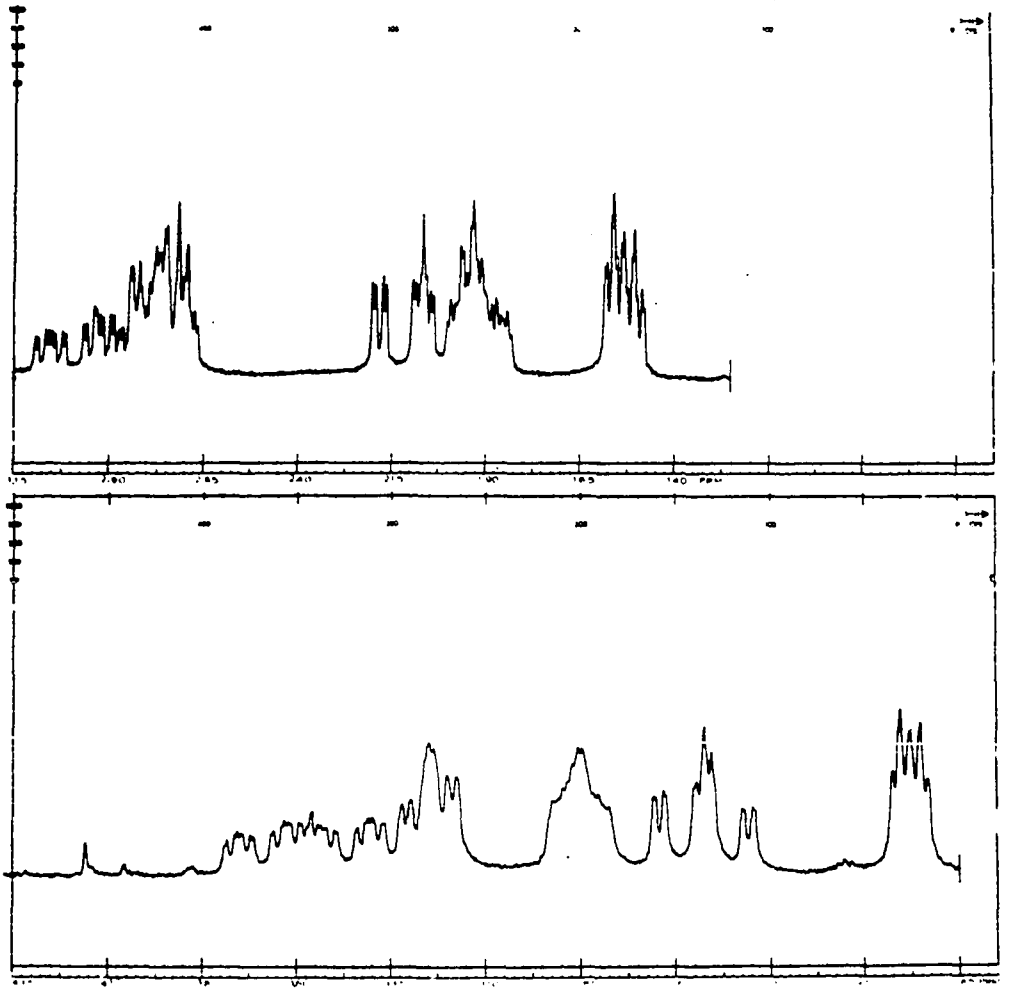
The fmr spectrum of 113 shown in Figure 11A is seen to be fundamentally an AB pattern with J_{FF} = 196 Hz, well within the known range of geminal fluorine coupling in cyclobutanes (126). The higher field fluorine (F_A) is strongly coupled to at least four protons giving a total of 32 well resolved lines. By contrast the lower field (fluorine (F_B) is coupled only very weakly to hydrogens and at the sweep width shown appears to

Figure 11A. 56.4 MHz fmr spectrum of 1-carbomethoxy-3,3-difluorobicyclo[2.1.0]pentane (113)

Figure 11B. 100 MHz pmr spectrum of 113 in CCl_4

Figure 11C. 100 MHz pmr spectrum of 113 with $Eu(dpm)_3$ added





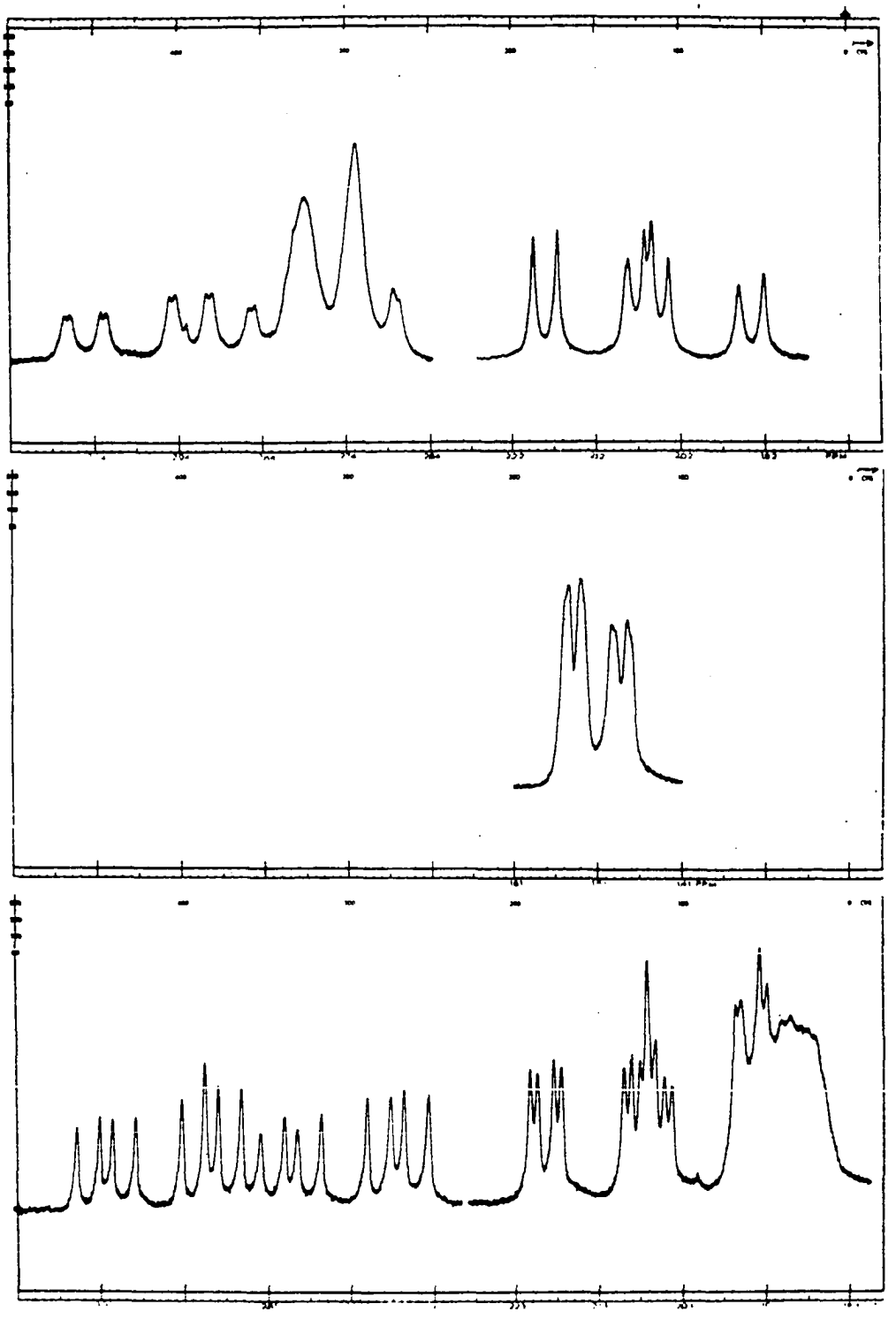
be a doublet. Even at narrow sweep widths the F_B multiplets were not sufficiently resolved to be analyzable although comparisons with the fmr spectra of the deuterium compounds indicated coupling of F_B to at least three hydrogens. The 100 MHz pmr spectrum of 113 shown in Figure 11B consists of five one-proton multiplets with the first centered at δ 1.52, the second at ca. δ 1.9 superimposed on the third at δ 2.07 and the fourth at ca. δ 2.7 superimposed on the fifth at δ 2.87 (ester methyl at δ 3.65 not shown). In the following discussion the five multiplets of 113 and the corresponding hydrogen atoms have been numbered from 1 through 5 in order of decreasing field. All attempts to simplify the spectrum of 113 through proton-proton decoupling were unsuccessful. However, superimposition of the multiplets were eliminated by employing the shift reagent Eu $(dpm)_3$ (127,128); as can be seen from that spectrum in Figure 11C, the relative positions of H_4 and H_5 are reversed. Unfortunately, the loss of resolution caused by shift reagent induced line broadening precluded the determination of coupling constants from that spectrum.

However, introduction of deuteriums at C-4 and C-5 served the dual purpose of providing decoupled spectra and permitting unambiguous assignments of chemical shifts. The 100 MHz pmr spectra of 113-5,5-d_2 and 113-4-d are shown in Figures 12A and 12B and C respectively. Complications arising

Figure 12A. 100 MHz pmr spectrum of 113-5,5-d_2

Figure 12B. 100 MHz pmr spectrum of 113-4-d

Figure 12C. 100 MHz pmr spectrum of 113-4-d continued



from superimposition of H_2 and H_3, and H_4 and H_5 in 113 made it impossible to complete the analysis of that spectrum, but the combination of substituting a cyano group for the carbomethoxyl and employing acetone-d_6 as the solvent eliminated the superimposition of multiplets without significantly altering the coupling constants. Thus the coupling data inferred from the labeled esters is directly transferable to the cyano derivative. It can be observed from the 100 MHz pmr spectrum of 140 shown in Figure 13 that the relative positions of H_4 and H_5 are reversed with respect to their positions in the ester.

The individual multiplets of each spectrum were analyzed by inspection to determine the apparent first-order coupling constants giving rise to the observed splitting pattern. In each case the first-order splitting networks drawn from the measured coupling constants gave an excellent visual fit with the experimental spectrum. The measured splittings in the individual multiplets are summarized in Table 5. In the case of 140 the two values of a coupling constant determined from the multiplets of coupled protons did not differ by more than 0.2 Hz. Comparison of the data in Table 5 leads to the coupling constants for 140 summarized in Table 6.

In the discussion which follows it will be shown that the multiplets should be assigned as shown below:

Figure 13. 100 MHz pmr spectrum of 1-cyano-3,3-difluoro-bicyclo[2.1.0]pentane

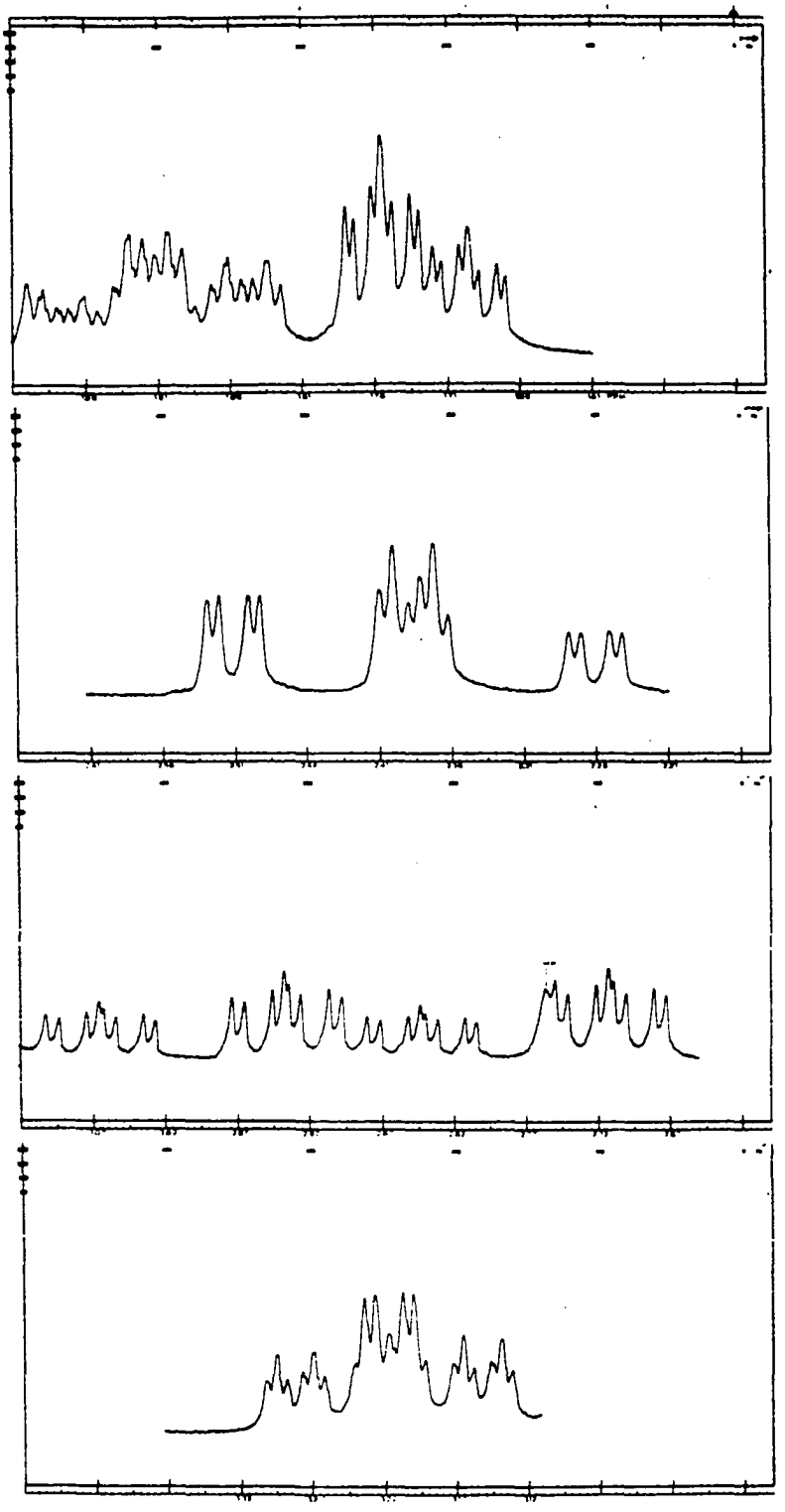


Table 5. Coupling constants in multiplets of 3,3-difluorobicyclopentanes

Compound	H_1	H_2	H_3
113-5,5-d_2	___	___	2.9
			11.2 13.2
113-4-d	.5 1.5	___[b]	.9 2.9
	5.5		11.2 13.2
113	.5 1.9	___[b]	.8 2.8
	2.5 5.3		10.9 12.8
140	.6 1.8	.2 .9 .9	.9 2.8
	2.5 6.0	2.8 5.9 6.9	11.9 12.9

[a]Due to inherent limitations in the instrumentation coupling constants measured from fluorine spectra are less accurate than those obtained from proton spectra.

[b]Values could not be obtained because of complete overlap with another multiplet.

[c]Not sufficiently resolved to obtain meaningful proton coupling data.

H_4			H_5			F_A[a]			F_B[a]	
	---[b]		.7		4.3		4.9	9.9	3.1	4.8
			12.6	21.9		19.9	196		196	
	——			2.8	4.3			10.4	---[c]	
			12.6	22.0		21.2	196		196	
	---[b]		.8	2.7	4.3	1.9	5.1	10.4	---[c]	
			12.7	22.4		20.5	196		196	
.75	.75	2.7	.9	2.8	4.0	1.3	5.2	10.4	---[c]	
6.2	6.9		12.9	22.2		18.5	192		192	

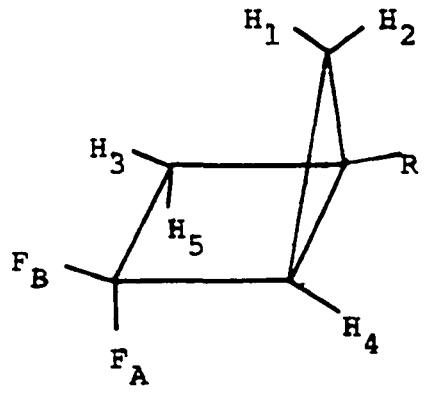
Table 6. Chemical shifts[a] and coupling constants[b,c] (Hz) for 1-cyano-3,3-difluorobicyclo[2.1.0]pentane (140)

δ_1	1.63	J_{12}	6.0	J_{23}	0.9	J_{34}	0	J_{45}	0.8	J_{5A} 22.2
δ_2	1.77	J_{13}	0	J_{24}	6.9	J_{35}	12.9	J_{4A}	6.2	J_{5B} 4.0
δ_3	2.27	J_{14}	2.6	J_{25}	2.8	J_{3A}	11.9	J_{4B}	.75	J_{AB} 192
δ_4	3.02	J_{15}	0	J_{2A}	0.2	J_{3B}	2.8			
δ_5	2.82	J_{1A}	1.8	J_{2B}	0.9					
δ_A	107	J_{1B}	0.6							
δ_B	98.4									

[a]Carbon tetrachloride solvent; reported for protons in ppm downfield from internal tms, for fluorine in ppm upfield from internal $CFCl_3$.

[b]From spectra where acetone-d_6 was the solvent.

[c]Where measured values in the two multiplets differed the average value is reported; proton-fluorine coupling constants are values measured from the proton spectra only.



R = CO_2CH_3, CN

It is apparent from the spectra and the data in Table 5 that the H_1 and H_2 multiplets arise from the cyclopropyl methylene hydrogens and that the H_4 multiplet arises from the bridgehead hydrogen. The fact that β-carboxyl substituents are known (114, pp. 228-229) to deshield cis hydrogens more strongly than trans hydrogens in cyclopropanes suggests that H_1 and H_2 arise from the endo and exo cyclopropyl methylene hydrogens respectively. The observation that J_{24} is appreciably larger than J_{14} confirms these assignments since cis vicinal coupling is always larger than trans vicinal coupling in cyclopropanes (114, p. 286).

The remaining hydrogens, 3 and 5, must then be the cyclobutyl methylene hydrogens. Other factors being equal, the endo cyclobutyl hydrogens in bicyclopentanes appear at higher field than the exo hydrogens (125). It has already been pointed out that a β-carboxyl substituent deshields cis hydrogens more strongly than trans hydrogens in three membered

rings, and the same trend is observed in planar five-membered rings (114, p. 223). Thus it would be reasonable to expect the same effect in a planar four-membered ring. Both effects would then work in the same direction to shield the endo cyclobutyl methylene hydrogens more strongly than the exo hydrogens. Thus H_3 and H_5 are assigned respectively to the endo and exo hydrogens on C-2. This argument is supported by the observation that reduction of ester 113 to the bridgehead carbinyl alcohol 107 is accompanied by a 0.5 ppm upfield shift of H_4 and H_5 while the chemical shift of H_3 is essentially unchanged. The fact that J_{25} is significantly larger than the other long-range coupling constants further supports these assignments since this type of geometry is known to be required for long range coupling (114, pp. 334-336).

This leaves only the stereochemistry of the fluorines unassigned. Williamson et al. (117) have determined vicinal proton-fluorine coupling constants in several rigid systems where the dihedral angle was 0°. Values ranged from 10.5 to 30.8 Hz with values near 20 Hz being typical. This suggests that the J_{5A} coupling of 22.2 Hz is a cis coupling constant from which it must be inferred that F_A occupies the exo position. Thus the J_{3A} value of 11.9 Hz must arise from a proton and a fluorine in a vicinal trans relationship in a planar cyclobutane. Judging from a molecular model the dihedral angle would be close to 120°. The 11.9 Hz value

then compares very favorably to the value of 12.2 Hz previously reported (117) in a case where the dihedral angle was 120°. It may also be noted that the J_{4A} value of 6.2 Hz seems consistent with this assignment with the dihedral angle between the bridgehead hydrogen and the exo fluorine estimated to be about 30°.

The interproton coupling constants determined for 140 are generally in excellent agreement with those previously reported for endo-bicyclo[2.1.0]pentan-2-ol (125), suggesting that similar values can be expected for other bicyclopentanes. The largest discrepancy occurs in the relative values of J_{34} and J_{45}, 0 and 0.8 Hz respectively with the corresponding values in the bicyclopentanol reported to be 1.00 Hz and .10 Hz respectively. The magnitudes are similar but reversed. The discrepancy should not be regarded as serious, however, since the differences in substitution are considerable and could easily be responsible for the small differences observed.

Perhaps the most astounding feature of the spectrum of 140 is the extremely small coupling between the endo-fluorine (F_B) and the cyclobutyl methylene hydrogens, H_3 and H_5. The cis coupling of only 2.8 Hz (J_{3B}) contrasts sharply with the 22.2 Hz value for the other cis coupling. Indeed the cis coupling here is even smaller than the trans coupling of 4.0 Hz (J_{5B}) which itself seems astonishingly small compared to the other trans coupling of 11.9 Hz. The small value for

J_{4B} is not unexpected since the dihedral angle between the endo fluorine and the bridgehead hydrogen approaches 90°, a relationship where vicinal proton-fluorine coupling is minimized (117). Values as small as .91 Hz have been reported for vicinal proton-fluorine coupling constants in some flexible cyclobutanes (129,130). However in each case puckered conformations were proposed in which the dihedral angle between the two weakly coupled nuclei was approximately 90° (diequational relationship). In the nmr spectrum of a difluorocyclobutanone, assumed to be a relatively planar molecule, none of the vicinal proton-fluorine coupling constants were smaller than 10.28 Hz. Although small local distortions of the bicyclopentane nucleus to relieve steric crowding of the substituents probably does occur, large deviations from a planar cyclobutane ring would undoubtedly be prevented by the accompanying increase in torsional strain. At the present time the small values of J_{3B} and J_{5B} would appear to be anomalous.

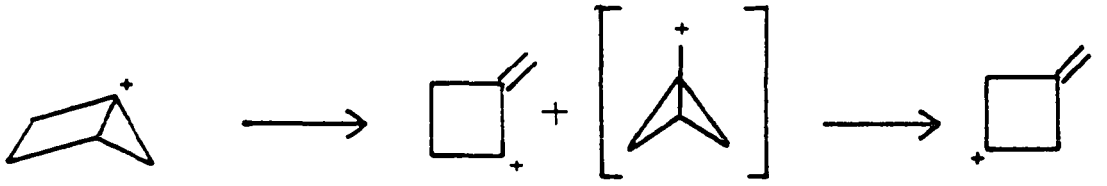
With regard to the long range proton-fluorine coupling in 140 it is noteworthy that the largest of these values are all relatively small and that the largest (1.8 Hz) is significantly smaller than the largest long-range H-H coupling (2.8 Hz). From a study of 5-substituted 7,7-difluoro-1,2,3,4-tetrachlorobicyclo[2.2.1]hept-2-enes Williamson (131) has concluded that H-F coupling over four bonds is maximized for nuclei in the

coplanar zigzag or W conformation analogous to the geometric requirement for maximum interproton coupling. Further, as with geminal and vicinal coupling in saturated systems the absolute magnitude of $^4J_{HF_{max}}$ (ca. 5Hz) was significantly larger than the corresponding long range H-H coupling (2-3 Hz) previously observed in bicycloheptenes. It is clear that despite similar geometries the four-bond proton-fluorine coupling in 140 differs significantly from the pattern found in the bicycloheptenes. Thus while the largest four-bond interproton coupling (J_{25}) does occur between nuclei in the zigzag relationship that geometry results in the smallest four-bond H-F coupling. This in turn suggests that four-bond H-F coupling may be more sensitive than interproton coupling to factors other than relative geometry of the nuclei. The F-C-C and H-C-C bond angles, strain in the carbon nucleus, and/or type of substitution may be important factors. Until additional data from other systems is available for comparison the long range proton-fluorine coupling observed here must be interpreted on a fragmentary and preliminary basis only.

Synthesis and Deamination of a 1-Aminobicyclo[2.1.0]pentane and 1-Aminobicyclo[3.1.0]hexane

The 1-bicyclo[2.1.0]pentyl cation (56) (or a nonclassical analog) has been postulated by Applequist and co-workers (79, 83) and others (80,82) as an intermediate in the rearrangement of the spiropentyl cation generated on deamination of

spiropentyl amine. That proposal rests chiefly on the assumption that 56 should undergo rearrangements characteristic of cyclopropyl and cyclobutyl cations to give products derived from cations 64 and 65 with the latter arising from the



56 64 66 65

initially formed intermediate 66. Although a recent deuterium labeling study (83) has provided some indirect support for the intermediacy of 56 in the spiropentyl cation rearrangement, that support is seriously undermined by the observation of Kinstle and co-workers (11,85) that anodic oxication of 3,3-dimethylbicyclo[2.1.0]pentane-1-carboxylate at carbon electrodes gives no products analogous to those obtained in the spiropentyl amine deamination. Despite the fact that only secondary products could be isolated, the electrolysis results directly suggest that similar bicyclopentyl cations are not involved in the two reactions and therefore imply that a 1-bicyclopentyl cation is not an intermediate in the spiropentyl cation rearrangement. However, an unambiguous mechanism to account for the electrolysis products has not been proposed and there might even be reason to doubt that a discrete

bridgehead cation is actually the specie undergoing rearrangement. Any mechanism which could reasonably account for the electrolysis products would seemingly have to involve an initial rearrangement of the bicyclopentyl cation which has no precedent in known rearrangements of either cyclobutyl or cyclopropyl cations. It is nevertheless conceivable that extreme distortion at the trigonal carbon and/or other factors associated with strain could result in unusual behavior for a 1-bicyclopentyl cation.

Questions which naturally arise are 1) is the bicyclopentyl cation unique in its arrangements or do less strained homologs behave similarly 2) are in fact bridgehead cations the actual intermediates in the electrolysis reactions and if so 3) do the electrolytically generated cations behave much differently from the corresponding cations generated by other methods.

It seemed likely that the first two questions might be answered by studying the electrolyses of homologous bicyclo-[n.1.0]alkane-1-carboxylic acids. The formation of 2-methylenecycloakanols and/or cycloalkene-1-methanols, normal products of cyclopropyl cation ring opening, would be strong evidence that bridgehead cations are indeed intermediates in the electrolyses and at the same time would establish the unique behavior of the bridgehead bicyclopentane cation. We therefore attempted the electrolysis of bicyclo[3.1.0]hexane-

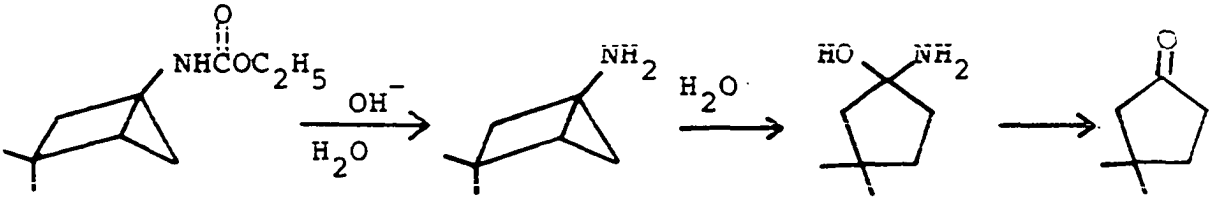
1-carboxylic acid prepared *via* a pyrazoline route from methyl cyclopentene-1-carboxylic acid and diazomethane. All attempts to prepare a pyrazoline from methyl cyclohexene-1-carboxyate and diazomethane failed, and original plans to study the electrolysis of bicyclo[4.1.0]heptane-1-carboxylic acid were abandoned. Unfortunately, meaningful results were not obtained in the electrolysis of the bicyclohexane acid as a result of exceedingly low material balances and/or extremely complex product mixtures. In a typical experiment 2.04g of acid in 500 ml of water was neutralized with a slight excess of potassium hydroxide and then electrolyzed employing a copper cathode and carbon anode with electrode potential differences of 40 to 100 volts [conditions similar to those previously employed for the bicyclopentane acid (11,85)]. While .91g (45%) of unchanged acid was recovered only .110g of neutral products accounting for approximately 10% of the reacted acid could be found. The infrared spectrum of the crude product mixture indicated both carbonyl and hydroxyl containing products, and a preliminary vpc analysis indicated at least four major components, but further attempts to characterize these products were not made. On the assumption that the low material balance was a result of extensive degradative oxidation of the alcoholic primary electrolysis products, the electrolysis was conducted in methanol in order to trap the intermediate cations as methyl ethers, expected to be stable

under the reaction conditions. In a preliminary experiment electrolysis of phenylacetic acid in methanol with sodium methoxide as the supporting electrolyte produced the expected benzyl methyl ether in 80% yield. By contrast electrolysis of the bicyclohexane acid under similar conditions resulted in only a relatively small improvement in material balance and the production of a complex mixture of products consisting of at least ten poorly resolved components in approximately equal amounts (vpc). The nmr spectrum of the apparent major component consisted of a broad aliphatic envelope centered at δ 1.6 and no less than seven lines of similar intensity plus several smaller absorptions in the O-methyl region, δ 3.1-3.4. Electrolyses of olefinic substrates in methanol frequently leads to poly O-methylated products resulting from addition of methanol across the double bonds (132) and it seems likely that that is what occurred in this instance. Although with considerable effort it might have been possible to identify these products, the absence of significant amounts of primary products would have made any mechanistic interpretation ambiguous at best.

With the failure of electrolysis to provide meaningful results, an alternative unambiguous method of generating the cations applicable to both bicyclopentane and its homologs was sought. Although deamination of bridgehead amines would normally be the method of choice, results of previous attempts (11) to synthesize 1-amino-3,3-dimethylbicyclo[2.1.0]pentane

(141) had indicated that that molecule was highly unstable in protic media making the possibility of its isolation for reaction purposes remote at best. Nevertheless, the absence of other more attractive alternatives necessitated the reconsideration of a bridgehead amine synthesis.

In an earlier attempt to prepare 141 by basic hydrolysis of the bridgehead carbamate 142 (prepared via a Curtius route from the bridgehead methyl ester) 3,3-dimethylcyclopentanone was obtained as the only product. It was suggested that 141 formed upon hydrolysis of 142 undergoes a rapid electrophilic attack by water as a result of enhanced nucleophilicity of the 1,4 bond induced by the amino substituent to give a hemiaminal which is converted by further hydrolysis to the ketone. It is well known that hydrocarbon bicyclopentanes are readily

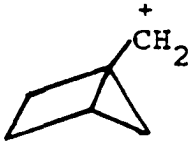


142 141

attacked at the bridgehead bond by a variety of electrophiles and that these reactions are severely retarded by electron withdrawing bridgehead substituents (11). It would therefore be expected that susceptibility to electrophilic attack at the 1,4 bond would be enhanced by electron donating substituents.

Consequently it might seem illogical to expect a bicyclopentane bridgehead amine to be stable in strongly acidic media. Nevertheless we speculated that the bridgehead amine, generated *in situ* in strong acid, as for example by hydrolysis of an isocyanate, might exist as a stable ammonium ion 143. The strong negative inductive effect of the ammonium substituent would make the bridge bond extremely resistant to further electrophilic attack. Although some free amine would be present at equilibrium, effective competition of N-protonation with C-protonation would result in long term stability for the amine in acid solution. It is interesting to contrast the expected stability of the bridgehead ammonium ion with that of the structurally analogous bridgehead carbinyl cation 106.

143

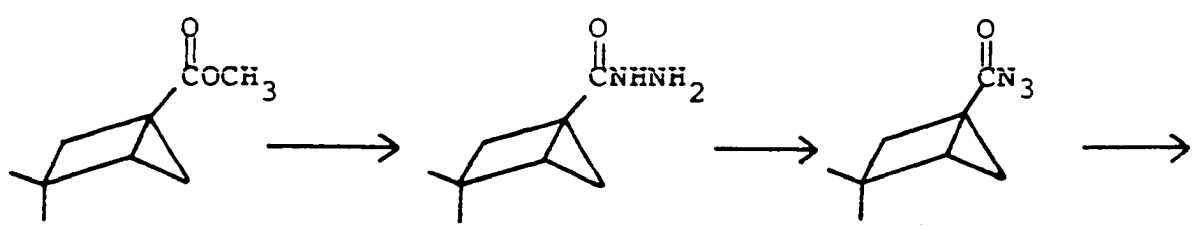


106

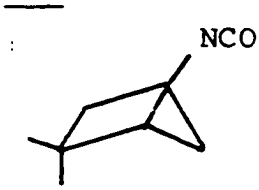
While the latter ion rearranges in its nascent state to a species closely resembling the 3-methylenecyclopentyl cation with considerable relief of strain, the analogous rearrangement of 143 would be prevented by the inability of nitrogen to expand its valence shell.

The 3,3-dimethylbicyclopentyl system was chosen for actual study because of advantages in availability and diagnostic utility of the methyl substituents in structure determinations

and mechanistic considerations. Acid hydrolysis of the bridgehead isocyanate seemed the most suitable means of generating the amine in situ since isocyanates are rapidly hydrolyzed to amines in aqueous acid and the electron withdrawing effect of the isocyanate substituent would retard electrophilic attack on the bicyclic nucleus before the ammonium ion could be generated. 3,3-Dimethylbicyclo[2.1.0]-pentane-1-isocyanate was synthesized via the Curtius route outlined in Scheme 15 using modified procedures of Welch (11). Treatment of 1-carbomethoxy-3,3-dimethylbicyclo[2.1.0]pentane 144 with 95% hydrazine at room temperature produced the acid hydrazide 145 as a crystalline compound easily purified by recrystallization. The pure hydrazide on treatment with nitrous acid gave the acyl azide 146 (ν = 2142 cm^{-1}) which on pyrolysis in refluxing benzene was slowly converted to the isocyanate 147 (ν = 2275 cm^{-1}). When crude 147 was treated with 6 M



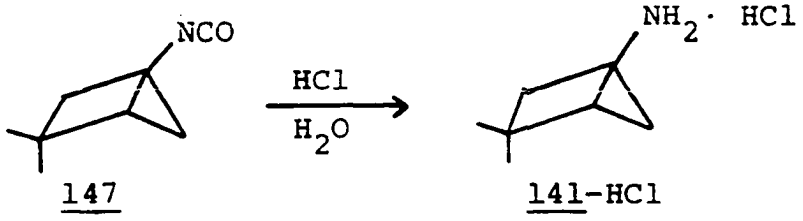
144 145 146



147

Scheme 15

aqueous hydrochloric acid at 75° for 1 hour followed by extraction of neutral impurities, treatment with decolorizing carbon, and removal of water under vacuum, the bicyclic amine hydrochloride 141-HCl was obtained as a pale yellow crystalline solid in 38-41% yield. Titration of the product so obtained with aqueous sodium hydroxide to a phenolphthalein end point indicated a purity of 95%. The 100 MHz pmr spectrum of 141-HCl in trifluoroacetic acid shown in Figure 14 shows the characteristic pattern of 1-substituted 3,3-dimethylbicyclo[2.1.0]-pentanes. Especially diagnostic are the positions of the methyl singlets at δ 0.9 and 1.4. The chemical shift of the amine protons at δ 6.7 is typical for amine salts in trifluroacetic acid (133). The appearance of the amino protons as a triplet (J_{NH} = 53 Hz) is indicative of a very slow rate of exchange.



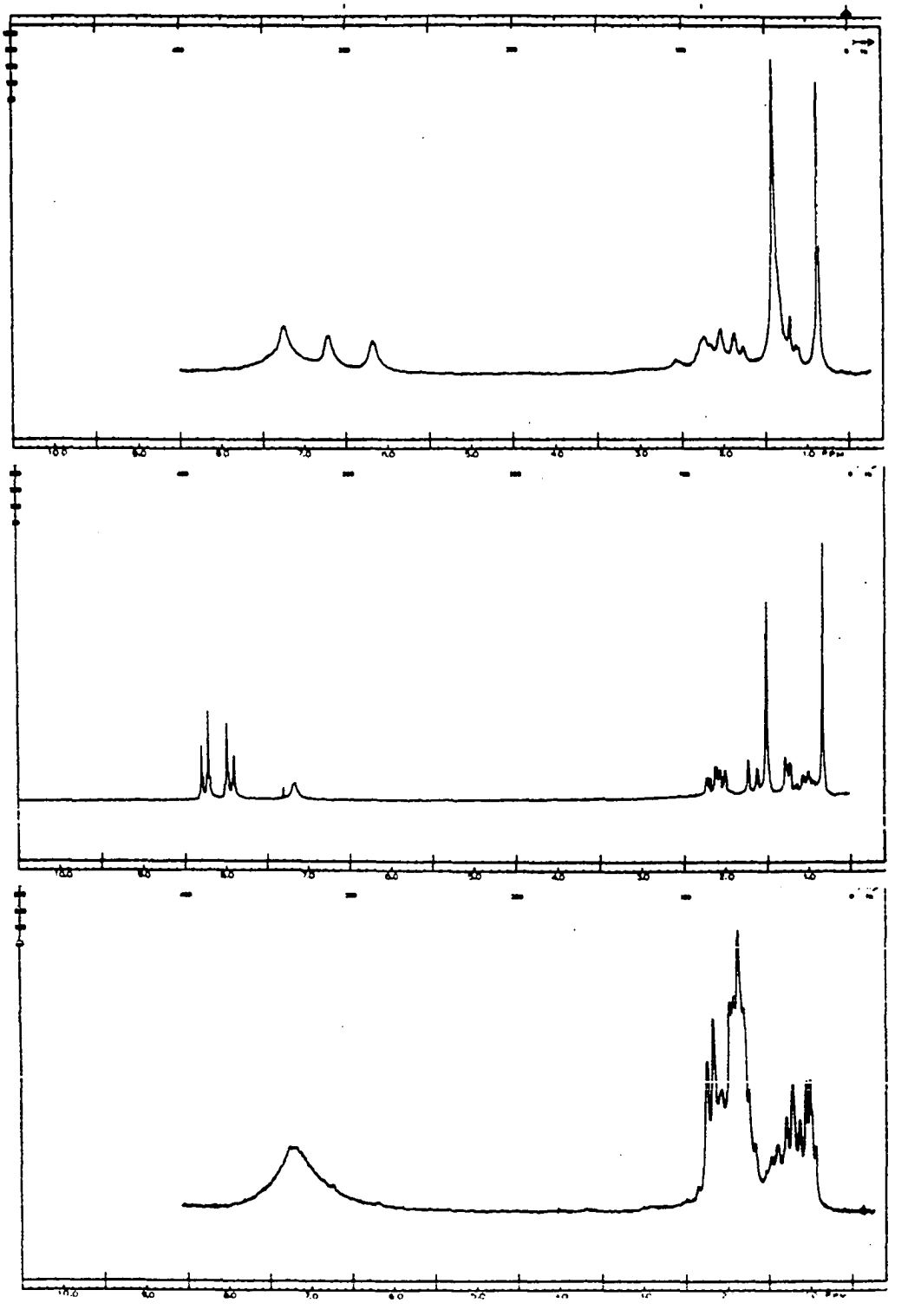
147 141-HCl

Although the hydrochloride salt was indefinitely stable when stored as the solid at 0° and showed only minor decomposition after several weeks in aqueous solution at room

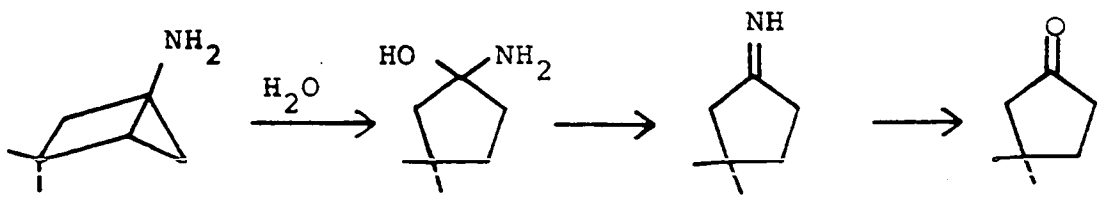
Figure 14. 100 MHz pmr spectrum of 3,3-dimethylbicyclo-[2.1.0]pentane-1-amine hydrochloride (141-HCl)

Figure 15. 100 MHz pmr spectrum of 1-p-nitrobenzamido-3,3-dimethylbicyclo[2.1.0]pentane (148)

Figure 16. 100 MHz pmr spectrum of bicyclo[3.1.0]hexane-1-amine hydrochloride

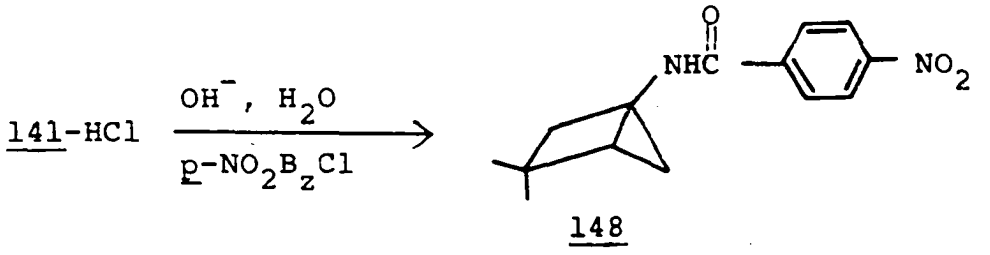


temperature, all attempts to liberate the free amine 141 by treatment of the hydrochloride with aqueous base resulted in the immediate destruction of the bicyclic nucleus and eventual formation of 3,3-dimethylcyclopentanone. When an aqueous solution of 141-HCl was treated with a slight excess of aqueous base followed by immediate extraction with ether, a nonbicyclic product (nmr) was obtained which on standing in the presence of moisture for several minutes was converted to 3,3-dimethylcyclopentanone. It seems likely that the observed intermediate product is either the hemiaminal or the imine resulting from a facile addition of water across the 1,4 bond of 141 as suggested previously (11).



141

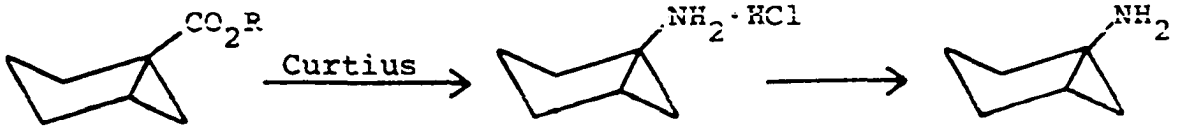
Despite its ready destruction in aqueous media the free amine could be trapped as its p-nitrobenzamide 148 when generated in the presence of p-nitrobenzoyl chloride. Amide 148 gave a satisfactory combustion analysis and exhibited a molecular ion at m/e 260 in its mass spectrum. The nmr spectrum of 148 (Figure 15) again shows the characteristic



148

pattern of 3,3-dimethylbicyclopentanes being very similar to that reported for the bridgehead ethyl urethane 142 (11). These data place the structure of 141-HCl on firm ground.

1-Aminobicyclo[3.1.0]hexane hydrochloride (149-HCl) was synthesized by an analogous Curtius route starting with methyl or ethyl bicyclo[3.1.0]hexane-1-carboxylate. The nmr spectrum of 149-HCl in trifluoroacetic acid (Figure 16) contains a



149-HCl 149

broad hump for the amino protons indicative of a faster rate of exchange than observed for 141-HCl. The benzamide derivative of 149 gave spectral and combustion analytical data consistent with its structure. In contrast to the bicyclopentyl case the free bicyclohexyl amine 149 (cyclopropyl

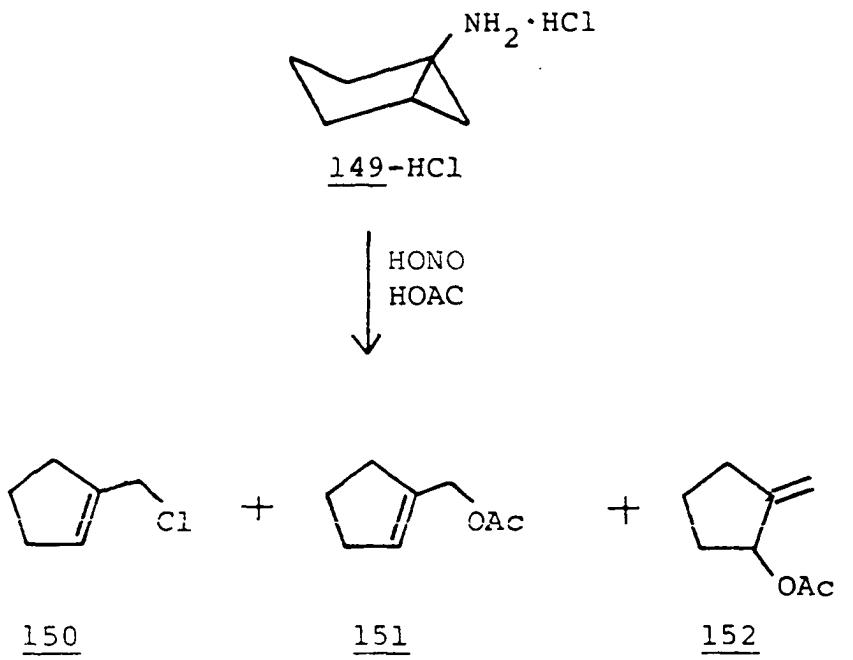
methylene protons at δ 0.3-0.7) could be isolated from basic aqueous solution without difficulty and indeed could be distilled at 70° without appreciable decomposition. The vast difference in stability between the free bicyclopentyl and bicyclohexyl bridgehead amines underscores the importance of strain in controlling the reactions of bicyclopentanes.

Deaminations

Glacial acetic acid was chosen as the deamination solvent in favor of the more common aqueous media on the assumption that certain acetates might be more stable than their corresponding alcohols under the reaction conditions and/or during isolation. Nitrous acid was generated in situ by the portionwise addition of granular sodium nitrite to solutions of the amines at room temperature. Products were analyzed and isolated by gas chromatography and identified in most cases by comparison with authentic specimens.

Bicyclohexyl amine Deamination of 149-HCl (Scheme 16) proceeded smoothly to give three major products 150, 151, and 152 along with smaller amounts of three components which were not investigated (Table 7). Deamination of 149 gave a product mixture consisting of 98% 151 and 152 in a ratio of 43/57.

The structure of 151 was confirmed by comparison of its spectral properties with those of an authentic specimen prepared by the method of Piaux (134). The structure of 150 follows clearly from its mass spectrum (molecular ions at m/e



149-HCl

150 151 152

Scheme 16

Table 7. Deamination products of 1-aminobicyclo[3.1.0]hexane (hydrochloride)

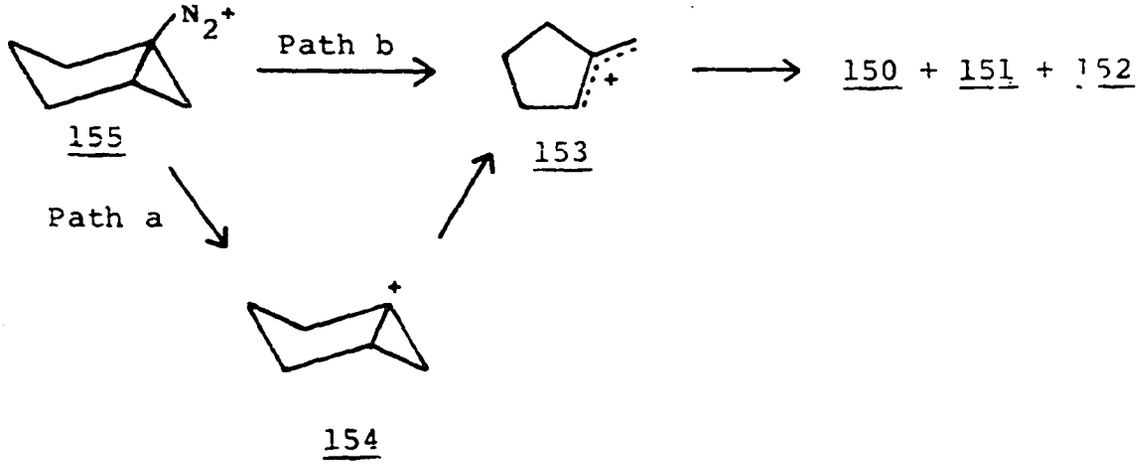
Component[a]	Relative abundance[b]	Identification
1	2.6	unidentified
2	19.0	150
3	.8	unidentified
4	34.3	152
5	3.5	unidentified
6	39.8	151

[a]Listed in order of increasing retention time (FFAP column).

[b]Relative peak areas in the gas chromatogram uncorrected for differences in detector response.

116 and 118) and nmr spectrum which is virtually identical in its common features with that of 151. The structure of 152 was confirmed by spectral comparisons with an authentic specimen prepared by treating 2-methylenecyclopentanol (135) with acetic anhydride/pyridine.

The deamination products of 149 and 149-HCl appear to result exclusively from electrocyclic fission of the C_5-C_6 bond in the fashion commonly observed in carbonium ion reactions of cyclopropane derivatives (Scheme 17). The products clearly arise from trapping of the intermediate secondary allylic cation 153 which in turn can arise either from ring opening of the bridgehead cation 154 (Scheme 17, path a) or from concerted nitrogen loss and ring opening in the diazonium ion 155 (Scheme 17, path b). Our data do not

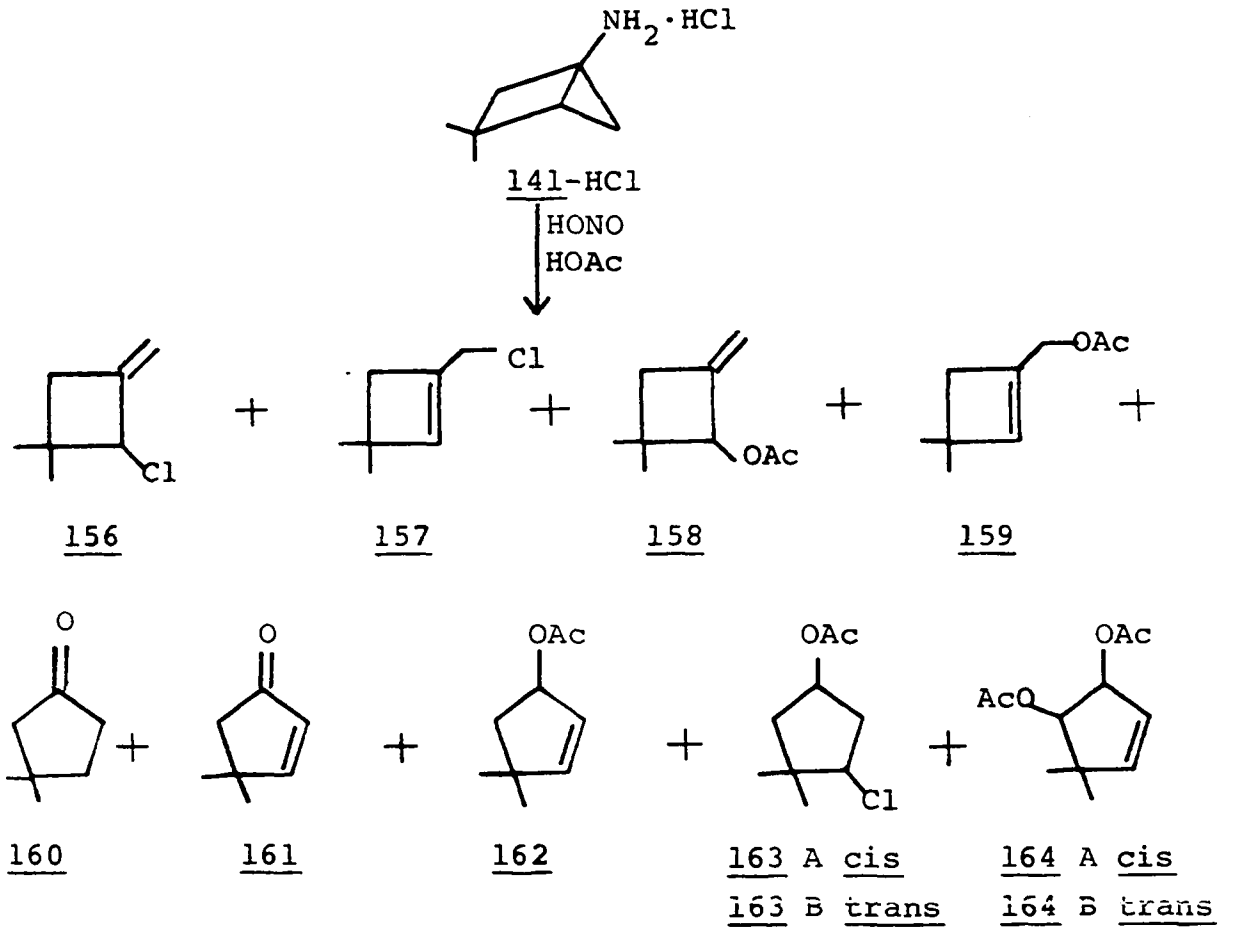


Scheme 17

distinguish between the two paths but Kirmse et al. (48,49,50) have recently offered evidence that cyclopropyl diazonium ions decompose at least in part via a two step pathway with cyclopropyl cations as discrete intermediates. In these cases cyclopropyl cation trapping products are sometimes observed, though in very low yield. The possibility that one or more of the minor products (Table 7) formed on deamination of 149-HCl arise from trapping of 154 cannot presently be completely excluded, although cyclopropanes were not detected in nmr spectra of the crude reaction mixtures.

Bicyclopentyl amine Deamination of 141-HCl (Scheme 18 and Table 8) gave a complex mixture of products consisting of 156, 157, 158, 159, 160, 161, and 162 as well characterized products along with four other products tentatively assigned structures 163A, 163B, 164A, 164B and three minor products which were not obtained in sufficient quantity for investigation.

Compounds 160 and 161 were identified by spectral comparisons with authentic specimens prepared by literature procedures (136,137). Compounds 159 and 162 gave spectra identical to authentic specimens obtained on treating 3,3-dimethylcyclobutene-1-methanol (11) and 4,4-dimethyl-2-cyclopenten-1-ol (136) respectively with acetic anhydride/pyridine. The structure of 158 rests on its spectra. The mass spectrum of 158 contains a weak molecular ion at m/e 154;



Scheme 18

its infrared spectrum contains a carbonyl absorption at 1746 cm^{-1}, absorptions for the exocyclic methylene at 3100, 1695 and 898 cm^{-1}, and a gemdimethyl band at 1378 cm^{-1}. Most informative is the 100 MHz spectrum which consists of three three-proton singlets at δ 1.01, 1.26 and 2.04 (ring and ester methyl groups) a two proton multiplet at δ 2.20 (ring

Table 8. Deamination products of 1-amino-3,3-dimethylbicyclo-[2.1.0]pentane hydrochloride

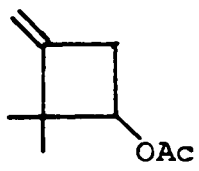
Component[a]	Relative abundance[b]	Identification
1	3.76	156
2	8.94	157
3	1.0	unidentified
4	17.25	158
5	11.05	160
6	26.10	159
7	3.18	162
8	9.51	161
9	1.0	unidentified
10	.7	unidentified
11	6.76	163A or B[c]
12	4.35	163A or B[c]
13	4.47	164A or B[c]
14	2.87	164A or B[c]

[a]Listed in order of increasing retention time (FFAP column).

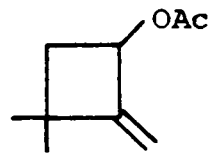
[b]Relative peak areas in the cromatogram uncorrected for differences in dector response.

[c]Tentative identification.

methylene), and one proton multiplets at δ 4.85, 4.99 and 5.05 (the latter two overlap) for the remaining hydrogens. Significantly, each of the multiplets in the nmr spectrum of 158 resembles a quartet with splittings of 2.2 ± .2 Hz. This suggests that each hydrogen is coupled about equally to three nonvicinal hydrogens. The 2.2 Hz coupling is well within the range of allylic and cyclobutane cross ring coupling but is too small for cyclobutane vicinal coupling (114, p. 287). Thus the absence of vicinal coupling distinguishes 158 from the isomeric alternatives 165 and 166. The nmr spectra of 1-carbomethoxy-2-methylene-3,3-dimethylcyclobutane (11), a



165



166

model for 166, and 2,2-dimethyl-3-acetoxycyclobutanone which we prepared as a model for 165 did clearly show the expected vicinal coupling and were completely dissimilar to the nmr spectrum of component 4 (Table 8) confirming the above assignment.

Although components 1 and 2 (Table 8) were not clearly resolved, the presence of molecular ions at m/e 130 and 132 in the mass spectrum of the two component mixture and a comparison

of the mixture's nmr spectrum with spectra of 158 and 159 leaves no doubt that these components are the corresponding chlorides 156 and 157. The only significant difference between the nmr spectra of acetates 158 and 159 and the chlorides 156 and 157 (other than the obvious absence of ester methyls in the latter) is the expected upfield shift of hydrogens on the heteroatom bearing carbon in the chlorides relative to the acetates.

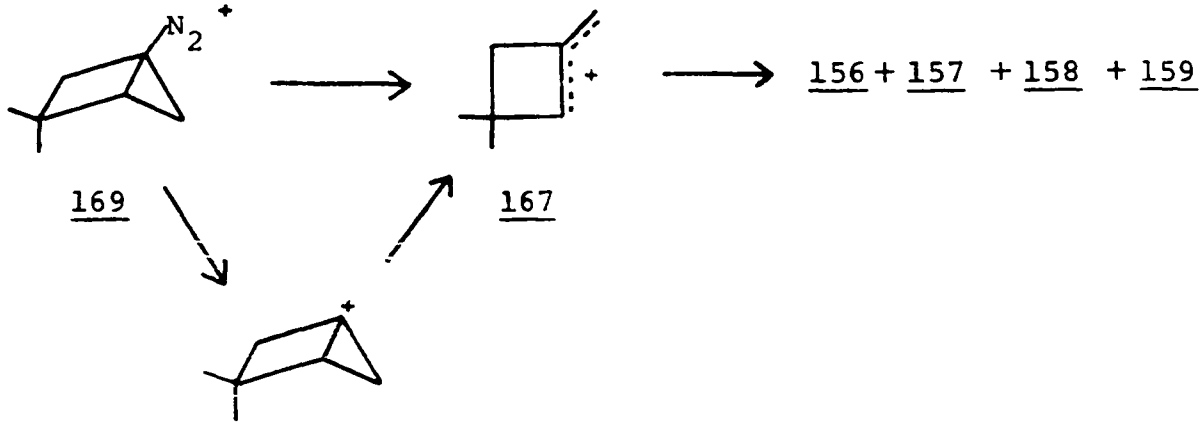
Components 11 and 12 (Table 8) had nearly identical infrared spectra and very similar nmr spectra indicative of closely related isomers. Only component 11 exhibited apparent molecular ions (very weak) at m/e 190 and 192 in its mass spectrum. The infrared spectra of both components contained a strong carbonyl absorptions at 1750 cm^{-1} and a gem-dimethyl doublet at 1365 and 1375 cm^{-1}, but no evidence of olefinic unsaturation. The 100 MHz nmr spectrum of component 11 consisted of singlets at δ 1.04 (3H), 1.15 (3H) and 1.96 (3H) and multiplets at δ 1.5 (1H, doublet of doublets, J = 5 Hz and 14 Hz), δ 1.95-2.45 (3H, complex), δ 3.95 (1H, triplet, J = 8 Hz) and δ 5.11 (1H, heptet). Unfortunately, sufficient analytically pure quantities of this component were not obtained for combustion analysis so that a completely unambiguous structure assignment cannot be made. Nevertheless the spectral data are readily interpreted in terms of compounds 163 A or B. The multiplet at δ 5.11, assigned to the proton

on the acetoxy bearing carbon, consists of a symmetrical seven line pattern with the inner five lines broadened; spacings and intensities are consistent with coupling to four vicinal hydrogens with approximate coupling constants of 5,5,8, and 8 Hz. The triplet at δ 3.95 is assigned to the proton α to the chlorine, with 8 Hz coupling to the two vicinal hydrogens. The 5 and 14 Hz splittings in the doublet of doublets at δ 1.5 is indicative of coupling to one geminal and one vicinal hydrogen requiring that this multiplet be assigned to one of the hydrogens of the ring methylene adjacent to the methyl groups. The remaining multiplet is assigned to the remaining three hydrogens. In the nmr spectrum of component 12 the proton on the acetoxy bearing carbon appears at δ 4.95 and though not well resolved has the same overall appearance as the corresponding multiplet in component 11. The proton α to chlorine in component 12 appears as a doublet of doublets at δ 3.72 with splittings of 7 and 8.7 Hz. One of the protons of the δ 1.95-2.45 multiplet in component 11 is shifted downfield to δ 2.77 in component 12 and appears as a symmetrical multiplet of five broadened lines equally spaced at 7.5 Hz. The relative intensities indicate that this is actually a doublet of triplets with fortuitous overlap of the two inner lines. This pattern can be interpreted as arising from coupling to two vicinal protons (J = 7-7.5 Hz each) and one geminal proton (J = 15 Hz), and is therefore assigned to one

of the hydrogens of the methylene adjacent to the chlorine. The remaining ring hydrogens appear as a complex multiplet from δ 1.5-2.2 and the methyl singlets appear at δ 1.08, 1.15, and 1.99. Although it should be reemphasized that these assignments are only tentative, we are unable to suggest alternative structures which are consistent with the spectral data or mechanistically reasonable.

Components 13 and 14 also gave very similar infrared and nmr spectra which indicated they were a closely related isomeric pair. The mass spectra were also very similar but neither contained a molecular ion. The infrared spectra of both components contained sharp carbonyl absorption at 1751 cm^{-1} and a gem-dimethyl band at 1378 cm^{-1}. Although the C=C stretching region was transparent there was a band at 3080 cm^{-1} in both spectra attributable to an olefinic C-H stretch. The 100 MHz nmr spectrum of component 13 consisted of singlets at δ 1.0 (3H), 1.2 (3H), 2.02 (3H), and 2.07 (3H) along with a doublet at δ 4.95 (1H, 5 Hz) a multiplet at δ 5.55 (2H) and a perterbed doublet at δ 5.7 (1H, 5 Hz). Component 14 gave a nearly identical nmr spectrum containing essentially the same bands with slightly different chemical shifts. Although the absence of molecular weight data and good combustion analytical data makes definitive structure assignments impossible, the data suggest structures 164 A and B as likely possibilities.

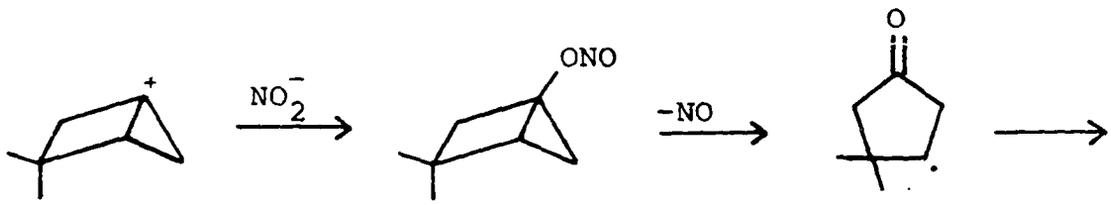
It is clear that chlorides 156, and 157 and acetates 158 and 159, which together amount to more than 56% of the deamination products, must be derived from trapping of the intermediate allylic cation 167 which in turn would result from the electrocyclic opening of the bicyclopentyl bridgehead cation 168 or the corresponding diazonium ion 169 (Scheme 19) as was observed with the bridgehead bicyclohexyl amine. However, the ketones 160 and 161 are completely unexpected products which indeed cannot arise through purely carbonium ion processes, and whose origin is not at all obvious. It



Scheme 19

will be recalled that 160 and 161 were major products from the electrolytic generation of the bridgehead cation (11,85) suggesting perhaps a common origin in the two reactions. However, electrolysis of an alcoholic primary product, the

explanation advanced previously, obviously cannot apply here. Our present feeling is that the ketones arise from unrelated processes in the electrolysis and deamination reactions. The observation by DePuy (41) that cyclopropyl nitrites at -50° spontaneously rearrange to nitrosoketones via presummed cyclopropoxy radicals or their ring-opened analogs suggests the possible explanation for 160 and 161 which is outlined in Scheme 20. Trapping of the bridgehead cation 168 by nitrite



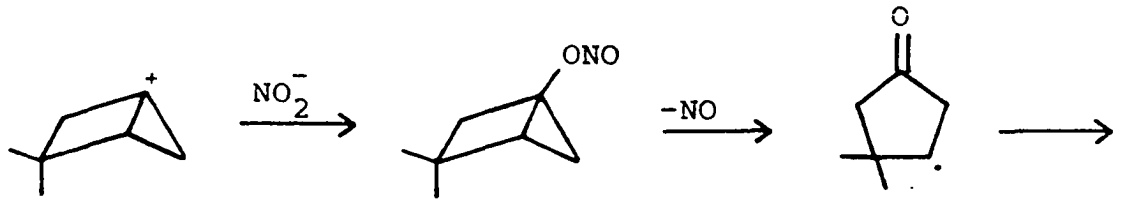
168 170 171

160 + 161

Scheme 20

ion would produce the cyclopropyl nitrite ester 170 which would undergo a spontaneous loss of NO followed by or in concert with fragmentation of the bridge bond to give the ketonic radical 171. Simple disproportionation of 171 would then give 160 and 161 directly. An attractive feature of this explanation is that it requires 160 and 161 to be formed in similar amounts as is actually observed. The effectiveness in trapping of 168 by nitrite ion could stem from the fact that

explanation advanced previously, obviously cannot apply here. Our present feeling is that the ketones arise from unrelated processes in the electrolysis and deamination reactions. The observation by DePuy (41) that cyclopropyl nitrites at -50° spontaneously rearrange to nitrosoketones via presummed cyclopropoxy radicals or their ring-opened analogs suggests the possible explanation for 160 and 161 which is outlined in Scheme 20. Trapping of the bridgehead cation 168 by nitrite



168 170 171

160 + 161

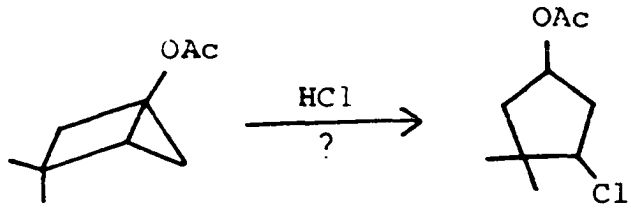
Scheme 20

ion would produce the cyclopropyl nitrite ester 170 which would undergo a spontaneous loss of NO followed by or in concert with fragmentation of the bridge bond to give the ketonic radical 171. Simple disproportionation of 171 would then give 160 and 161 directly. An attractive feature of this explanation is that it requires 160 and 161 to be formed in similar amounts as is actually observed. The effectiveness in trapping of 168 by nitrite ion could stem from the fact that

nitrite may be the predominant counter ion paired with the diazonim ion 169. Loss of nitrogen would then result in a bridgehead cation-nitrite ion pair. The considerable distortion at the trigonal carbon of the cation would undoubtedly result in a high degree of reactivity for that specie leading to a fairly efficient collapse of the ion pair.

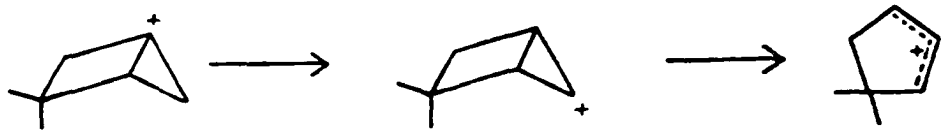
The above explanation would imply that other trapping products of 168, notably the bridgehead acetate 172, should be found if 168 becomes solvated before it rearranges. Although the existence of 172 as one of the unidentified minor products cannot be completely excluded, it is unlikely that it would have been stable under the reaction conditions. Welch (11) prepared 172 and found that it underwent slow decomposition in the presence of protic solvents even at subzero temperatures. It is highly probable that 172 would succumb to electrophilic attack on the bridgehead bond in the presence of strong acid catalysts such as hydrogen chloride which is present in the reaction mixture. Although the direction of attack would be difficult to predict, it is quite possible that 163 would be formed in such a process.

Acetate 162, though a minor product in the deamination is particularly interesting since it corresponds to alcohol 72, the supposed primary product in the anodic oxidation of the bridgehead carboxylate 68. A mechanism suggested earlier by



172 163

Welch to account for the alcohol and which could also apply in the present case involved a hydride shift in the bridgehead cation followed by or in concert with an electrocyclic opening of the bridgehead bond and trapping of the resulting cation by



solvent. Whatever the actual mechanism it is clear that a hydrogen migration must be involved at some stage. Deuterium labeling would appear to be the most promising method of attacking this problem.

Although plausible mechanisms have now been advanced to account for greater than 90% of the deamination products of 141-HCl, the presence of 164 defies adequate explanation. Since the structure assignment for 164 is highly tentative it

would be inappropriate to indulge in excessive speculation as to its origin. Considering, however, that components 13 and 14 are minor secondary reaction products, it is unlikely that they are significant in considering the important characteristics of the bicyclopentane bridgehead cation.

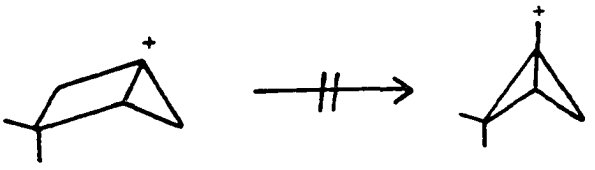
It is of significance that nearly all the deamination products of the bicyclopentyl amine can be explained in terms an initial trapping or electrocyclic opening of a bicyclopentyl bridgehead cation. Thus except for an apparently greater susceptibility to trapping which could result from strain enhanced reactivity, the bicyclopentyl ion is essentially the same in its behavior as the less strained bicyclohexyl bridgehead cation. The latter ion shows only the characteristic electrocyclic ring opening reactions of cyclopropyl cations.

It would appear then that the deaminatively generated bicyclopentyl bridgehead cation and the species produced on anodic oxidation of the bicyclopentane bridgehead carboxylate are dissimilar since products derived from the latter apparently do not arise either from trapping or an electrocyclic ring opening of the bridgehead cation. However, a possibility which has not been ruled out is that the ketonic electrolysis products 70 and 71 arise from the third electrolysis product, 3,3-dimethylcyclopentanone under the electrolyses conditions. The latter compound could arise from the

rearrangement of 3,3-dimethylbicyclo[2.1.0]pentan-1-ol which would undoubtedly occur in an aqueous environment. Although this possibility seems unlikely, it must be experimentally disproven before it can be rigorously concluded that the deamination and electrolysis intermediates are different species.

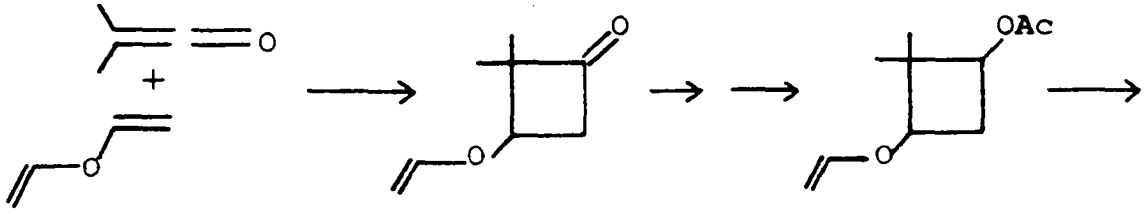
The electrolysis results had previously been interpreted (11) as strong evidence against the intermediacy of a bicyclopentyl bridgehead cation in the spiropentyl cation rearrangement. In direct contrast to that conclusion the deamination results reported here are entirely consistent with an intermediate bicyclopentyl cation in the spiropentylamine deamination, though not exactly as proposed by previous authors (79,80,82,83). The 2-methylenecyclobutanol formed in this reaction was attributed solely to the electrocyclic ring opening of the bicyclopentyl bridgehead cation which is consistent with the deamination results for the bicyclopentylamine. However, it was suggested that the 3-methylenecyclobutanol observed in this reaction arises from parallel routes involving rearrangements of both the spiropentyl cation and the bicyclopentyl cation to the bicyclo[1.1,0]butane-1-methyl cation. This proposed rearrangement of the bicyclopentyl cation is not supported by the observation of 2,2-dimethyl-3-methylenecyclobutyl acetate (165) among the deamination products of 141-HCl. Admittedly, unfavorable nonbonded

interactions between the endo hydrogen and the endo methyl substituent in the 2,2-dimethylbicyclo[1.1.0]butane-1-methyl cation (173) might reduce the tendency of the 3,3-dimethyl-bicyclo[2.1.0]pentane-1-cation (168) to rearrange to that

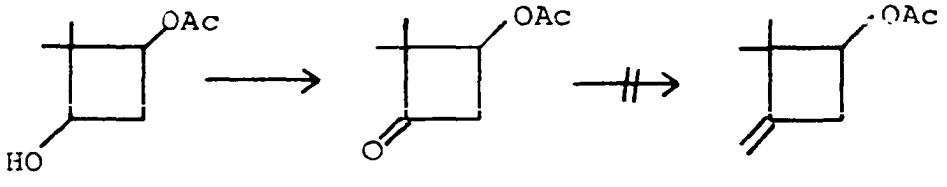


168 173

specie, but it would not be expected to eliminate it altogether. In order to check this point more carefully by confirming the absence of 165 by vpc analysis, a synthesis of 165 was attempted but failed in the final step. The initial step in the attempted synthesis was the cycloaddition of dimethyl-ketene with divinyl ether to give 174. The feasibility of this step depended on the fact that ketenes and vinyl ethers are known to give head-to-tail cycloadducts (137). It was originally intended to convert 174 to 177 in two steps by acid hydrolysis of the vinyl ether functions followed by acetylation of the resulting keto alcohol. However, the first step in that sequence was unsuccessful giving what appeared to be a cyclobutenone instead of the desired keto-alcohol. Thus the more indirect sequence involving reduction of 174 with lithium aluminum hydride followed by acetylation to give 175, acid



174 175



176 177 165

hydrolysis of 175 to 176, and Jones oxidation of 176 to 177 was employed. The nmr spectrum of 176 clearly did show that the oxygen functionalities were in a 1,3 (head-to-tail cycloaddition) and not a 1,2 (head-to-head cycloaddition) relationship since nearly identical triplets were observed for both methine hydrogens. Unfortunately, the critical Wittig reaction of 177 failed, possibly as a result of a deleterious steric influence of the methyl substituents. A Wittig reaction of 174 was likewise unsuccessful, despite the fact that a Wittig reaction of cyclobutanone under the same conditions gave methylenecyclobutane in good yield.

EXPERIMENTAL

General

All boiling points and melting points are uncorrected. The 60 MHz nmr spectra were recorded on Varian A-60 or Hitachi-Perkin Elmer R-20B instruments; 100 MHz spectra were obtained on a Varian HA-100 spectrometer usually in the frequency sweep mode; fmr spectra at 56.4 MHz were recorded on a modified Varian HR-60 instrument. Proton and fluorine chemical shifts are reported in ppm downfield from tetramethylsilane and in ppm upfield from chlorotrifluoromethane internal standards respectively. Infrared spectra (reported in wavenumbers) were recorded on a Perkin-Elmer model 21 or Beckman IR 12 spectrometer. Mass spectra were obtained on an Atlas CH-4 spectrometer. High resolution mass measurements were made on an associated Electronics Industries MS 902 instrument. GLPC analyses were performed on a Varian Aerograph instrument with thermal conductivity detector and 1/4" x 6-8 ft aluminum columns. Combustion analyses were performed by Chemalytics, Inc., Tempe, Arizona.

Addition of dichlorocarbene to 1-methylcyclobutene

1-Methylcyclobutene was prepared from cyclopropylmethyl ketone tosylhydrazone (96) and distilled from sodium hydride to give a dry, methanol free product.

Into a 50-ml, four-necked flask equipped with a thermometer, ice-cooled condenser, septum, nitrogen inlet, and magnetic stir bar has was placed 2.72g (0.0645 mole) of 56.9% sodium hydride dispersion in mineral oil. The mineral oil was removed by successive washings with pentane, with the pentane being removed after each wash by pipette and finally under a stream of nitrogen. Then 10.4g (0.0586 mole) of methyltrichloroacetate and 8.00g (0.117 mole) of 1-methylcyclobutene was introduced with stirring. To the resulting suspension was added over a period of Ca. 4h 2.25g (0.0705 mole) of methanol at such a rate that the temperature was maintained at 25-35°. After the addition was complete the mixture was stirred for an additional 1 hr at room temperature. Throughout the reaction period aliquots of the mixture were withdrawn, concentrated under reduced pressure, and their nmr spectra recorded. At no time were signals assignable to a bicyclopentane observed. Particularly significant was the absence of a methyl singlet above δ 1.5.

At the end of the reaction period the flask was fitted with a short path distillation head, cooled in an ice bath and gradually evacuated to 0.2 torr. The bath temperature was then gradually increased to 40° and all volatile naterials were collected as a single fraction in a Dry Ice/isopropanol cooled receiver. The mixture of volatiles was subjected to a bulb to bulb distillation at 0° and 0.1 torr. The volatile

materials under these conditions consisted chiefly of 1-methylcyclobutene, chloroform, and dimethylcarbonate as determined by vpc and nmr analysis. The residue (1.65g) consisted of greater than 90% of a compound whose nmr spectrum is shown in Figure 1 along with an undetermined number of minor components characterized by a continuous complex absorption from δ 5.0-6.3. Attempts to analyze the corresponding mixture from previous runs by vpc on a carbowax 20M column at temperatures down to 65° had resulted in destruction of the major component and nearly all the minor components. Extensive decomposition likewise occurred on silica gel. A reasonably clean separation of the labile major component from the more volatile minor components was finally achieved through low temperature vacuum distillation. The nmr spectrum of that sample is shown in Figure 1. The mass spectrum of this compound contained molecular ions at m/e 150, 152, and 154, with major fragment ions at m/e 117, 116, 115, 114, 99, and 79 (base peak), and 77. On the basis of its spectral data and labile behavior this compound was assigned structure 76, 2,3-dichloro-1-methylcyclopentene.

6,6-Dichloro-1-methylbicyclo[3.1.0]hexane (79)

In a procedure analogous to that described above, 8.21 g (0.100 mole) of 1-methylcyclopentene, 8.89 g (0.050 mole) of methyltrichloroacetate, 1.39 g (0.055 mole) of sodium hydride

(mineral oil free) and 1.89 g (0.059 mole) of methanol were reacted at 25-30° over a period of 5 hr. The volatile components of the reaction mixture were then removed by a bulb to bulb distillation and collected in two fractions, the first at .6 torr with the pot cooled to 0° and the second at .6 torr with the pot warmed to room temperature (receivers at -78°). The second fraction contained the title compound along with substantial amounts of dimethylcarbonate. The more volatile dimethylcarbonate was removed in a second bulb to bulb distillation at 0° and .6 torr to give 2.0 g (24%) of 6,6-dichloro-1-methylbicyclo[3.1.0]hexane whose nmr spectrum is shown in Figure 2. ir (film) 3022, 2160, 2870, 1479, 1460, 1449, 1385, 1315, 1255, 1165, 1103, 1050, 1008, 917, 895, 875, 845, 825. The mass spectrum contained very weak molecular ions at m/e 164 and 166 and major fragment ions at m/e 128, 113, 92 (base peak), 90, and 76.

Addition of difluorocarbene to 1,2-dimethylcyclobutene

1,2-Dimethylcyclobutene was prepared through the photolysis of 2,3-dimethyl-1,3-butadiene (101). Trimethyl(trifluoromethyl)tin was prepared through the sunlamp photolysis of a mixture of hexamethylditin (Columbia) and trifluoroiodomethane (Pierce) in a sealed tube for 17 hr as described by Kaesz et al. (138). The workup was modified by substituting fractional distillation of the reaction mixture for chromatography. This method gives a product bp 54-57° (170 torr)

which is virtually 100% pure (vpc, nmr) in 84% yield compared to the 42% yield reported by the original authors.

Into a 50-ml, three-necked flask equipped with a reflux condenser and nitrogen inlet and containing a magnetic stir bar was placed 12 ml of dimethoxyethane (freshly distilled from potassium) 4.37 g (0.0290 mole) of powdered, vacuum-dried sodium iodide, 2.95 g (0.0360 mole) of 1,2-dimethylcyclobutene, and 6.80 g (0.0290 mole) of trimethyl(trifluoromethyl)tin. The mixture was heated in a 50° oil bath for 21 hr at which time an nmr spectrum of the reaction mixture indicated a 60% conversion of trimethyl(trifluoromethyl)tin (singlet near δ 0.4) to trimethyl tin iodide. Further heating at 62° for 5 hr increased in the conversion to 69% and after an additional 7 hr at 68° the conversion was 85%. Ammonia was bubbled through the cooled reaction mixture until precipitation of the trimethyltin iodide ammoniate was complete and then all the volatile components of the mixture were transferred to a Dry Ice/isopropanol cooled receiver at .1 mm without applying external heat to the pot. Analysis of this mixture of volatiles on carbowax 20 M and SE 30 columns at 100° showed five products A, B, C, D, and E (increasing retention times) in respective area ratios of 106 : 54.5 : 10 : 16.8 : 2.9.

Component A had an pmr spectrum shown in Figure 4 and an infrared spectrum (CCl_4) with major bands at 2925, 1675, 1450, 1388, 1365, 1340, 1235, 1150, 1126, 1036, 1000, 948, and

867 cm^{-1}.

The mass spectral molecular weight was 112. This compound was reasonably stable when stored as a dilute solution in carbon tetrachloride in the cold but rapidly polymerized at room temperature when neat. On the basis of spectral data and a probable reaction mechanism this compound was assigned structure 83, 1,3-dimethyl-2-fluorocyclopentadiene.

Component B had an pmr spectrum shown in Figure 5 and an fmr spectrum consisting of two complex multiplets at ca. 120 ppm upfield from $CFCl_3$. The infrared spectrum (CCl_4) contained major absorption bands at 2945, 1628, 1595, 1486, 1463, 1380, 1337, 1305, 1282, 1242, 1212, 1177, 1145, 1108, 1070, 1038, 1010, 915, 903, 888, and 862 cm^{-1}. The mass spectral molecular weight was 142. On the basis of spectral comparisons with an authentic specimen (see below) component B was identified as 2,4-difluoro-m-xylene (84).

Component D gave the pmr spectrum shown in Figure 6 and a fmr spectrum consisting of a single complex multiplet at 143 ppm. The mass spectral molecular weight was 142. This compound was identified as 2,3-difluoro-p-xylene (85) by vpc retention time and nmr spectral comparisons with an authentic specimen (see below).

The minor components C and E were not investigated. A comparison of the nmr spectra of purified compounds 83, 84, and 85 with nmr spectra of the crude reaction mixture at

various stages of heating showed that xylenes 84 and 85 increased at the expense of 83 as the reaction progressed.

2,4-Dinitro-m-xylene (87)

To a stirred mixture of 54.2 g (0.360 mole) of 2-nitro-m-xylene (Aldrich) and 100 ml of concentrated sulfuric acid colled in an ice bath was added 100 ml of concentrated nitric acid at such a rate that the temperature of the mixture remained below 50°. When all the nitric acid had been added the mixture was heated on a steam bath for 15 min and then cooled and poured into an equal volume of crushed ice. The pale yellow crystalline product was collected on a filter, washed with cold water and dried to give 70.4 g (100%) of the title compound mp 80-81° lit. (102) 83-84°.

2,4-Diamino-m-xylene (88)

To a stirred mixture of 140 g (0.715 mole) of 2,4-dinitro-m-xylene, 50 ml of 95% ethanol, and 202 g (1.70 mole) of granular 20 mesh tin was added 715 ml of concentrated hydrochloric acid dropwise, with ice bath cooling as required to prevent the reaction from becoming too violent. When the addition was complete the mixture was heated on a steam bath for 30 min. Upon workup of a portion of the reaction mixture the reduction was found to be only 75% complete. An additional 100 g of tin and 300 ml of hydrochloric acid was added and reacted as before, heating for 1 hr on the steam bath after

the second addition of hydrochloric acid was complete. After cooling one-half of the solution was made basic with 50% potassium hydroxide solution and then extracted with ether. The etheral extracts was dried over anhydrous magnesium sulfate and the solvent was removed on a rotary evaporator to give 27.7 g (57%) of the title compound mp 59-62° lit (103) 65-66°. The crude material was of satisfactory purity to be used in the following reaction. The 60 MHz nmr spectrum of 88 ($CDCl_3$) consisted of: 1.95, singlet (3H), 2.15 singlet (3H); 3.4, broad singlet (4H); 6.1, doublet, J = 8 Hz (1H); 6.7, doublet, J = 8 Hz (1H).

2,4-Difluoro-m-xylene (84)

To a stirred suspension of 6.5 g (0.048 mole) of 2,4-diamino-m-xylene, in 37 ml of water contained in a 400 ml beaker was added 8.5 ml of 12 M hydrochloric acid and 50 ml of 48% fluroboric acid. The mixture was cooled to -10° in an ice/salt bath and then an ice-cold solution of 7.00 g (0.102 mole) of sodium nitrite in 50 ml of water was added at such a rate that the temperature did not rise above -9°. When the addition of sodium nitrite was complete the mixture was immediately filtered. The dark brown solid which was collected was washed with 175 ml of ice-cold methanol followed by 25 ml of ice-cold ether. The resulting light brown solid was placed in a vacuum desiccator overnight where it darkened slightly.

The yield of the bisdiazonium salt 89 was 5.3 g (33%).

A mixture of 5.0 g (0.015 mole) of 89 and 15 g of sand was placed in a flame dried apparatus consisting of a 200-ml flask connected through a short path distillation head to a Dry Ice/isopropanol cooled receiver. The system was thoroughly flushed with and maintained under nitrogen while the solid mixture was gently heated with a luminous flame. After a short time brown fumes began to evolve and intermittent heating was continued as necessary to sustain the reaction. Finally strong heat was applied to drive the volatile products into the receiver. The receiver was then allowed to come to room temperature to allow boron trifluoride to escape. The apparatus was washed with ether and the washings added to the liquid in the receiver. Concentration of the resulting solution on a steam bath resulted in the precipitation of a white solid with a phenol-like odor which was filtered off. After further concentration of the solution on a steam bath vpc analysis on a Carbowax 20M column showed in addition to solvent one major component with a retention time equal to that of component B in the difluorocarbene/1,2-dimethylcyclobutene reaction and two minor components with slightly longer retention times which were not clearly resolved from the major component. A sample of the major component isolated by preparative vpc gave spectral data identical to component B from the difluorocarbene/dimethylcyclobutene reaction.

High resolution mass spectral analysis: calcd for $C_8H_8F_2$: m/e 142.059401; Found m/e 142.057401.

2,3-Difluoro-p-xylene (85)

O-Difluorobenzene (4.73 g, 0.0415 mole) and 42 ml of dry tetrahydrofuran were placed in a 250-ml, three-necked flask equipped with a mechanical stirrer, addition funnel, thermometer, and nitrogen inlet. The solution was stirred and cooled to -50° by means of a Dry Ice/isopropanol bath and then 25 ml (0.0415 mole) of 1.67 M n-butyl lithium solution in hexane was added over 20 min at such a rate that the temperature did not rise above -48°. When the addition of butyl lithium was complete the solution was stirred for an additional 7 hr at -48° to -52° then poured onto a slurry of Dry Ice in ether. After acidifying with 6 M hydrochloric acid the ether layer was separated, the aqueous layer was extracted with additional ether and the ether solutions were combined and dried ($MgSO_4$). Removal of the solvent on a rotary evaporator gave 5.00 g (76%) of 2,3-difluorobenzoic acid (91) as a white crystalline solid. 60 MHz pmr (ether) 6.9-7.9, complex, (3H); 10.6, singlet (1H).

A solution of 5.00 g (0.311 mole) of 91 in 20 ml of ether was added dropwise to a solution of 1.20 g (0.316 mole) of lithium aluminum hydride in 40 ml of ether and the resulting mixture was refluxed overnight. After cooling successive portions of water and hydrochloric acid were added to

decompose the excess lithium aluminum hydride and the insoluble aluminum salts were removed by filtration. The ether layer was separated; the aqueous layer was extracted with additional ether, and the combined ethereal solutions were dried ($MgSO_4$). Removal of the solvent on a rotary evaporator gave 4.60 g (100%) of 2,3-difluorobenzyl alcohol (92) as a colorless oil. 60 MHz pmr (neat) 4.6, doublet or triplet, J = 1.4 Hz (2H); 5.2, singlet (1H); 6.7-7.3, complex (3H). A vpc analysis of this compound on a carbowax 20M column at 196° indicated it was 95% pure.

The entire portion of 2,3-difluorobenzyl alcohol was reacted with 38.3 ml (0.0638 mole) of 1.67 M n-butyl lithium in hexane and excess solid carbon dioxide as described above to give upon workup a mixture of starting material and 2,3-difluoro-4-hydroxymethylbenzoic acid (93). The starting material was removed by washing with chloroform to give 1.57 g (26%) of 93 as a white crystalline solid mp 154-156.5°, 60 MHz pmr (DMSO-d_6) 4.65, broadened singlet (2H); 7.2-7.9, complex (3H). The signals from the hydroxyl and carboxyl protons were apparently broadened beyond detection since they were not observed as low as 16 ppm. However, the ir spectrum (nugol mull) did contain a characteristic strong, broad band at 3500-2200 cm^{-1} along with a strong carbonyl absorption at 1690 cm^{-1}.

The reduction of 1.49 g (0.00792 mole) of 93 with 0.600 g (0.0158 mole) of lithium aluminum hydride as described above for 91 gave 1.20 g (87%) of 2,3-difluoro-1,4-benzenedimethanol (94), 60 MHz pmr (acetone-d_6) 4.7, singlet (4H); 4.8, broad singlet (2H) 7.25, 4 line multiplet (2H).

To a stirred suspension of 1.10 g (0.00634 mole) of 94 in 17 ml of benzene under nitrogen was added a solution of 1.15 g (0.00425 mole) of phosphorus tribromide in 5 ml of benzene. The resulting mixture was stirred for 1 hr at room temperature, then heated to 40° for an additional 1 hr, cooled, and poured onto crushed ice. The benzene layer was removed and the aqueous layer was extracted with several portions of ether. After combining and drying ($MgSO_4$) the ether and benzene solutions the solvent was removed on a rotary evaporator to give 1.31 g (70%) of crude α,α'-dibromo-2,3-difluoro-p-xylene (95). The crude product was dissolved in 20 ml of dry tetrahydrofuran and added dropwise to a suspension of .675 g (0.0178 mole of lithium aluminum hydride in 14 ml of tetrahydrofuran under nitrogen. The mixture was heated to reflux for 19 hr and then worked up by the usual procedure to give .52 g of a crude liquid mixture. Analysis of the crude product by vpc on a carbowax 20M column at 125° revealed two components in a 64:36 ratio. The nmr spectrum of the major component indicated that it was not aromatic, and it was not further investigated. The pmr and mass spectra of

the second component indicated that it was indeed authentic 2,3-difluoro-p-xylene (85). The spectra and vpc retention time of authentic 85 were identical to those of component D from the difluorocarbene/1,2-dimethylcyclobutene reaction. Anal. Calcd for $C_8H_8F_2$: C, 67.60; H, 5.67; Found: C, 67.64; H, 6.26.

Addition of chlorocarbene to methylcyclopentadienes

Into a 500-ml, three-necked flask equipped with a mechanical stirrer, reflux condenser, addition funnel, and nitrogen inlet was placed 200 ml of methylene chloride and 8.0 g (0.10 mole) of an approximately 1:1 mixture of 1- and 2- methylcyclopentadiene (obtained from the thermal cracking of the commercial dimer). The mixture was stirred and 65 ml (0.091 mole) of 1.4 M methyl lithium in ether was added dropwise over 1 hr (gentle reflux). When the addition of methyl lithium was complete the mixture was stirred for an additional 1 hr at room temperature, then filtered and concentrated on a rotary evaporator to give 11.85 g of a crude mixture. Analysis of the mixture by vpc on a carbowax 20M column revealed four major products in the ratio 71:19:4:6 in order of increasing retention times along with solvent and starting materials. The major product was collected and identified as toluene by vpc and spectral comparisons with an authentic specimen. The second component was also collected but was not obtained in sufficient quantity for complete characterization. The 60 MHz

nmr spectrum of the second component consisted of a sharp singlet at δ 1.43, a multiplet at δ 2.45, and a multiplet at δ 5.4. The sample was too dilute for an accurate integration. The mass spectrum of this component contained as the highest ion of significant intensity m/e 93, which was also the base peak. Major fragment ions were observed at m/e 91, 79, and 77.

Addition of chlorofluorocarbene to 1-methylcyclobutene

To a stirred suspension of 1.30 g (0.055 mole) of mineral oil free sodium hydride in a mixture of 8.05 g (0.050 mole) of methyl dichlorofluoro acetate and 6.44 g (0.0950 mole of 1-methylcyclobutene was added dropwise over 2 hr 1.92 g (0.060 mole) of methanol. The addition was controlled so that the temperature of the mixture remained below 30°. After stirring for an additional hour at room temperature an nmr spectrum of the crude mixture showed what appeared to be considerable amounts of olefinic material (complex resonances 4.1-5.5 and methyl resonances near 1.65) in addition to the starting olefin. No evidence for a bicyclo[2.1.0]pentane through appropriate signals above δ 1.5 were observed. The mixture appeared to be complex and on attempted workup through low temperature fractionation techniques it became apparent that the major products were thermally labile. No further characterization of the products of this reaction were attempted.

6,6-Difluoro-1-methylbicyclo[3.1.0]hexane (100)

An apparatus consisting of a 50-ml, three-necked flask fitted with a nitrogen inlet, reflux condenser, and magnetic stir bar was flame-dried under a stream of nitrogen. Then 12 ml of dimethoxyethane (freshly distilled from potassium) 3.00 g (0.20 mole) of vacuum dried sodium iodide, 4.66 g (0.020 mole) of trimethyl(trifluoromethyl)tin, and 2.05 g (0.025 mole) of 1-methylcyclopentene was introduced and heated at 90° for 8 hr. Then ammonia gas was bubbled into the cooled mixture to convert the trimethyltin iodide to the insoluble solid ammoniate. The volatile components of the resulting mixture were transferred to a Dry Ice/isopropanol cooled receiver by means of a bulb to bulb vacuum distillation at room temperature. Analysis of this volatile fraction by vpc on an SE30 column at 100° indicated only one component in addition to solvent. Purification of the title compound was effected by preparative gas chromatography. The vpc determined yield was 72%. The 60 MHz pmr spectrum of 100 shows a doublet of doublets at 1.25 for the methyl group with couplings (apparently to fluorine) of 2.0 and 3.5 Hz, and a broad envelope at 1.4-2.4 for the remaining hydrogens. The infrared spectrum (CCl_4) contains major bands at 2949, 1477, 1450, 1439, 1315, 1300, 1274, 1235, 1200, 1182, 1145, 1120, 1078, 1055, 1005, 1005, 976, 940, 911, and 861 cm^{-1}. The mass spectrum contained a molecular ion at m/e 132. Anal. Calcd for $C_7H_{10}F_2$: C, 63.62; H, 7.63. Found:

C, 63.00; H, 7.51.

Thermal rearrangement of 6,6-difluoro-1-methylbicyclo[3.1.0]-hexane (100)

A solution of 100 in dry tetraglyme was heated at 200° in the probe of a Varian A 60 spectrometer for 40 min without suffering any change in its nmr spectrum. After heating an additional 15 min in an oil bath at 250°, the nmr spectrum contained new band of significant intensity in the 2-2.5 and 4.4-5.8 regions. After an additional hour at 230° (oil bath) 100 was completely destroyed and there were new bands at .8-2.6 (complex), 5.4 (broad hump) and 6.7 (broad hump) and the bands in the 4.4-5.2 region had greatly diminished in intensity. The dark color of the solution at this point and the broadness of the nmr bands suggested that.

Addition of chlorocarbene to 1,2-dimethylcyclobutene

To a stirred solution of 11.61 g (0.142 mole) of 1,2-dimethylcyclobutene and 6.04 g (0.0710 mole) of dichloromethane at room temperature under nitrogen was added dropwise over 2 hr 25 ml (0.035 mole) of 1.4 M etheral methyl lithium. After standing at room temperature overnight an nmr spectrum of the crude mixture showed the presence of m and p-xylene and resonances at 1.88, doublet; 1.98, doublet; 2.7, multiplet; 5.65, multiplet; and 5.9, multiplet readily assignable to

1,3-dimethylcyclopentadiene as the major features. There were no resonances assignable to vinylcyclopropanes 10 and 11. The volatile components of the mixture were transferred to a Dry Ice/isopropanol cooled receiver under reduced pressure and excess dichloromethane and 1,2-dimethylcyclobutene were subsequently removed under reduced pressure to give 0.36 g of a crude product mixture whose nmr spectrum contained the same features as that of the crude mixture minus methylene chloride and 1,2-dimethylcyclobutene. Analysis of this mixture by vpc on a carbowax 20M column showed nine resolvable components with retention times ranging from 3 to 29 min. Comparison of nmr spectra of the collected components with that of the crude mixture indicated that m and p-xylene were the only components present in the crude mixture. Although the xylenes were not resolvable as under the vpc conditions employed comparison of the nmr spectrum of the collected mixture with an authentic mixture indicated that the m/p xylene ratio was approximately 3:1.

1,1-Difluoro-2-chloro-3-vinylcyclobutane (109)

Tri-n-butyltin hydride was prepared by the lithium aluminum hydride reduction of tri-n-butyltin chloride according to the procedure of Kuivila and Beumel (139).

The tin hydride employed was freshly distilled. 1,1-Difluoro-2,2-dichloro-3-vinylcyclobutane 108 (20.4 g, 0.110 mole) (Pierce) and 2,2'-azobis (2-methylpropronitrile) (.05 g)

were placed in a 100-ml three-neck flask equipped with a thermometer, reflux condenser, nitrogen inlet, magnetic stir bar, and addition funnel containing 31.9 g (0.110 mole) of tri-n-butyltin hydride. Approximately 10 ml of the tin hydride was added and the mixture was heated slowly to 50° whereupon an exothermic reaction begain and the temperature of the mixture increased to 85°. The heat was removed and the tin hydride was added at a sufficient rate to maintain the temperature at 85-90°. When the addition was complete, external heat was again applied to maintain the temperature at 90° for an additional 75 min. The reaction flask was then equipped with a short-path distillation head and the mixture was distilled at 60 torr with bath temperatures up to 200°. A single 13.0 g fraction, bp 55-65° was collected. Analysis of this fraction by vpc (SE-30 column) indicated three components in ratios of 47:48:5 in order of increasing retention times. The retention time of the third component was identical to that of the starting material. The pmr spectrum of the distillate indicated it was a mixture of isomeric 1,1-difluoro-2-chloro-3-vinylcyclobutanes. 60 MHz pmr (neat), 1.9-3.4, complex (3H); 3.9-4.9, multiplet (1H); 4.9-5.4, complex (2H); 5.6-6.3, multiplet (1H). The mass spectrum of the mixture contained very weak molecular ions at m/e 152 and 154 and a base peak at m/e 54. The yield was 74%.

Reduction of 108 with triphenyltin hydride produced a similar mixture of monochlorides in 64% yield.

3,3-Difluorocyclobutenecarboxylic acid (111)

Both permanganate oxidation and ozonolysis procedures are described. The latter is more convenient and produces better yields, but the former is a satisfactory alternative if ozone is not available.

A. Permanganate oxidation

The procedure is adapted from the method of Smith and Rouault (140).

Into a 500-ml, three-necked flask equipped with thermometer and mechanical stirrer was placed 16.8 g (0.110 mole) of 1,1-difluoro-2-chloro-3-vinylcyclobutane, 3.48 g (0.0415 mole) of sodium bicarbonate and 120 ml of acetone. The solution was stirred and cooled to 5° (ice bath) and a total of 66 g (0.420 mole) of potassium permanganate was added in small portions over 2 hr with the temperature maintained at 5-15°. When the addition was complete most of the solvent was removed on a rotary evaporator. Then 200 ml of ice water was added to the dark residue followed by the cautious addition (foaming) of a few ml of 6 M sulfuric acid. Sulfur dioxide was then bubbled into the dark suspension (ice bath cooling) until a homogeneous solution was obtained. The solution was then acidified and extracted with several portions of ether. The

combined extracts were washed with water, dried over anhydrous magnesium sulfate and filtered. After removal of the solvent on a rotary evaporator 14.14 g of a viscous, nearly colorless oil remained. The 60 Hz pmr spectrum of the oil was consistent with that expected for 2-chloro-3,3-difluorocyclobutane-carboxylic acid (110): 60 MHz pmr (acetone d_6) 2.3-3.8, complex (3H); 4.5-5.1, multiplet (1H); 9.15 singlet (1H).

To 11.96 g of this crude chloro acid was added a solution of 10.5 g of 87.7% potassium hydroxide in 60 ml of methanol. The mixture was stirred at room temperature for 75 min and the solvent was then removed on a rotary evaporator. The residue was taken up in 100 ml of ice water and acidified with 6 M hydrochloric acid. The acidic solution was extracted with several portions of ether and the combined ethereal extracts were washed with brine, dried ($MgSO_4$) and filtered. The solid residue which remained after removing the ether at reduced pressure was triturated with several portions of boiling hexane to eventually give 5.7 g (50%) of 3,3-difluorocyclobutene carboxylic acid which was very pure by nmr analysis (see below).

B. Ozonolysis

A solution of 5.0 g (0.033 mole) of 1,1-difluoro-2-chloro-3-vinylcyclobutane 40 ml of acetic acid, and 21 ml of acetic anhydride was cooled to 0°, and ozone from a Wellsbach ozonator was slowly bubbled into the solution until ozone

absorption ceased. Times on several runs varied from 8-12 hr. After flushing the solution with oxygen a solution of 10 ml of 30% hydrogen peroxide in 62 ml of water was added dropwise over 15 min at 0°. The mixture was then allowed to come to room temperature and then heated at reflux overnight. The acetic acid and water were then removed on a rotary evaporator taking care to remove as much acetic acid as possible since it is difficult to remove in later stages. The residual oil was taken up in ether and the resulting solution was extracted with an excess of 10-15% aqueous potassium hydroxide. After standing at room temperature for 2.5 hr the basic solution was acidified with 12 M hydrochloric acid and then extracted with several portions of ether. The combined ethereal extracts were washed with brine, dried ($MgSO_4$) and filtered. The solvent was removed on a rotary evaporator without external heat and taking care to avoid loss of the product through sublimation. The crude acid was purified by sublimation at 50-70° and 20 torr to give 3.16 g (72%) of 3,3-difluorocyclobutenecarboxylic acid, mp 80-87°. As an alternative or additional method of purification the acid can be recrystalized from petroleum ether. Acetic acid is the major contaminant. An analytically pure sample obtained after repeated sublimations and recrystallizations melted at 88-89.5° and gave the following data: 60 MHz pmr (acetone d_6) 3.18, triplet, J = 3.7 Hz (2H), 6.70, triplet, J = 1.3 Hz (1H), 13.48, singlet (1H). fmr

(acetone d_6) 107 ppm, triplet of doublets, J = 3.7, 1.3 Hz. ir($CHCl_3$) 3050, 1728, 1626, 1616, 1300,1225, 710. A molecular ion at m/e 134 is observed in the mass spectrum.

Anal. Calcd for $C_5H_4F_2O_2$: C, 44.79; H, 3.00. Found: C, 44.48, H, 2.91.

1-Carbomethoxy-2,3-diaza-6,6-difluorobicyclo[3.2.0]hept-2-ene (112)

Diazomethane generated from N-nitroso-N-methylurea was distilled into an ethereal solution of 5.57 g (0.0415 mole) of 3,3-difluorocyclobutenecarboxylic acid at 0° until a faint yellow color persisted. Excess diazomethane was decomposed by the dropwise addition of ethereal formic acid until the yellow color was discharged. The resulting solution was washed with successive portions of saturated sodium bicarbonate solution and saturated sodium chloride solution, then dried ($MgSO_4$) and filtered. Removal of the solvent on a rotary evaporator gave 7.9 g (100%) of the title pyrazoline which required no further purification. 60 MHz pmr (CCl_4) 2.3-3.7, complex (3H); 3.78, singlet (3H); 4.3-5.3, perturbed AB portion of an ABX pattern, J_{AB} = 19 Hz (2H). ir(film) 3020, 2970, 1750, 1550, 1444, 1420, 1325, 1265, 1210, 1190, 1160, 1130, 1105, 1060, 920.

1-Carbomethoxy-3,3-difluorobicyclo[2.1.0]pentane (113)

A solution of 4.91 g (0.0259 mole) of 112 and 4.71 g (0.0259 mole) of benzophenone in 250 ml of benzene contained in a pyrex immersion well was irradiated with a 450 watt Hanovia 679A-36 lamp until nitrogen evolution ceased (ca. 2.5 hr). Benzene was removed on a rotary evaporator and the residual oil was distilled in vacuo to give 3.07 g of a colorless sweet smelling liquid, bp 68-72° (22 torr). The distillate consisted of 95% of the title ester along with 5% of three other uninvestigated components in approximately equal amounts as determined by vpc analysis on an SE-30 column. The yield of 113 was 69%. The spectral data reported for 113 was obtained on vpc collected samples. The nmr spectra of 113 is shown in Figure 11 and discussed at length in the "Results". The infrared spectrum (film) contained major bands at 3085, 3000, 2955, 1730, 1442, 1360, 1320, 1190, 1120. The mass spectrum contained a molecular ion at m/e 162 and a base peak at m/e 131.

Anal. Calcd for $C_7H_8F_2O_2$: C, 51.85; H, 4.97. Found: C, 52.12; H, 4.81.

1-Carbomethoxy-3,3-difluorobicyclo[2.1.0]pentane-5,5-d_2 (113-5,5-d_2)

A 50% solution of NaOD in D_2O was prepared by adding 37 g of sodium in small portions to 100 g of deuterium oxide under nitrogen and with ice-bath cooling. Diazomethane from 10 g of

N-nitroso-N-methylurea in 150 ml of ether was treated with 40 ml of 50% NaOD solution at room temperature for 35 min with vigorous magnetic stirring. Treatment of a small sample of benzoic acid with the resulting diazomethane solution gave methyl benzoate with 60% d_2 incorporation by nmr analysis. The NaOD solution was removed and replaced with 40 ml of fresh solution. After an additional 65 min of vigorous stirring the deuterium incorporation as determined above was 90% d_2.

Methyl 3,3-difluorocyclobutenecarboxylate prepared from the acid through a standard thionyl chloride, methanol sequence was treated with the diazomethane-d_2 solution to give following workup 1-carbomethoxy-2,3-diazo-6,6-difluorobicyclo-[3.2.0]hep-2-ene-4,4-d_2. The 60 MHz pmr spectrum of the pyrazoline contained only faint absorption in the 4.4-5.1 region where the methylene protons on C-4 are observed. Irradiation of the deuterated pyrazoline (Hanovia 450 watt lamp, pyrex) in the presence of one molar equivalent of benzophenone in benzene solution gave the title ester which was purified by vpc collection. The nmr spectra of 113-5,5-d_2 is discussed at length in the "Results".

1-Carbomethoxy-3,3-difluorobicyclo[2.1.0]pentane-4-d

(113-4-d)

3,3-Difluorocyclobutenecarboxylic acid-2-d was prepared according to the procedure given for the nondeuterated analog

with the following modifications: Triphenyltin deuteride prepared from triphenyltin chloride and lithium aluminum deuteride was employed in the reduction of 108. After ozonolysis of the resulting deuterated monochloride and oxidative workup a solution of NaOD in deuterium oxide was employed in the elimination step. The pmr spectrum of the deuterated acid showed only a trace absorption in the olefinic region.

The pyrazoline ester produced on treatment of the deuterated acid with diazomethane gave the following 60 MHz pmr spectrum (CCl_4) 2.3-3.6, complex (2H); 3.77, singlet (3H); 4.4-5.3, perturbed AB quartet, J = 19 Hz (2H). Comparison of the nmr spectra of the monodeuterio pyrazoline and the non-deuterated pyrazoline indicated that the chemical shift of the C-5 methine to be ca. 3.4.

Photolysis of the pyrazoline as before gave the title compound which was purified by preparative gas chromatography. The nmr spectrum of 113-4-d is shown in Figure 12 and discussed in the "Results".

1-Carboxamido-3,3-difluorobicyclo[2.1.0]pentane

A mixture of 4.57 g (0.0282 mole) of 1-carbomethoxy-3,3-difluorobicyclo[2.1.0]pentane, 7 ml of concentrated ammonium hydroxide and 0.7 g of ammonium chloride was stirred for 24 hr at room temperature and then heated to 50° for 3 hr. The mixture was then cooled in an ice bath to crystallize the crude amide which was collected on a filter and sucked dry. The

crystals were then washed with cold hexane to give after drying 2.53 g of the crude amide. An additional 0.6 g of amide was isolated from the mother liquor to give a total of 3.13 g (75%) of the title compound which was quite pure by nmr analysis and used without further purification. An analytical sample obtained after treatment of the crude product with decolorizing carbon and recrystallization from water melted at 136-138° and gave the following 60 MHz pmr spectrum (acetone-d_6) 1.4, multiplet (1H); 1.6-2.4, overlapping multiplets (2H); 2.5-3.2, overlapping multiplets (2H); 6.9, broad singlet (2H). Anal. Calcd for $C_6H_7F_2NO$: C, 48.98; H, 4.80. Found: C, 48.80; H, 4.62.

1-Cyano-3,3-difluorobicyclo[2.1.0]pentane (140)

A mixture of 2.83 g (0.0193 mole) of crude 1-carboxamido-3,3-difluorobicyclo[2.1.0]pentane and 4.0 g (0.028 mole) of phosphorus pentoxide from a freshly opened bottle was placed in a 50-ml distilling flask and shaken to obtain a uniform mixture. The flask was equipped with a short-path distillation head with a receiver cooled in a Dry Ice/isopropanol bath. The system was connected through a calcium chloride drying tube to a water aspirator and evacuated to 25 torr. The contents of the flask were then heated with a soft flame to initiate the reaction, and intermittent heating was continued as necessary to maintain a steady rate of distillation. Finally, strong heat was applied to insure complete transfer of all

volatile materials to the receiver. The distillate was taken up in ether and washed with successive portions of saturated sodium bicarbonate solution and water, then dried ($MgSO_4$) and filtered. The solvent was removed first by distillation at atmospheric pressure and finally under reduced pressure on a rotary evaporator. The residual liquid (1.01 g, 41%) was nearly pure 140 with only trace impurities visible on vpc analysis on a FFAP column. Purification was effected by preparative gas chromatography. The pmr spectrum of 140 is shown in Figure 13. The ir spectrum (CCl_4) contained major bands at 3095, 3010, 2970, 2250, 1435, 1358, 1315, 1240, 1205, 1145, 1085, 1010, 925, 890. The mass spectrum contained a molecular ion at m/e 129 and a base peak at m/e 102.

Anal. Calcd for $C_6H_5F_2N$: C, 55.81; H, 3.90. Found: C, 55.76; H, 3.98.

3,3-Difluorobicyclo[2.1.0]pentane-1-methanol (107)

A solution of 1.50 g (0.00926 mole) of 1-carbomethoxy-3,3-difluorobicyclo[2.1.0]pentane in 10 ml of ether was added slowly to a stirred solution of 0.228 g (0.0060 mole) of lithium aluminum hydride in 20 ml of ether at 0°. Shortly after the addition of the ester was complete the gray suspension coagulated into a sticky mass which could not be stirred. The mixture was kept at 0° for an additional 45 min and then warmed to room temperature for 30 min. The mixture was again cooled to 0° and in succession were added 0.23 ml of water,

0.23 ml of 15% aqueous sodium hydroxide and 0.69 ml of water. The solid salts were filtered off and solvent was removed from the filtrate on a rotary evaporator to give 1.16 g (93%) of the title alcohol which was pure by nmr analysis and used without further purification. This alcohol was generally used soon after its preparation although it could be kept for a few days at -30° without appreciable decomposition. Storage at room temperature resulted in complete decomposition after about three days. 100 MHz pmr ($CDCl_3$) 1.05-1.40, complex (2H); 1.85-2.85, complex (4H); 3.80,AB quartet, J_{AB} = 13 Hz (2H). ir(film) 3380, 3000, 2950, 2880, 1315, 1235, 1185, 1125, 1040, 920. The mass spectrum contained a molecular ion at m/e 134 and a base peak at m/e 57.

Behavior of 3,3-difluorobicyclo[2.1.0]pentane-1-methanol (107) under vpc conditions

When a sample of the title alcohol which contained no detectable impurities in its nmr spectrum was injected onto a DEGS column at 115° with the injector block temperature at 200° the chromatogram consisted of three peaks in area ratios of 83.0:6.1:10.9. The major component was collected and identified as aldehyde 125 on the basis of its spectral data: nmr ($CDCl_3$) 2.4-3.3, complex (5H); 4.95, multiplet (1H); 9.67, unsymmetrical triplet, J = 1.4 Hz, (1H). The appearance of the aldehydic proton as a triplet results from coupling to the proton α to the carbonyl and apparently from long range

coupling to the fluorine. ir ($CHCl_3$) 2940, 2870, 2830, 2730, 1732, 1690, 1345, 1185, 910.

The 2,4-dinitrophenylhydrazone of 125 was prepared by standard methods and recrystallized from aqueous ethanol, mp 136-138°. High resolution mass spectral analysis: Calcd for $C_{12}H_{11}FN_4O_4$: m/e 294.0764244. Found: m/e 294.057394.

3,3-Difluorobicyclo[2.1.0]pentane-1-methyl p-nitrobenzoate (114)

To a stirred solution of 2.76 g (0.0149 mole) of freshly recrystallized p-nitrobenzoyl chloride in 25 ml of dry pyridine cooled in an ice bath was added a solution of 1.05 g (0.00715 mol) 3,3-difluorobicyclo[2.1.0]pentane-1-methanol and the mixture placed in a refrigerator overnight. The mixture was then poured into water and extracted with several portions of petrolium ether. The extracts were washed with saturated sodium bicarbonate solution and then dried over anhydrous $MgSO_4$. The solvent and last traces of pyridine were removed on a rotary evaporator and finally at .1 mm pressure overnight. The crude product was recrystallized from hexane to give 1.66 g (79%) of nearly colorless crystals, mp 77-78.5°, ir($CHCl_3$) 3120, 3050, 2960, 1731, 1609, 1532, 1345, 1315, 1270, 1240, 1130, 1115, 1102, 1015, 870; 100 MHz pmr ($CDCl_3$) 1.25-1.55, multiplet, (2H); 2.15, multiplet (1H); 2.35-2.9, multiplet (2H), 4.6, AB portion of ABX (CH_2-O)(2H); 8.25 AA'BB'

multiplet (4H); mass spectral molecular weight 283.

Anal. Calcd for $C_{13}H_{11}F_2NO_4$: C, 55.12; H, 3.92. Found: C, 55.13; H, 4.02.

Solvolysis of 3,3-difluorobicyclo[2.1.0]pentane-1-methyl-p-nitrobenzoate

A solution of 1.025 g of the title ester in 30 ml of 60% aqueous acetone (prepared by mixing two volumes of water with 3 volumes of acetone) in a sealed glass ampoule was placed in an oil bath at 100° for 72 hr. The contents of the ampoule were then poured into 50 ml of saturated sodium bicarbonate solution and extracted with six 15 ml portions of ether. The combined ethereal extracts were washed with saturated bicarbonate solution and then dried ($MgSO_4$). The solvent was removed under reduced pressure to give 0.931 g of nonvolatile residue. The nmr spectrum of the residue was essentially that shown in Figure 7 and assigned to 115. The product was freed from colored impurities by chromatography on silica gel and subsequent recrystallization from hexane to give white crystals mp 81-82°; mass spectral molecular weight 281, ir($CHCl_3$) 3610 3450, 3125, 2960, 2935, 2870, 1732, 1688, 1610, 1537, 1350, 1320, 1280, 1118, 1102, 1015, 972, 875. The fmr spectrum consisted of a complex multiplet centered at 119 ppm.

The α-napthyl urethane of 115 was prepared by treating 115 with an excess of α-napthyl isocyanate in refluxing hexane.

The residue which remained after removal of the solvent was triturated with hot chloroform and the chloroform soluble material was chromatographed on a silica gel column with chloroform eluant to give the soild α-napthylurethane. After recrystallization from hexane the product melted at 150.5-152°. The mass spectral molecular weight was 450; 100 MHz nmr ($CDCl_3$) 2.6-3.4, complex (4H); 4.80, singlet (2H); 5.00, multiplet (1H); 7.00, singlet (1H); 7.25-8.00, complex (7H); 8.18, AA'BB' (4H).

Addition of bromine to 115

A solution of bromine in chloroform was added dropwise to a solution of 115 in chloroform until the bromine color persisted. The yellow solid which remained after removal of the solvent on a rotary evaporator appeared to be a single product by TLC analyses. Purification by silica gel chromatography followed by recrystallization from carbon tetrachloride afforded dibromide 118 as white crystals mp 100-110°, 100 MHz pmr ($CDCl_3$): 2.3-3.3, complex (5H), 4.45, doublet (2H), 4.4-4.95, multiplet (1H); 8.3, AA'BB' multiplet (4H); fmr: 104 ppm, multiplet. ir ($CHCl_3$) 3600, 3400, 2970, 1730, 1613, 1545, 1350, 1320, 1278, 1120, 1103, 1018, 940, 872, 856. Anal. Calcd for $C_{13}H_{12}Br_2FNO_5$: C, 35.42; H, 2.71; Br, 36.20; N, 3.18. Found: C, 35.28; H, 2.99; Br 36.24; N 2.88.

3,3-Difluorobicyclo[2.1.0]pentane-1-carboxylic acid (120)

The title acid was prepared by stirring 2.20 g of the corresponding ester at room temperature for 12 hr with 5 ml of a potassium hydroxide solution prepared by mixing one volume of 50% potassium hydroxide solution with two volumes of water. The basic solution was extracted with ether then cooled in an ice bath and acidified with 12 M hydrochloric acid. The resulting solution was extracted with a total of 50 ml of ether. The latter ethereal solution was washed with saturated sodium chloride solution and dried ($MgSO_4$). Removal of the solvent on a rotary evaporator afforded 1.70 g (84%) of the crude acid. The crude product was recrystallized from petroleum ether to give 1.03 g of white crystals mp 66-69°. The 100 MHz pmr spectrum was nearly identical to that of the corresponding ester: (CCl_4) 1.65, multiplet (1H); 1.9-2.25, overlapping multiplets (2H); 2.7-3.2, overlapping multiplets (2H); 12.0, singlet (1H). The mass spectral molecular weight was 148.

Solvolysis of 3,3-difluorobicyclo[2.1.0]pentane-1-carboxylic acid (120)

The title acid (0.773 g) was dissolved in 15 ml of 1 M aqueous sodium hydroxide and the resulting solution heated at 55° for 4 hr. The solution was then cooled and acidified with 12 M hydrochloric acid. Continuous extraction with ether afforded 0.789 g of crude products. A portion of the crude

mixture (0.302 g) upon treatment with an excess of ethereal diazomethane and removal of the solvent gave 0.311 g of a liquid found to consist of two components in a 93:7 ratio by vpc analysis (carbowax 20M column). The major component was collected and identified as 1-carbomethoxy-3-fluorocyclopent-3-en-1-ol (121). 100 MHz pmr ($CDCl_3$) 1.8-2.8, complex (4H); 3.6, singlet (1H, disappears with D_2O); 3.85, singlet (3H); 4.95 multiplet (1H); ir(CCl_4) 3610, 3545, 3100, 3010, 2955, 2930, 2860, 1745, 1693, 1440, 1340, 1305, 1272, 1220, 1193, 1090, 1040, 990, 970, 915. The highest ion and also the base peak in the mass spectrum was m/e 142 which corresponds to a loss of water from the molecular ion.

Anal. Calcd for $C_7H_9FO_3$: C, 52.53; H, 5.66. Found: C, 52.35; H, 5.67.

A portion of the crude solvolysis product of 120 was recrystallized from carbon tetrachloride to give a white crystalline solid, mp 83-84.5°. The nmr and ir spectrum indicated that this compound was indeed the acid corresponding to ester 121.

Reduction of 1-carbomethoxy-3-fluorocyclopent-3-en-1-ol (121)

A solution of 0.150 g ($.937 \times 10^{-3}$ mole) of 121 in 2.5 ml of ether was slowly added to a stirred solution of 0.050 g (1.32×10^{-3} mole) of lithium aluminum hydride in 5 ml of ether at 0°. When the addition was complete the solution was warmed to room temperature and stirred for 1.5 hr. Then in

successive portions was added 0.05 ml of water, 0.05 ml of 15% sodium hydroxide solution, and .150 ml of water. The resulting suspension was filtered and solvent was removed from the filtrate on a rotary evaporator to give 0.124 g (100%) of glycol 122, which gave a positive periodate test. The 100 MHz pmr spectrum of 122 (acetone d_6) consisted of: 1.5-2.8, complex (4H); 3.5, singlet (2H); 4.2, broad hump (2H); 4.9 multiplet (1H), and was identical to the nmr spectrum of the alcohol obtained on saponification of 115, the solvolysis product of p-nitrobenzoate 114.

3,3-Difluorobicyclo[2.1.0]pentane-1-methyl benzoate (123)

A solution of 1.15 g (0.0117 mole) of 3,3-difluorobicyclo-[2.1.0]pentane-1-methanol in 10 ml of pyridine was added dropwise to a stirred solution of 2.5 ml (.021 mole) of benzoyl chloride in 25 ml of pyridine at 0°. The solution was kept at 0° for 4 hr and then warmed to room temperature for 1 hr. The mixture was poured into ice water and extracted with a total of 120 ml petroleum ether. The combined extracts were washed with successive portions of saturated sodium bicarbonate solution, water, 6 M hydrochloric acid, and water then dried ($MgSO_4$). Removal of the solvent on a rotary evaporator afforded 2.78 g (100%) of the ester as a colorless oil. The product showed a single spot on TLC analysis and no impurities could be detected in the nmr spectrum which differed from that

of the p-nitrobenzoate only in the aromatic region: 7.5, complex multiplet (3H); 8.05, complex multiplet (2H). The mass spectral molecular weight was 238. The product so obtained was used in the kinetic studies without further purification.

3,3-Difluorobicyclo[2.1.0]pentane-1-methyl acetate (124)

3,3-Difluorobicyclo[2.1.0]pentane-1-methanol (.808 g) was dissolved in 5 ml of acetic anhydride containing .5 ml pyridine and let stand for 20 hr at room temperature. Then 15 ml of saturated sodium bicarbonate solution was added slowly followed by several small portions of solid sodium bicarbonate to neutralize most of the acetic acid. The resulting solution was extracted with a total of 60 ml of ether. The combined ethereal extracts were washed with successive portions of saturated sodium bicarbonate solution, 4N hydrochloric acid, and again sodium bicarbonate solution and then dried ($MgSO_4$). Removal of the ether on a rotary evaporator afforded 0.948 g (89%) of the acetate as a colorless liquid. The product was used in the kinetic studies without further purification since no impurities could be detected in the nmr, ir, or mass spectrum, ir(film) 3080, 3010, 2960, 2900, 1750, 1440, 1378, 1320, 1245, 1192, 1138, 1050, 1035, 915; mass spectral molecular weight 176 (very weak molecular ion); 100 MHz pmr ($CDCl_3$) 1.1-1.4, complex multiplet (2H); 1.85-2.75, complex multiplet (3H); 2.10, singlet (3H); 4.24, singlet (2H). The

portion of the pmr spectrum corresponding to the bicyclopentane nucleus is essentially identical to that of the benzoate and p-nitrobenzoate.

Solvolysis of 3,3-difluorobicyclo[2.1.0]pentane-1-methyl p-nitrobenzoate, benzoate, and acetate in 60% aqueous acetone at 100°-kinetics

The following procedure for the p-nitrobenzoate ester was also applied to the benzoate and acetate. Reagent grade acetone (Baker) was further purified by treatment with potassium permanganate and anhydrous calcium sulfate according to the procedure of Hammond and Kochi (141). 2,6-Lutidine was freshly distilled, the center cut fraction bp 141° being used. The 60% aqueous acetone was prepared by mixing three volumes of the purified acetone with two volumes of distilled water.

A 0.60 g sample of the p-nitrobenzoate ester and 0.34 g of 2,6-lutidine were dissolved in 60 ml of 60% aqueous acetone, then 10 ml of this solution was transferred to each of six glass ampoules which were then sealed. The ampoules were completely immersed in a 100.0° oil bath. At timed intervals the ampoules were withdrawn, cooled quickly with cold water, opened, and the contents poured into 10 ml of saturated sodium bicarbonate solution. The aqueous solution was extracted with three 10 ml portions of ether. The combined ethereal extracts were washed with 5 ml of water and dried ($MgSO_4$).

After removing the solvent under reduced pressure the residue was taken up in $CDCl_3$, and the integrated 100 MHz pmr spectrum was obtained. The ratio of starting material to the substituted fluorocyclopentene product was determined from the relative area of the olefinic multiplet in the product at δ 5.0 and the total area of the $-OCH_2-$ resonances in the starting material and product near δ 4.5. This region of the spectrum was recorded at 250 Hz sweep width and the product/starting material ratio was determined from the average of five integrations. A plot of log (mole percent of starting material) vs. time was linear. The half-life of the starting material was determined from the plot to be 49.7×10^3 sec from which the first order rate constant is calculated to be 1.39×10^{-5} sec^{-1}.

3,3-Difluorobicyclo[2.1.0]pentane-1-methyl tosylate (127)

To a stirred solution of 7.8 g (0.041 mole) of p-toluenesulfonyl chloride in 20 ml of dry pyridine at 0° was added dropwise over 8 hr 1.10 g (0.00821 mole) of 3,3-difluorobicyclo[2.1.0]pentane-1-methanol in 5 ml of pyridine. When the addition was complete the solution was placed in a refrigerator at 0° for 8 hr and then poured into 100 ml of ice water and extracted with a total of 175 ml of ether in small portions. The combined ethereal extracts were washed successively with two 15 ml portions of ice cold 6 M hydrochloric acid, 15 ml of saturated sodium chloride solution,

and 20 ml of saturated sodium bicarbonate solution, then dried over anhydrous magnesium sulfate. After removing the solvent on a rotary evaporator the only residue was taken up in 40 ml of ether and treated with decolorizing carbon. Filtration followed by removal of the solvent on a rotary evaporator and finally at ca. 1 torr for several minutes gave 1.255 g of a colorless oil. The crude product was taken up in the minimum amount of petrolium ether at room temperature and gradually cooled to -78° whereupon the tosylate separated as a colorless oil. The solvent was decanted and the above process repeated once. The last traces of solvent were removed at room temperature and .1 torr to give 0.663 g (31%) of analytically pure 127. 100 MHz pmr ($CDCl_3$) 1.05-1.4, overlapping multiplets (2H); 1.8-2.15, multiplet (1H); 2.2-2.8, complex multiplet superimposed on aromatic methyl at 2.48 (5H total); 4.25, singlet (2H); 7.35 doublet (2H); 7.80, doublet (2H). ir($CHCl_3$) 3070, 2960, 1603, 1375, 1350, 1320, 1230, 1195, 1140, 1100, 955.

Anal. Calcd for $C_{13}H_{14}F_2O_3S$: C, 54.16; H, 4.89. Found: C, 54.03; H, 4.89.

The solvent was removed from the combined petroleum ether fractions to give an oil whose nmr spectrum ($CDCl_3$) consisted of 1.1-1.45, multiplet (2H); 1.9-2.85, complex (3H); 3.75, singlet (2H), with the multiplets being almost identical to those in 3,3-difluorobicyclo[2.1.0]pentane-1-methanol. The ir

spectrum was also very similar to that of the alcohol but did not contain a hydroxyl band. On the basis of spectral data this product was characterized as ether 128.

Solvolysis product study of 3,3-difluorobicyclo[2.1.0]pentane-1-methyl tosylate (127)

A solution of 0.420 g of 127 in 15 ml of 80% aqueous acetone was heated at 50° for 5 hr then cooled and concentrated on a rotary evaporator. The solution was made basic with saturated sodium bicarbonate solution, then saturated with sodium chloride and finally extracted with a total of 35 ml of ether. After drying the combined ethereal extracts over anhydrous magnesium sulfate, the solvent was cautiously removed at reduced pressure to give 0.269 g of crude neutral products. A 0.212 g sample of the crude product mixture was separated into a volatile fraction (0.101 g) and nonvolatile fraction (.111 g) by molecular distillation at 5 torr and 65° bath temperature. The 100 MHz pmr spectrum of the nonvolatile fraction indicated that it consisted of ca. 90% of a single component assigned structure 129, the pmr spectrum of which is shown in Figure 8. The minor components of the nonvolatile fraction, which were characterized by a series of complex absorptions in the region 3.5-4.4 and 4.8-5.1, could be separated from the major component on a silica gel column with chloroform eluant after treating the mixture with bromine.

The fmr spectrum of 129 consisted of a triplet (J = 12 Hz) 100.5 ppm upfield of $CFCl_3$. The infrared spectrum of 129 contained major bands at 3050, 2990, 1605, 1380, 1340, 1290, 1240, 1190, 1110, 1070, 1040, 1010, 985, 943, 911, and 850. The mass spectrum of 129 contained a molecular ion at m/e 288 and a base peak at m/e 155. High resolution mass spectral analysis: Calcd for $C_{13}H_{14}F_2O_3S$: m/e 288.066318. Found: m/e 288.074339.

The crude mixture of volatiles gave three peaks A, B, and C in respective area ratios of 10:45.5:44.5 in order of increasing retention time on a DEGS column. Each component was collected for spectral analysis. Component A was shown to be aldehyde 125 derived from pyrolysis of 3,3-difluorobicyclo-[2.1.0]pentane-1-methanol (107) in the gas chromatograph. The presence of 107 in the crude product mixture was established by nmr spectroscopy, while the same method showed that the aldehyde was absent in the crude mixture. Component B gave the following spectral data: 100 MHz pmr ($CDCl_3$) 2.1, broad singlet (1H); 2.25-3.1, complex (4H); 4.17, multiplet (1H); 5.03, multiplet (2H) (shown in Figure 10). fmr ($CDCl_3$) 106.5 ppm doublet of multiplets; 116.5 ppm doublet of multiplets. The doublet splitting was 240 Hz. Because the samples was very dilute resulting in slow S/N ratio, only the upfield multiplet in the low field doublet was sufficiently resolved to be meaningfully analyzed. It consisted of a

triplet of doublets with approximate J values of 19 Hz and 9 Hz. The multiplets of the high field doublet had the same general outline as the low field pair. The ir spectrum of component B ($CHCl_3$) contained major absorptions at 3610, 3420, 3050, 2942, 1675, 1610, 1432, 1362, 1290, 1245, 1135, 1078, 1055, 985, 895, and 877. The mass spectrum of this component was not obtained. Component B has been tentatively assigned structure 131 on the basis of its spectra.

Component C gave the 100 MHz pmr spectrum shown in Figure 9 and an fmr spectrum ($CDCl_3$) consisting of a symmetrical triplet J = 12 Hz at 100 ppm upfield from $CFCl_3$. The ir spectrum of component C ($CHCl_3$) contained major absorption bands at 3612, 3003, 2968, 1335, 1290, 1220, 1200, 1155, 1105, 1037, 978, and 947 cm^{-1}. The mass spectrum of component C did not contain a molecular ion; major fragmentation ions were observed at m/e 86, 77, 73, and 72 (base peak).

On treatment of component C with p-toluenesulfonyl chloride and pyridine followed by the usual workup a product was obtained whose pmr spectrum was identical to that of tosylate 129. On the basis of the spectral and chemical data component C is assigned structure 130. Each of the solvolysis products was shown to be present in the crude solvolysis product mixture by nmr spectroscopy.

Solvolysis kinetics of 3,3-difluorobicyclo[2.1.0]pentane-1-methyl tosylate (127) at 39.9°

Aqueous acetone (80%) was prepared by mixing four volumes of reagent acetone further purified by the method of Hammond and Kochi (141) with one volume of doubly distilled water. Aqueous 80% acetone (25 ml) contained in a stoppered 25-ml volumetric flask was placed in an oil bath at 39.9° and allowed to equilibrate for 15 min. Then 0.2544 g of tosylate 127 was pipetted into the solution, the flask inverted several times to obtain a uniform mixture and a timer started. At timed intervals 2.00 ml aliquots were removed by means of a pipette and transferred to a flask containing 2 ml of ice cold 80% acetone and a magnetic stir bar. Bromthymol blue indicator solution was added and the resulting solution titrated with 0.208 N aqueous sodium hydroxide. The experimental infinity titer was 2.17 ml or 64% of theory.

The titrimetric rate data was analyzed by assuming that the solvolysis of 127 proceeds by a series of parallel first-order reactions. The sum of the rate constants for each of the solvolysis and internal return steps then corresponds to the apparent rate constant (k_{app}) for initial ionization. Since a reactant decomposing through a series of parallel first-order reactions has a half-life equal to the half-growth time of each of the products which in turn is equal to $\ln 2/k_{app}$, determination of the half-growth time of any product is

sufficient to determine k_{app} (142). The half-growth time of p-toluenesulfonic acid was determined from the linear plot of log/ml base used at time T - ml of base used at infinity/ vs. time. The time corresponding to 1.085 ml of base is the half-growth time for p-toluene-sulfonic acid and was found to be 3.57×10^3 sec from which k_{app} is calculated to be 1.94×10^{-4} sec^{-1}.

The limited amount of 127 available permitted only one run at each of two temperatures. A second run at 50.0° gave a half-growth time for p-toluenesulfonic acid of 1.35×10^3 sec from which a k_{app} of 5.13×10^{-4} sec^{-1} was calculated.

Attempted preparation of 1-carbomethoxy-8,9-diazobicyclo-[4.3.0]non-8-ene

A solution of diazomethane generated 16.0 g (0.155 mole) of nitrosomethylurea in the usual way was mixed with a solution of 6.35 g (0.0450 mole) of methyl cyclohexene-1-carboxylate in 50 ml of ether and allowed to stand 19 hr at room temperature. Excess diazomethane was decomposed by the gradual addition of formic acid until the yellow color was discharged. The ethereal solution was washed with saturated sodium bicarbonate solution and water then dried. Ether was removed on a rotary evaporator to give 6.54 g of an oil whose nmr spectrum indicated it was almost entirely the starting ester. There was minor absorption in the δ 4-5

region attributable to the desired pyrazoline. The above procedure was repeated but only a minor increase in the pyrazoline bands was observed after 3 days reaction time.

Electrolysis of bicyclo[3.1.0]hexane-1-carboxylic acid

In a typical experiment 2.04 g of bicyclo[3.1.0]hexane-1-carboxylic acid (prepared by saponification of the methyl ester (11) with 15% potassium hydroxide at room temperature) was dissolved in 500 ml of water and the solution was made slightly alkaline by addition of dilute aqueous potassium hydroxide solution. A copper cathode and carbon anode was immersed the solution and connected to a variable DC voltage source. The electrolysis was conducted at 40 volts for 4 hr then at 100 volts for an additional 2 hr. The basic aqueous solution was extracted continuously with ether to give after drying and removal of the solvent only 0.125 g of neutral products. Analyses of this mixture by vpc on a DC 550 column indicated four to six major products. The nmr spectrum of the mixture consisted of broad overlapping bands from δ 1.0-2.8, smaller absorption in the 3.2-3.7 range, a broad at 3.8-4.4, similar appearing multiplets at 4.8 and 5.0 a complex absorption centered at 5.7 and a complex absorption at 7.2. The infrared spectrum of the mixture contained major bands at 3430, 2900, 1740, 1708, 1440, 1402, 1380, 1350, 1255, and 1180-950 (broad continuous) cm^{-1}. The mass spectrum of the mixture contained visible ions at m/e 141-101 but the highest

m/e value of strong intensity was m/e 98. Other ions of significant intensity were observed at m/e 97, 96, 83, 81, 80, 68, 67, 57, 55 (base peak) 43, 41, and 39.

From the acidified aqueous solution, 0.911 g of crude starting acid was isolated by continuous ether extraction.

3,3-Dimethylbicyclo[2.1.0]pentane-1-carboxylic acid hydrazide (145)

To 13.5 g (0.40 mole) of 95% hydrazine at 40-45° was added 4.18 g (0.0272 mole) of 3,3-dimethyl-1-carbomethoxybicyclo[2.1.0]pentane (11) in portions over 4 hr. When the addition was complete the homogeneous solution was stirred for an additional 9 hr at room temperature then poured into 40 ml of ice water. The white crystalline product was collected on a filter and dried to give 2.0 g of material mp 57-58.5°. Upon cooling the mother liquor in a Dry Ice/isopropanol bath an additional 0.32 g of product mp 56-58.5° was obtained an additional 0.75 g of product mp 57-58 was obtained from the concentrated mother liquor. The total yield was 3.07 g (75%) of the title compound of sufficient purity to be used in the following reaction. After several recrystallizations from benzene/petroleum ether the melting point was raised to 59-60.5°; 100 MHz nmr ($CDCl_3$) 0.86, singlet (3H); 1.28, singlet superimposed on a multiplet (4H); 1.4-1.66, two overlapping multiplets (2H); 1.8, doublet of doublets, J's = 11 Hz,

1.8 Hz (1H); 2.05, doublet of doublets, J's = 6.5 Hz, 3Hz (1H); 3.55, broad hump (2H); 7.4, broad hump (1H); ir($CHCl_3$) 3460, 3340, 3030, 2970, 2940, 2870, 1660, 1630, 1490, 1470, 1375, 1310, 1255, 1030, 965.

High resolution mass spectrum: Calcd for $C_8H_{14}N_2O$: m/e 154.110596. Found m/e 154.111052.

3,3-Dimethylbicyclo[2.1.0]pentane-1-amine hydrochloride (141-HCl)

3,3-Dimethylbicyclo[2.1.0]pentane-1-carboxylic acid hydrazide, 3.00 g (0.0195 mole) was dissolved in 14 ml of 4 N hydrochloric acid which had been cooled to 0°. Then 13 ml of ether was added and the mixture stirred magnetically so as not to appreciably agitate the ether layer. While maintaining the temperature of the mixture below 5° (ice bath) a solution of 1.68 g (0.0244 mole) of sodium nitrite was slowly introduced through a pipette whose tip dipped into the aqueous layer. When the addition was complete the ether layer was separated, filtered to remove a small quantity of white solid, and dried ($MgSO_4$). The ethereal solution was concentrated to a volume of 5-10 ml on a rotary evaporator and then mixed with 50 ml of benzene. The benzene solution was heated at 70-80° while monitoring the infrared spectrum and gas evolution. After 5 hr the gas evolution was complete and the azide band at 2142 cm^{-1} had been almost completely replaced by an isocyanate band at 2275 cm^{-1}. The nearly colorless solution was then

concentrated to a volume of 5-10 ml on a rotary evaporator and mixed with 35 ml of 6 M hydrochloric acid. The resulting mixture was heated in a 75° oil bath for 1 hr, then cooled and extracted with ether until the extracts were nearly colorless. The ethereal extracts were washed with 6 M hydrochloric acid and the aqueous portions were combined. After concentrating the dark aqueous solution to ca. 25 ml under reduced pressure it was treated with decolorizing carbon until only a pale yellow color remained. Evaporation of the water under reduced pressure and final drying at 30-50° and .1 torr gave 1.165 g (41%) of 141-HCl as a pale yellow crystalline solid. The purity of the product obtained in this way was determined to be approximately 95% by titration with 0.208 N sodium hydroxide in aqueous solution to a phenolpthalein end-point. The nmr spectrum of 141-HCl in trifluoroacetic acid is shown in Figure 14.

1-p-nitrobenzamido-3,3-dimethylbicyclo[2.1.0]pentane (148)

A small portion of the amine hydrochloride (141-HCl) was suspended in a solution of excess p-nitrobenzoylchloride in 5 ml of benzene and the mixture cooled to 5-10°. Then 1-2 ml of 15% potassium hydroxide solution was added and the mixture shaken vigorously for 10 minutes. A small amount of a crystalline material which had separated soon after the addition of potassium hydroxide was filtered off and identified

as p-nitrobenzamide by spectral (nmr, ir) and mixture melting point comparisons with an authentic specimen. After drying ($MgSO_4$) the benzene solution, the solvent was removed on a rotary evaporator to give the crude bicyclic amide which was purified on a silica gel column with ether/hexane (1:3) elutant to give white crystals, mp 109-110°. Except for predictable differences in chemical shifts the nmr spectrum of 148 (Figure 15) is virtually identical to that of hydrazide 145. The ir spectrum of 148 ($CHCl_3$) contained major bands at 3450, 3050, 2970, 2942, 2880, 1685, 1610, 1537, 1515, 1490, 1353, and 1278 cm^{-1}, and the mass spectral molecular weight was 260.

Anal. Calcd for $C_{14}H_{16}N_2O_3$: C, 64.60; H, 6.20. Found: C, 64.52; H, 5.96.

Attempt to isolate 1-amino-3,3-difluorobicyclo[2.1.0]pentane (141)

A small portion of hydrochloride 141-HCl was dissolved in 3 ml of water; 5 ml of ether was added followed by several drops (excess) of 15% potassium hydroxide solution. The mixture was shaken vigorously for several seconds and the ether layer was removed and immediately concentrated on a rotary evaporator. The 60 MHz nmr spectrum of the residue in carbon tetrachloride consisted of an apparent methyl singlet at 1.0 and a complex absorption from 1.1-2.6. After standing

for 50 min at room temperature the nmr spectrum of a second portion of the residue was identical to that of authentic 3,3-dimethylcyclopentanone.

Bicyclo[3.1.0]hexane-1-carboxylic acid hydrazide

A quantity of 10.1 g (0.0655 mole) of 1-carboethoxybicyclo[3.1.0]hexane (11) was added dropwise over 20 hr to 20 ml of 95% hydrazine at 70°. When the addition was complete the mixture was heated to 100° for an additional 10 hr then cooled and poured into 75 ml of ice water. The solution was continuously extracted with ether to give 6.55 g (72%) of the title compound as a colorless, very viscous oil, 100 MHz nmr ($CDCl_3$) 0.77, triplet, J = 5 Hz (1H); 1.25, complex (2H), 1.85, complex (6H); 3.90, broad hump (2H); 7.5, broad hump (1H). ir($CHCl_3$) 3465, 3340, 3030, 2980, 2950, 2880, 1665, 1630, 1495, 1460, 1375, 1310, 1298, 1045, 992, 952, 913. Mass spectral molecular weight: 140.

Bicyclo[3.1.0]hexane-1-amine hydrochloride (149-HCl) and 1-aminobicyclo[3.1.0]hexane (149)

Bicyclo[3.1.0]hexane-1-carboxylic acid hydrazide 6.35 g (0.0453 mole) was dissolved in 33 ml of 4 N hydrochloric acid, 30 ml of ether was added, and the mixture was cooled in an ice/salt bath. The mixture was stirred with minimum agitation of the ether layer while a solution of 3.96 g (0.0574 mole) of sodium nitrite in 9 ml of water was introduced below the ether

layer at such a rate that the temperature did not rise above 5°. When the addition was complete the ether layer was separated, the aqueous phase was extracted with fresh ether and the combined etheral solution was dried ($MgSO_4$). After removing most of the ether under reduced pressure, the residue was taken up in 70 ml of benzene and heated in an 85° oil bath for 4.5 hr. After cooling and removing most of the benzene on a rotary evaporator, the residue was heated with 50 ml of 6 N hydrochloric acid for 45 min at 70°. The resulting dark mixture was cooled, then extracted with a total of 100 ml of ether. The ethereal phase was washed with two 10 ml portions of 6 N hydrochloric acid and the aqueous phases were combined. The dark aqueous solution was decolorized with activated carbon, concentrated to a volume of 60 ml on a rotary evaporator, decolorized once again, then evaporated to near dryness on a rotary evaporator. Final drying at 50° and 0.5 mm gave 3.05 g (51%) of the title hydrochloride whose nmr spectrum is shown in Figure 16.

The free amine (149) was obtained by an analogous procedure in which the aqueous phase after acid hydrolysis of the isocyanate was extracted with ether to remove neutral impurities then made alkaline with 50% potassium hydroxide solution. The liberated amine was isolated by ether extraction and purified by molecular distillation at 70° and 90 torr. The resulting product was colorless and gave the following

spectral properties: 60 MHz nmr (CCl_4) 0.3-0.7, multiplet (2H); 0.9-2.1, complex (7H); 2.88, broad singlet (2H). ir (film) 3350, 2920, 2860, 1665, 1600, 1477, 1445, 1377, 1355, 1305, 1247, 1225, 1018: mass spectrum m/e 97(M^+), 93 (base peak).

The benzamide of 149 was prepared by the reaction of 149 with benzoyl chloride in alkaline aqueous media and purified by recrystallization from methanol/water; mp 154.5-155°; 100 MHz nmr ($CDCl_3$) 0.60-1.00 complex (2H); 1.1-2.3, complex 7H, 6.66, broad hump (1H); 7.28-7.5, complex (3H); 7.65-7.85, complex (2H); ir($CHCl_3$) 3460, 3050, 2980, 2880, 1668, 1587, 1520, 1492, 1455, 1305, 1283, 1132; mass spectral molecular weight 201.

Anal. Calcd for $C_{13}H_{15}NO$: C, 77.58; H, 7.52. Found: C, 77.29; H, 7.52.

Deamination of bicyclo[3.1.0]hexane-1-amine hydrochloride

To a stirred solution of 1.11 g (0.00835 mole) of bicyclo[3.1.0]hexane-1-amine hydrochloride in a mixture of 20 ml of glacial acetic acid and 1 ml of acetic anhydride under nitrogen was added 2.6 g (0.038 mole) of sodium nitrite in small portions over 2.5 hr. When all the sodium nitrite had been added the solution was stirred for an additional 20 min then poured into 75 ml of saturated sodium bicarbonate solution. The aqueous solution was continuously extracted

with pentane and the pentane extract was washed with saturated sodium bicarbonate solution until the aqueous phase remained alkaline, then water and dried over anhydrous magnesium sulfate. Pentane was then removed first by distillation at atmospheric pressure and finally by brief exposure to water aspirator vacuum to give 0.772 g of a crude product mixture.

Analysis of the mixture by vpc on an FFAP column at 100-120° showed a small amount of residual pentane and six major products (A-F) in the ratio 2.6 : 19.0 : 0.8 : 34.3 : 3.5 : 39.8 (Table 7). The minor components A, C, and E were not obtained in sufficient quantities for characterization. Components D and F were identified as 2-methylenecyclopentyl acetate (152) and cyclopentene-1-methyl acetate (151) by comparison of their nmr and ir spectra with spectra of authentic specimens (v.i.). Component B was identified as cyclopentene-1-methyl chloride (150) on the basis of its spectra: 100 MHz nmr (CCl_4) 1.8-2.2, complex (2H); 2.2-2.6, complex 4H; 4.07, slightly broadened singlet (2H); 5.68 narrow, poorly resolved multiplet (1H); ir (CCl_4) 3108, 3050, 2960, 2855, 1448, 1272, 1260; mass spectrum (major ions) m/e 118 and 116 (M°), 79, 67 (base peak). The nmr spectrum of 150 was in good agreement with that reported earlier for cyclopentene-1-methanol (9).

Deamination of 1-aminobicyclo[3.1.0]hexane (149)

The title amine, 0.40 g (0.0041 mole) was dissolved in 5 ml of glacial acetic acid containing ca. .25 ml of acetic anhydride and 0.80 g (0.012 mole) of sodium nitrite was added in portions over 1 hr. When gas evolution appeared complete the acetic acid was neutralized with excess saturated sodium bicarbonate solution and the aqueous solution was extracted with several portions of hexane. The combined hexane extracts were washed with successive portions of saturated bicarbonate solution and water, then dried ($MgSO_4$). After concentration of the hexane solution on a rotary evaporator vpc analysis (SE-30) showed two major components A and B in a 57:43 ratio. Both components were collected and identified as 152 and 151 respectively by spectral (nmr, ir) comparisons with authentic specimens.

Cyclopentene-1-methyl acetate (151)

Ethyl cyclopentene-1-carboxylate 1.4 g (0.010 mole) in 10 ml of ether was added slowly to an ice cold solution of 0.304 g (0.00800 mole) of lithium aluminum hydride in 20 ml of ether to which had previously been added 0.368 g (0.00800 mole) of absolute ethanol. The mixture was stirred for 1 hr at 0°, then 30 min at room temperature, and finally worked up by the usual water, sodium hydroxide procedure to give cyclopentene-1-methanol whose nmr spectrum was identical to that previously reported (9). The crude product was taken up

in 15 ml of ether, mixed with 5 g of pyridine, and then treated dropwise with excess acetyl chloride. The mixture was poured into water, and the ether layer was separated and combined with ethereal extracts of the aqueous phase. The combined ethereal extracts were washed with saturated sodium bicarbonate solution and water then dried over anhydrous magnesium sulfate. The residue obtained on removal of the solvent at reduced pressure gave a single peak on vpc analysis. A pure sample of the title compound was obtained by preparative gas chromatography. 100 MHz nmr (CCl_4) 1.7-2.15, complex pattern with superimposed singlet at 2.00 (5H total), 2.15-2.6, complex (4H); 4.54, broadened singlet (2H); 5.60, narrow, poorly resolved multiplet (1H); ir (CCl_4) 3035, 2940, 2880, 2835, 1730, 1650, 1432, 1365, 1355, 1263, 1220, 1030, 1015, 950. Mass spectral molecular weight, 140.

2-Methylenecyclopentyl acetate (152)

Crude 2-methylenecyclopentanol, 1 g prepared by reduction of 2-carbethoxycyclopentanone with lithium aluminum hydride (135) was dissolved in 4 ml of acetic anhydride containing ca. 0.25 ml of pyridine and heated on a steam bath for 30 min. The solution was cooled, mixed with 7 ml of water, and heated on a steam bath to hydrolyze excess acetic anhydride. The resulting solution was extracted with ether and the ethereal extracts were washed with saturated sodium bicarbonate solution

and water. After drying ($MgSO_4$) and removing the ether on a rotary evaporator the product was purified by preparative gas chromatography (SE 30). 100 MHz nmr (CCl_4) 1.6-2.2, complex pattern with superimposed singlet at 1.98 (total 7H); 2.2-2.55, complex (2H); 5.0, narrow multiplet, 1H; 5.09, narrow multiplet (1H); 5.36, broad multiplet (1H). ir(CCl_4) 3095, 2980, 2890, 1745, 1665, 1440, 1378, 1250, 1142, 1050, 1030, 968, 910, 900. The mass spectrum of 152 did not contain a molecular ion; the highest ion of significant intensity was m/e 98 and the base peak was at m/e 80.

Anal. Calcd for $C_8H_{12}O_2$: C, 68.54, H, 8.63. Found: C, 68.33; H, 8.65.

Deamination of 3,3-dimethylbicyclo[2.1.0]pentane-1-amine hydrochloride (141-HCl)

To a stirred solution of 1.230 g (0.00835 mole) of the title amine salt in a mixture of 20 ml of glacial acetic acid and 1 ml of acetic anhydride was added 2.6 g (0.038 mole) of sodium nitrite in small portions over 3.25 hr. When the sodium nitrite addition was complete the mixture was stirred for an additional 1/2 hr at room temperature then poured into 80 ml of saturated sodium bicarbonate solution. The aqueous solution (still acidic) was extracted with a total of 75 ml of pentane in small portions. The pentane extract was washed with successive portions of saturated bicarbonate solution and water and then dried. Most of the pentane was removed by

distillation at atmospheric pressure followed by brief treatment on a rotary evaporator to give 0.52 g of a crude product mixture. Analysis of the mixture by VPC on an FFAP column showed 14 products as summarized in Table 8. The first two components were not well resolved and were collected together. A comparison of the nmr spectrum of the mixture with spectra of compounds later identified as 158 and 159 indicated that these products were the corresponding chlorides 156 and 157. The resonances arising from 156 appeared at 1.15, methyl singlet; 1.26, methyl singlet; 2.36, multiplet, ring methylene; 4.44, multiplet, allylic methine; 5.94, multiplet, olefinic; 5.14, multiplet, olefinic. Resonances arising from 157 appeared at 1.23, methyl singlet, 2.25, broad singlet, ring methylene; 3.93, multiplet, chloromethylene; 5.94, triplet, J = 1 Hz, olefinic. The infrared spectrum (CCl_4) of the mixture contained major bands at 3045, 2960, 2930, 2870, 1465, 1440, 1367, 1292, 1258, 940, and 895 cm^{-1}. The mass spectrum of the mixture contained molecular ions for at least one of the components at m/e 130 and 132. The third component was not identified.

The fourth component was identified as 158 on the basis of its spectra 100 MHz nmr (CCl_4) 1.01, singlet (3H); 1.26, singlet (3H); 2.04, singlet (3H); 2.19, four line multiplet with spacings of 2.0-2.4 Hz, (2H); 4.85, four line multiplet with spacings of 2.1-2.4 Hz (1H); 5.01, 7 line multiplet with

spacings of 2-2.4 Hz (2H). The infrared spectrum of 158 contained major bands at 3100, 2975, 2940, 2885, 1750, 1695, 1470, 1440, 1377, 1245, 1075, 1065, and 898 cm^{-1}. The mass spectrum of 158 contained a weak molecular ion at m/e 154 and major fragment ions at m/e 111, 94, 91, 79 (base peak), and 77.

The fifth and eighth components were identified as 3,3-dimethylcyclopentanone (160) and 5,5-dimethylcyclopenten-3-one (161) respectively by nmr, ir, and mass spectral comparisons with authentic specimens (11,136).

The sixth and seventh components were identified as 3,3-dimethylcyclobutene-1-methyl acetate (159) and 3-acetoxy-5,5-dimethylcyclopentene (162) also by nmr, ir and mass spectral comparisons with authentic specimens (see below).

The ninth and tenth components were not obtained in sufficient quantity for characterization.

Components eleven and twelve gave very similar nmr and mass spectra indicative of closely related isomers. Component eleven gave the following data: 100 MHz nmr (CCl_4) 1.04, singlet (3H); 1.15, singlet (3H); 1.5, doublet of doublets, J = 5 and 14 Hz (1H); 1.96, singlet (3H); 1.95-2.45, complex (3H); 3.95, triplet, J = 8 Hz (1H); 5.11, multiplet consisting of seven broad lines, spaced approximately equal at 4 Hz (1H). ir(CCl_4) 2975, 2945, 2880, 1750, 1470, 1460, 1440, 1395, 1375, 1365, 1250, 1195, 1042, 1020. Mass spectrum: m/e 190 (192)

(apparent M^+) 155, 132, 130, 115, 95, 94, 93, 91, 79 (base peak). Component twleve gave the following data: 100 MHz nmr (CCl_4) 1.08, singlet (3H); 1.14, singlet (3H); 1.75-2.15, complex with superimposed singlet at 1.99 (total 6 H); 2.74, multiplet consisting of five lines equally spaced at 7.5 Hz (1H); 3.72, doublet of doublets, J = 7 and 8.7 Hz (1H); 4.95, multiplet (1H). ir(CCl_4) 2975, 2945, 2890, 1750, 1472, 1460, 1438, 1391, 1375, 1365, 1250, 1195, 1160, 1070, 1047, 1025. Mass spectrum: m/e 92, 91 (base peak), 79, 77, 65. On the basis of the above data components eleven and twelve were tentatively assigned structures 163A and B.

Components thirteen and fourteen also gave very similar sets of spectra indicative of a second set of closely related isomers. Component 13 gave the following data: 100 MHz nmr (CCl_4) 1.0, singlet (3H); 1.20, singlet (3H); 2.02, singlet (3H); 2.07, singlet (3H); 4.95, doublet, J = 5 Hz (1H); 5.55, complex (2H); 5.1, perterbed doublet, J = 5 Hz (1H); ir (CCl_4) 3060, 2978, 2945, 2880, 1750, 1470, 1440, 1378, 1253, 1236, 1082, 1060, 1040, 983, 928, 907, 885. Mass spectrum: m/e 94, 93, 92, 91, 79 (base peak), 77. Component fourteen gave the following data: 1.08, singlet (3H); 1.14, singlet (3H); 1.99, singlet (3H); 2.05, singlet (3H); 4.88, doublet, J = 6 Hz (1H); 5.6, complex (2H); 5.86 doublet, J = 6 Hz (1H). ir(CCl_4) 3060, 2975, 2945, 2880, 1750, 1473, 1440, 1378, 1258, 1236, 1108, 1090, 1055, 1030, 1015, 970, 935, 912, 870. Mass

spectrum: m/e 95, 94, 93, 92, 91 (base peak) 79, 77, 65. On the basis of the above data components thirteen and fourteen were tentatively identified as 164.

3,3-Dimethylcyclobutene-1-methyl acetate (159)

3,3-Dimethylcyclobutene-1-carboxylic acid was prepared by the method of Brannock et al. (141) and converted to the methyl ester through a standard thionyl chloride-methanol sequence.

To a suspension of 0.204 g (0.0054 mole) of lithium aluminum hydride in 20 ml of ether at 0° to which had previously been added 0.246 g (0.0054 mole) of absolute ethanol was added 1.00 g (0.00715 mole) of methyl 3,3-dimethylcyclobutene-1-carboxylate in 6 ml of ether. As the addition was being completed the suspension coagulated into a gummy mass which could not be stirred. An additional 10 ml of ether was added without improvement. The cold bath was removed and the mass was allowed to remain at room temperature for 1.5 hr. Following the usual water-sodium hydroxide workup the solvent was removed on a rotary evaporator to give 0.86 g of crude 3,3-dimethylcyclobutene-1-methanol. A 0.39 g sample of the crude alcohol was dissolved in 4 ml of acetic anhydride, and 4 drops of pyridine was added. After heating the mixture on a steam bath for 1 hr it was worked up by the usual aqueous sodium bicarbonate procedure and the title compound was isolated by preparative vpc on an SF-96 column. 100 MHz nmr

(CCl_4) 1.20, singlet (6H); 2.00, singlet (3H); 1.68, broadened singlet (2H); 4.41, multiplet consisting of four lines equally spaced at 1.5 Hz; 5.94, triplet, J = 1.5 Hz (1H). ir (CCl_4) 3050, 2970, 2875, 1755, 1652, 1465, 1443, 1390, 1370, 1288, 1250, 1138, 1035, 910, 895. Mass spectral: molecular weight, 154.

3-Acetoxy-5,5-dimethylcyclopentene (162)

A solution of 0.095 g of 5,5-dimethylcyclopenten-3-ol (136) in 1 ml of acetic anhydride containing several drops of pyridine was heated at 80° for 30 min then cooled and the reaction mixture worked up by the usual aqueous sodium bicarbonate procedure. The title acetate was isolated by preparative vpc on an FFAP column. 100 MHz nmr (CCl_4) 1.12, singlet (3H); 1.16, singlet (3H); 1.65, doublet of doublets, J = 3.5 and 14 Hz (1H); 1.9-2.25, multiplet with superimposed singlet at 1.98 (total 4H), 5.5-5.65, complex (2H); 5.76, multiplet (1H). ir(CCl_4) 3080, 3030, 2970, 2943, 2840, 1741, 1460, 1440, 1368, 1350, 1250, 1138, 1100, 1050, 1027, 960, 932, mass spectrum m/e 154 (weak M^+), 112, 97, 96, 95, 94, 93, 91, 81, 80, 79 (base peak), 77.

Cycloaddition of dimethylketene and divinylether

To 67 g (0.96 mole) of divinyl ether was added 150 ml of a .965 M solution of dimethylketene in ethyl acetate (10.2 g 0.145 mole dimethylketene) under nitrogen. The mixture was

stirred and heated to gentle reflux overnight. The mixture was then distilled at atmospheric pressure to recover 51 g of unreacted divinyl ether. The distillation was continued at reduced pressure to give 8.16 g (40%) of cycloadduct 174, bp 65-70° at 55 mm contaminated with a small amount of dimethylketene dimer. A pure specimen of the cycloadduct was obtained by preparative vpc on an SF-96 column. 100 MHz nmr (CCl_4) 1.16, singlet (3H), 1.22, singlet (3H), 3.14, AB portion of an ABX pattern, J'_{AB} = 18 Hz, J_{AX} = 6 Hz, J_{BX} = 7 Hz (2H); 4.0-4.3, complex (2H), 6.5, doublet of doublets, J = 7 and 14 Hz (1H); ir (CCl_4) 3130, 3090, 3060, 2970, 2930, 2870, 1794, 1670, 1640, 1620, 1465, 1448, 1385, 1370, 1355, 1323, 1205, 1170, 1065, 1045, 962. Mass spectral molecular weight, 140.

2,2-Dimethyl-3-acetoxycyclobutanone (177)

The reduction of 1.42 g (0.010 mole) of cycloadduct 174 with 0.13 g of lithium aluminum hydride at room temperature afforded upon workup a quantitative yield of the alcohol which was acetylated by the usual acetic anhydride/pyridine method to give acetate 175 which was in turn taken up in ether and stirred overnight with 1 M aqueous sulfuric acid to give the crude acetoxy alcohol 176 in 63% overall yield from 174. The nmr spectrum of crude 174 contained resonances for the ring methine hydrogens at 3.6 and 4.33. Each was a triplet with

splittings of ca. 8 Hz. A Jones oxidation of 176 produced crude 177 in 57% yield. A sample of 177 purified by preparative gas chromatography on an SF-96 column gave the following spectral data: 100 MHz nmr (CCl_4) 1.08, singlet (3H); 1.25, singlet (3H); 2.07, singlet (3H); 3.20, AB portion of an ABX pattern, J_{AB} = 18 Hz, J_{AX} = 5.75 Hz, J_{BX} = 7.5 Hz (2H), 4.84, doublet of doublets (X portion of ABX), J = 5.7 and 7.5 Hz (1H). The ir spectrum contained strong carbonyl absorptions at 1798 and 1750 cm^{-1}. The mass spectrum of 177 did not contain a molecular ion; the highest ion of significant intensity was m/e 114 (M^+-42). Other intense fragment ions were observed at m/e 96, 81, 72, 70, 67, 60, 57, 53, and 43 (base peak).

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