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THE THERMAL DECOMPOSITION OF CYCLOBUTANECARBOXALDEHYDE p-TOSYLHYDRAZONE AND THE REACTION OF SILVER TETRAFLUOROBORATE WITH ORGANIC CHLORIDES

BY

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JUNE 30, 1966

CANDIDATE	SUPERVISOR
PETER W.N. KWOK, B.Sc.	D.H. PASKOVICH, Ph.D.

TO

MY DEAR PARENTS

WITHOUT WHOSE ENCOURAGEMENT

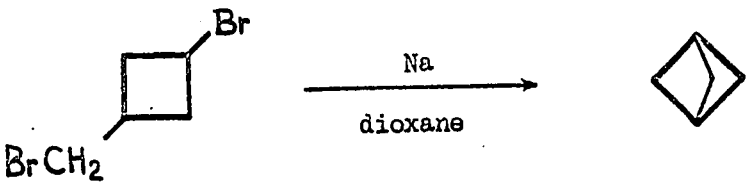
THIS WORK COULD NOT HAVE BEEN COMPLETED

PREFACE

In recent years, there has developed, from both a mechanistic and synthetic view point, an increasing interest in the chemistry of carbenoid and cationic species generated by thermal decomposition of p-tosylhydrazones. The synthetic utility of this reaction has been exploited in the synthesis of many new highly strained small ring compounds.

Our original aim was the synthesis of bicyclo(1.1.1)pentane (1) system, which was unknown at the time when this work was started, by thermally decomposing the cyclobutanecarboxaldehyde p-tosylhydrazone (2). This problem was challenging since many attempts to synthesize this highly strained bicyclic small ring system by many competent chemists were unsuccessful.

Our attempt was also unfortunately unsuccessful. During our research, K. B. Wiberg, D. S. Connor and G. M. Lampman[1] reported the successful synthesis of bicyclo(1.1.1)pentane by ring closure of 3-bromocyclobutane-1-methyl bromide (3) with sodium.



(3) (1)

The work in Part I of this thesis reports the effect of varying solvents and bases in the pyrolytic reaction of cyclobutanecarboxaldehyde p-tosylhydrazone.

Part II of this thesis is actually an extension of our interest in the chemistry of carbonium ions. By reacting silver tetrafluoroborate with organic chlorides in aprotic solvents we had hoped to produce conditions favorable for carbocyclic ring closure. The products formed, however, are those resulting from reaction of a carbonium ion with solvent and the tetrafluoroborate anion.

ACKNOWLEDGEMENT

The author wishes to thank his research director, Dr. D. H. Paskovich, and Dr. P. F. Morand for their guidance of this work, and to express to the Ontario Research Foundation his appreciation of the necessary financial assistance in the form of a Graduate Fellowship.

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Aldehyde and ketone p-tosylhydrazones react thermally with bases in aprotic solvents to give diazo-compounds which decompose by carbenic processes. In proton-donor solvents decomposition appears to occur primarily by cationic mechanisms involving diazonium and/or carbonium ion intermediates.

Thermal decomposition of cyclobutanecarboxaldehyde p-tosylhydrazone gives methylenecyclobutane by hydrogen migration, cyclopentene by ring expansion, bicyclo(2.1.0)pentane by intramolecular insertion, 2-methylbutene-1 by reorganization, methylcyclobutane by hydride transfer, along with ethylene and acetylene by fragmentation.

The effect of varying solvents and bases on the product compositions is reported.

A brief historical review is given and the mechanisms of this reaction are discussed.

PART II

A new method for the preparation of organic fluoro-compounds was discovered.

Reaction of cholesteryl chloride with silver tetrafluoroborate in monoglyme gave good yields of cholesteryl fluoride and cholesta-3,5-

diene. In a similar way, 4-chloromethylfluorenone gave the corresponding fluoride as a principal product.

PART I

THE THERMAL DECOMPOSITION OF CYCLOBUTANECARBOXALDEHYDE p-TOSYLHYDRAZONE

INTRODUCTION

The derivatives of tosylhydrazide (p-toluenesulphonylhydrazine) can be grouped in two categories: the tosylhydrazones (4) (derivatives of aldehydes and ketones: general formula Ts-NHN=CR_1R_2) and the substituted tosylhydrazides (5) (acyl, aryl or alkyl-tosylhydrazides: general formula Ts-NH-NH-R).[2]

The thermal decomposition reaction of a tosylhydrazide was first done in 1885 when Escales observed that benzenesulphonylphenylhydrazide (6) was decomposed by warm alkali, giving benzene, nitrogen, and benzenesulphinic acid (7).[3]

$$\underset{(6)}{Ph\text{-}SO_2\text{-}NH\text{-}NH\text{-}Ph} \longrightarrow PhH + N_2 + \underset{(7)}{Ph\text{-}SO_2H}$$

Based on this finding, Bamford and Stevens[4] in 1952 expected that the p-toluenesulphonylhydrazone of an enolisable ketone might analogously yield an olefin. For instance, the thermal decomposition of ethyl β-ketobutyrate p-tosylhydrazone (8) was studied.

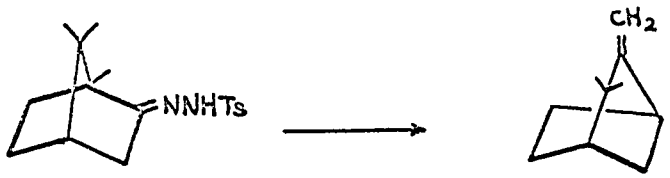
$$\underset{(8)}{Ts\text{-}NH\text{-}N{=}CMe\text{-}CH_2\text{-}COOEt} \longrightarrow \left[Ts\text{-}NH\text{-}NH\text{-}CMe{=}CH\text{-}COOEt\right] \longrightarrow$$

$$TsH + N_2 + \underset{(9)}{CHMe{=}CH\text{-}COOH} + EtOH$$

Ts = CH_3-C$_6$H$_4$-SO_2-

This reaction gave in fact a little crotonic acid (9). As a continuation of this work, they also found that the treatment of the tosylhydrazones of simple, not readily enolisable ketones with the sodium salt of ethylene glycol in ethylene glycol always leads to the formation of nitrogen, p-toluenesulphinic acid and olefins. Thus tosylhydrazones of acetone (10) and cyclohexanone (11) afforded propylene and cyclohexene in nearly quantitative yields. Carbon-skeleton rearrangements were observed in decomposition of pinacolone (12) and camphor (13) tosylhydrazones to give tetramethylethylene (14) (34% Yield) and camphene (15) (94% yield).

$$\underset{(12)}{Ts\text{-}NHN{=}C(CH_3)CMe_3} \longrightarrow TsH + N_2 + \underset{(14)}{Me_2C{=}CMe_2}$$



(13) (15)

The hydrazones of aromatic aldehydes and ketones, on the other hand, afforded arydiazoalkanes (16) or products of their decomposition:

$$Ts\text{-}NHN{=}CHPh \longrightarrow TsH + \underset{(16)}{N_2{=}CHPh}$$

By working at lower temperatures, substantial yields of the diazo-compounds could be attained from the derivatives of benzaldehyde (17), acetophenone (18), benzophenone (19) and fluorenone (20).

It was recently reported[5] that diazoalkanes and diazocycloalkanes can frequently be prepared conveniently and in high purity by vacuum pyrolysis (0.2-0.3 mm.) of dry (preferred) or suspended lithium or sodium salts of p-tosylhydrazones at 70 - 140°. The dry salts were obtained by precipitation after neutralization of the p-tosylhydrazone with butyllithium in tetrahydrofuran, sodium hydride in mineral oil, or sodium methoxide in absolute methanol-ether.

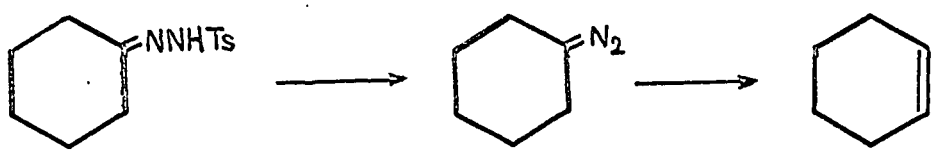
$$RCH{=}NNH\text{-}Ts + BuLi \longrightarrow RCH{=}NN(Li)Ts + Bu\text{-}H$$

$$RCH{=}NN(Li)Ts \longrightarrow RCH{=}N_2 + TsLi$$

The reaction discovered by Bamford and Stevens was intensively applied without substantial modifications, until in 1959, Powell and Whiting[6] in England and Friedman and Schechter[7] in U. S. A. described experiments designed to characterized this potentially useful reaction.

Acetone methanesulphonylhydrazone (21) was found to have pK_a ca. 8.5 by potentiometric titration. Accordingly, sulphonylhydrazones are highly ionized under the basic condition used for the reaction. The decompositions of the methane and p-toluene derivatives of cyclohexanone (11) and camphor (13)were studied kinetically. These two reactions were found to be of first-order with respect to the conjugate anions of the sulphonylhydrazones, proceeding at virtually the same

rate, and were independent of initial alkali concentration as the hydrazones were present essentially as the anions.



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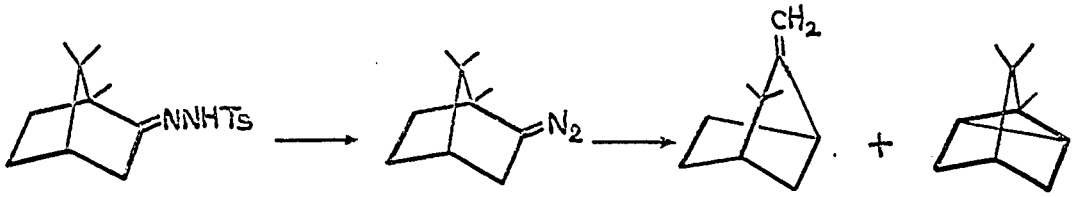


(13) (22) (15) (23)

Powell and Whiting therefore classed this reaction as a E_1cb mechanism and stressed the view that it was always the chosen route for the conjugate anion of a sulphonyl hydrazone to break down, in an initial rate-determining stage, to give an aliphatic diazo-compound.

Positive evidence for such a mechanism was provided by the finding that diazocamphane (22) and camphor methane and p-toluenesulphonylhydrazones (13) gave identical results.

Powell and Whiting also observed the important fact that the course of this thermal decompositions is very drastically affected by the solvent used and showed that changing the solvent markedly changed

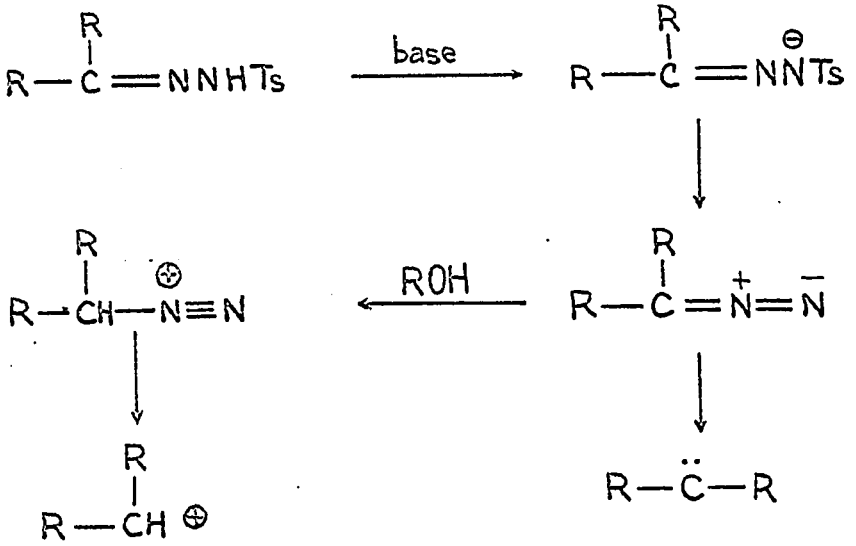
Table 1. Products from camphor sulphonylhydrazone decomposition[6]

Hydrazone	Solvent	Temperature	% Tricyclene
Ts	Glycerol	132°	12
Ts	Ethylene glycol	124	15
Ts	Ethylene glycol	139	20
Ms	Ethylene glycol	139	21
Ts	Ethylene glycol	195	23
Ts	Trimethylene glycol	132	46
Ms	Diethylene glycol	139	53
Ts	Ethanolamine	132	91
Ts	2-Ethoxyethanol	132	92
Ms	Acetamide	181	97
Ts	Acetamide	181	97
Ms	Acetamide	156	98
Ts	Acetamide	156	99

Ts = p-toluenesulphonyl; Ms = methanesulphonyl.

the camphene (15) : tricyclene (23) ratios from camphor p-toluenesulphonylhydrazone decomposition. Generally, the formation of camphene is promoted by a high concentration of acidic protons (Table 1).

The explanation is that the diazo-compound can decompose either with or without acid catalysis, undergoing: (a) proton transfer from proton donor solvents and cationic decomposition involving diazonium and/or carbonium ion intermediates, and (b) carbenic decomposition in aprotic solvents.

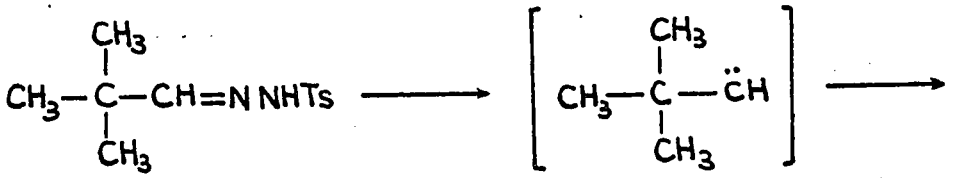


In both cases, p-toluenesulphinic acid and nitrogen are obtained. The cationic decomposition leads to olefins and Wagner-Meerwein rearrangement products whereas the carbenic decomposition gives olefins and insertion products.

In an investigation of the product compositions from the decomposition of tosylhydrazones of a series of simple aliphatic aldehydes

and ketones, Friedman and Shechter[7] concluded that (1) rearrangements in carbenoid decomposition of diazo-compounds involving hydrogen migration occur more readily than do carbon-skeleton rearrangements, (2) carbenoid decomposition of diazo-compounds results in extensive intramolecular cyclization to give cyclopropanes, and (3) the secondary carbenes presumably formed as reaction intermediates are more selective in their decomposition than are their primary analogs.

For example, the carbenoid decomposition of 2,2-dimethylpropanal p-tosylhydrazone (24) in sodium methoxide – diethyl carbitol gave 1,1-dimethylcyclopropane (25) (92%), 2-methyl-2-butene (26) (7%) and 2-methyl-1-butene (27) (1%).



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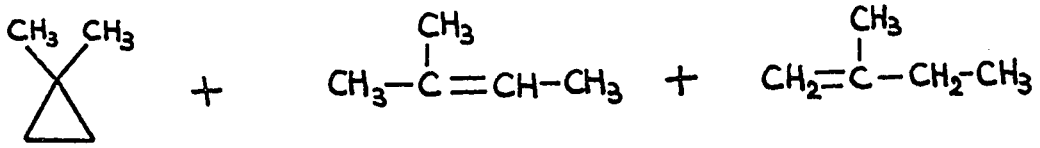
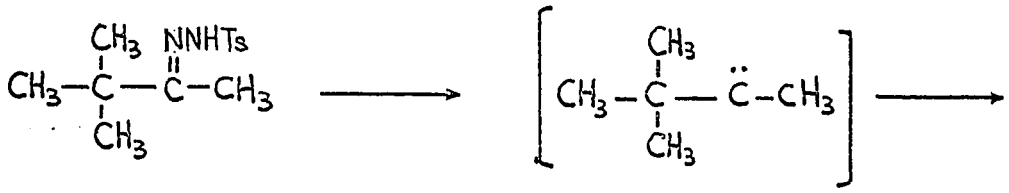


(25), 92% (26), 7% (27), 1%

On the other hand, decomposition of 3,3-dimethyl-2-butanone p-tosylhydrazone (12) gave 3,3-dimethyl-1-butene (28) (52%) and 1,1,2-trimethylcyclopropane (29) (47%).



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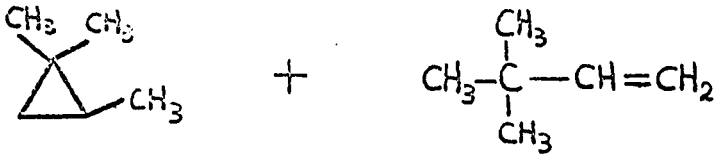


(29), 47% (28), 52%

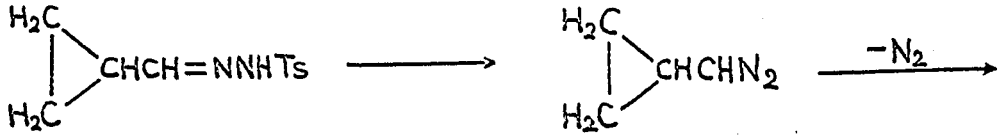
Since that time, the topic of the thermal decomposition of tosylhydrazones has attracted a great deal of interest, especially the carbenic decomposition in aprotic solvents because of its unusual capability of undergoing intramolecular insertion reaction to form highly strained polycyclic small ring systems.

The reaction mechanisms suggested by Powell-Whiting[6,8] and Friedman-Shechter[7,9,10,11] have been generally accepted until recently. Work is still in progress, however, in order to find more detailed and satisfactory explanation for the mechanisms of this potentially useful reaction.

A survey of the types of reactions which have been observed in the decomposition of diazo-compounds will now be made:

I FRAGMENTATION

Friedman and Shechter have observed that acetylene and ethylene are formed in the carbenoid decomposition of cyclopropanecarboxaldehyde p-tosylhydrazone (30) and methylacetylene and ethylene from the related reaction starting with cyclopropyl methyl ketone (31) by requisite shifts of electrons and bond breaking.[9]



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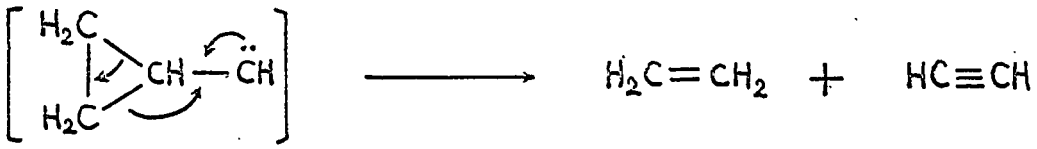

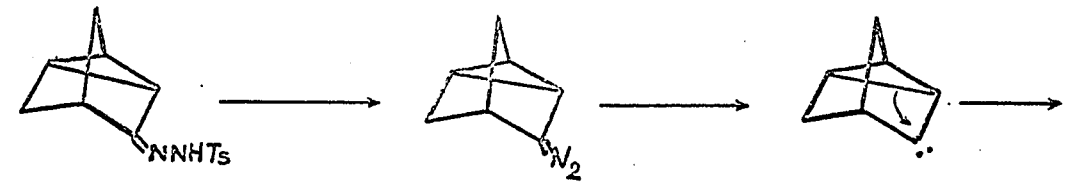

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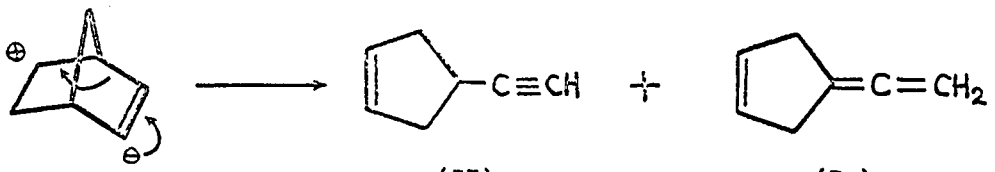


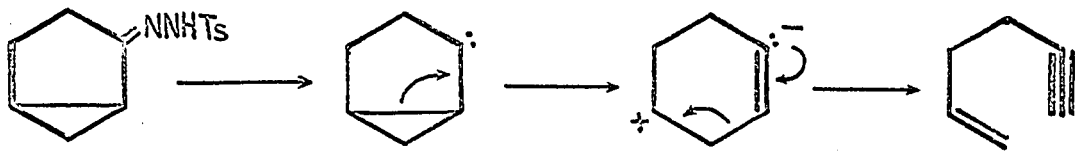
(33) (34)

II RING RUPTURE

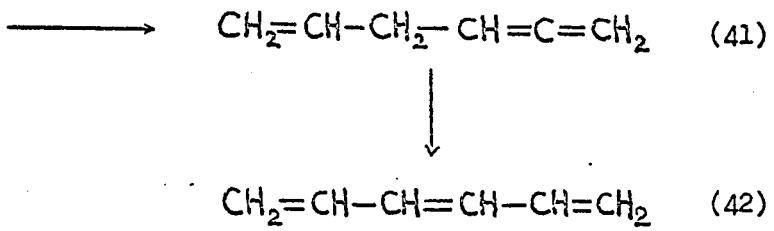
A representative of this type of reaction is the formation of 1,3-butadiene (35) as minor reaction product from carbenoid decomposition of cyclobutanone tosylhydrazone (36) or cyclopropanecarboxaldehyde p-tosylhydrazone (30).[9] Allene was also found as the principal product in thermal decomposition of diazocyclopropane (37).[10,14] It has not yet been established whether butadiene is formed directly in decomposition of cyclobutanone tosylhydrazone (36) or by subsequent decomposition of the cyclobutene (38).

A 67.2% yields of open-chain isomers has been obtained from the decomposition of 2-bicyclo(3.1.0)hexanone p-tosylhydrazone (39).[15] 1-hexen-5-yne (40) was produced as the primary product which isomerized

to give some 1,2,5-hexatriene (41) and 1,3,5-hexatriene (42) under the reaction conditions employed. This type of ring-cleavage mechanism may possibly involve the electronic shift pictured below.

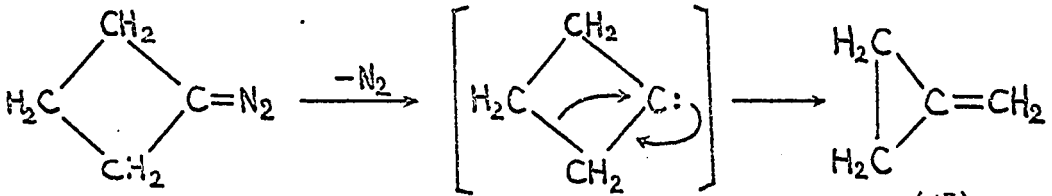


(39) (40)



III RING CONTRACTION

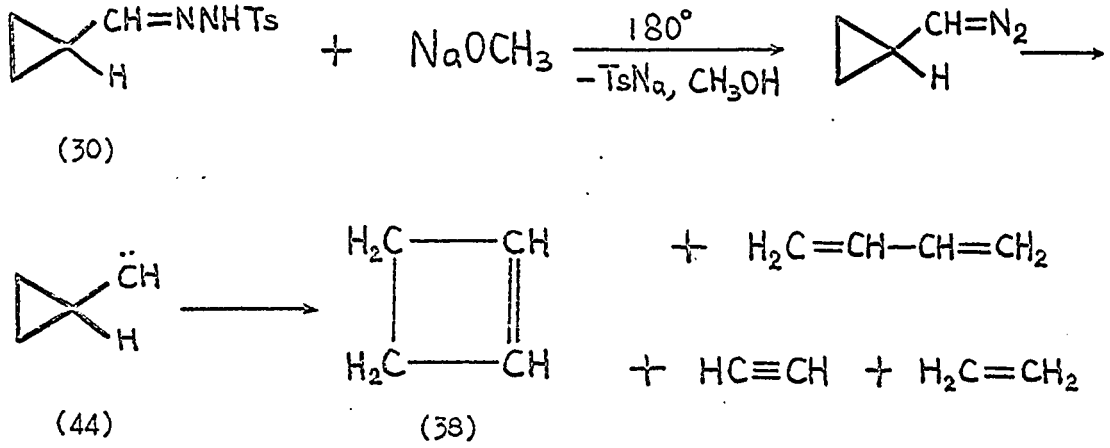
Carbenoid decomposition of cyclobutanone p-tosylhydrazone (36)[9] in diethyl carbitol or N-methylpyrrolidone is of significance in that ring-contraction to give methylenecyclopropane (43) (79,80%) occur; hydrogen-migration to yield cyclobutene (38) (18,20%) and formation of 1,3-butadiene (35) (2,1% yield) are also reported to be minor reactions.



(43)

IV RING EXPANSION

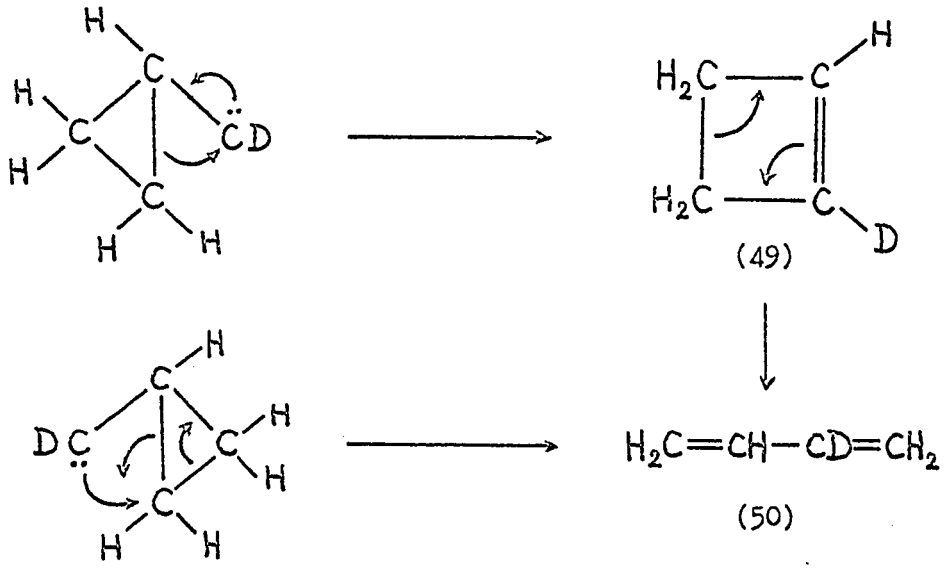
Formation of cyclobutene (38) from cyclopropanecarboxaldehyde p-tosylhydrazone (30) reacting with sodium methoxide in aprotic solvent is a prime example of ring expansion rearrangement in a simple carbenoid system.[9] The ability of a cyclopropylcarbenyl system (44) to undergo ring-expansion is also illustrated in the base-catalyzed reaction of cyclopropyl methyl ketone p-tosylhydrazone (45) in diethyl carbitol to give 1-methyl-1-cyclobutene (46) (92%).



Smith, Shechter, Bayless and Friedman[16] later proved that this ring expansion occurs by direct carbon-skeleton rearrangement of the carbenic species (Figure 1, Scheme A) and excluded the possibility that the ring expansion product, cyclobutene (38), is formed by β carbon-hydrogen insertion involving bicyclo(1.1.0)butane (47) as intermediate which isomerizes to cyclobutene via reorganization of external carbon-

Figure 1

Scheme A :



Scheme B :

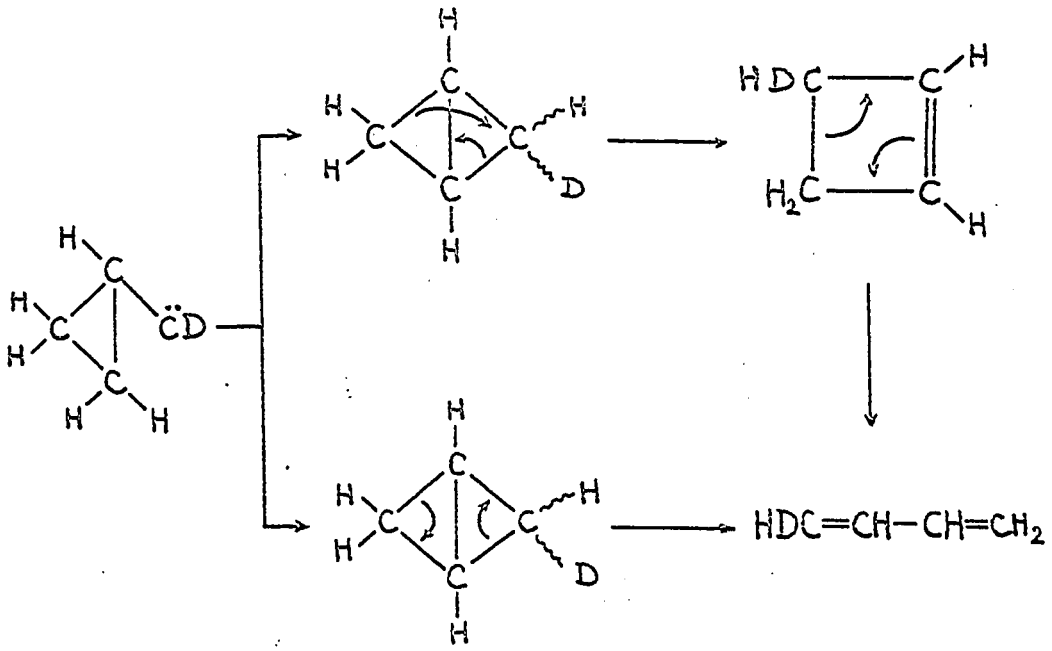
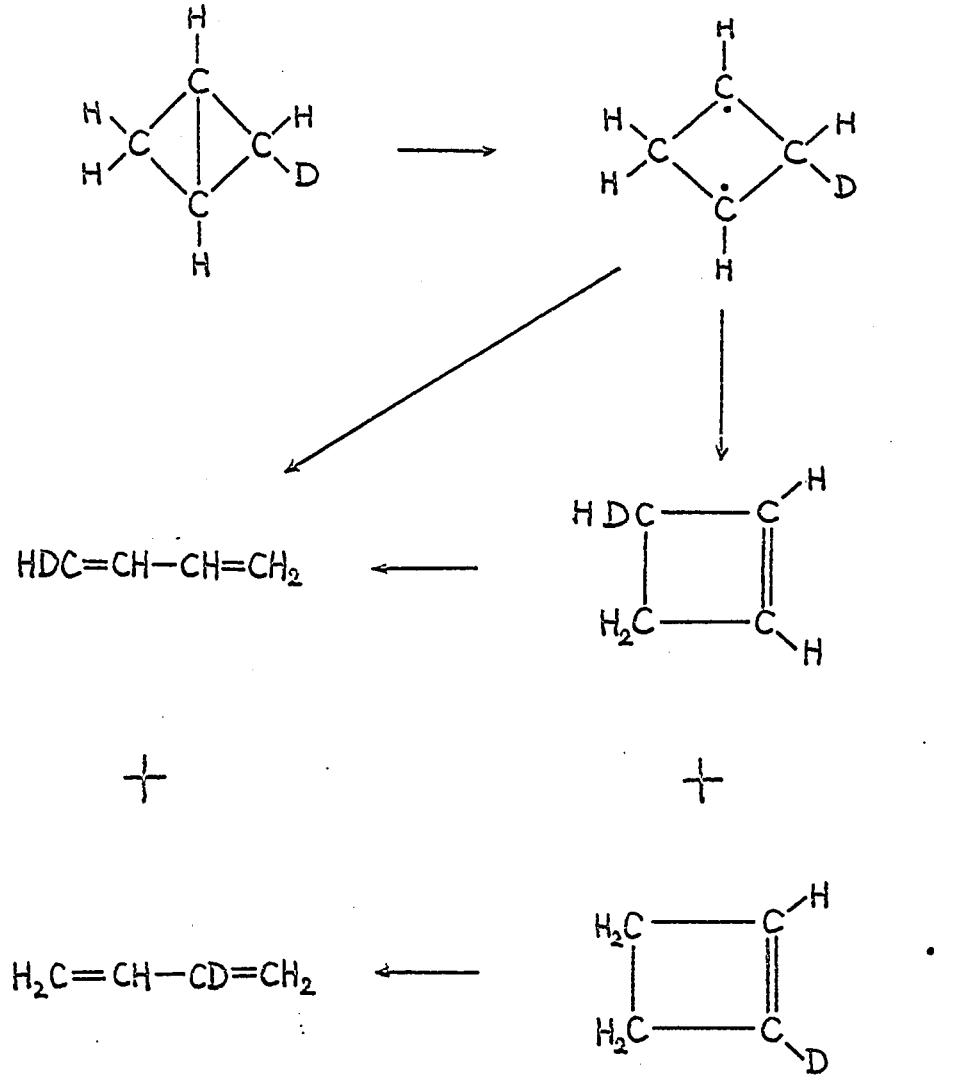


Figure 1 (continued)

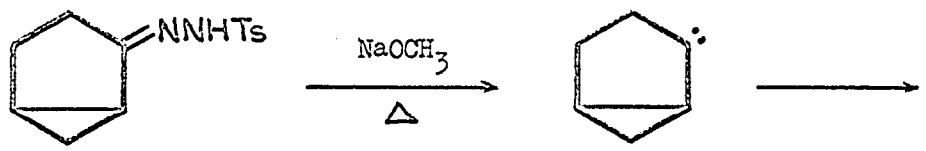
Scheme C :



carbon bonds (Figure 1, Scheme B) or rupture of the internal carbon-carbon bond and subsequent rearrangement (Figure 1, Scheme C).

These conclusions were based on the finding that pyrolysis of lithium cyclopropanecarboxaldehyde-d tosylhydrazone (48) (125°, 8 mm.) yielded cyclobutene-1-d (49) (44%) and 1,3-butadiene-2-d (50) (56%) as the only C_4 products.

The generation of the cyclopropylcarbene system does not always result in formation of a cyclobutene derivative if the carbene site is in incorporation in a second ring. Decomposition of the p-tosylhydrazone of 2-bicyclo(3.1.0)hexanone (39)[15] with sodium methoxide in bis(2-ethoxyethyl)ether at 160° produced a 49.0% yield of C_6H_8 hydrocarbons: 18.6% bicyclo(3.1.0)hexene-2 (51), 14.2% 1,3-cyclohexadiene (52), 13.1% 1-hexen-5-yne (40), 12.3% 1,2,5-hexatriene (41), and 41.8% trans-1,3,5-hexatriene (42). No cyclobutene derivative was obtained.



(39)

(51)

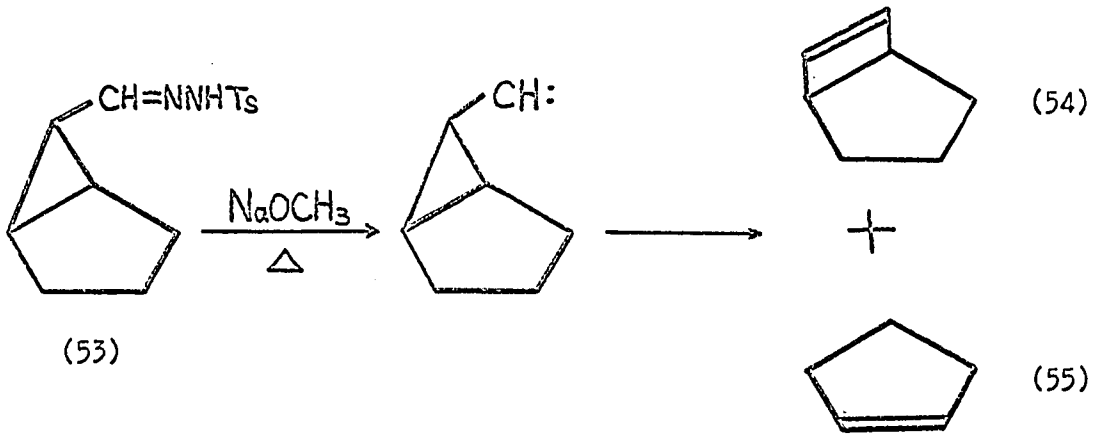
$CH_2=CH-CH_2-CH_2-C\equiv CH$ (40)

$CH_2=CH-CH_2-CH=C=CH_2$ (41)

(52)

$CH_2=CH-CH=CH-CH=CH_2$ (42)

This result is obviously different from the finding that decomposition of the p-tosylhydrazone of bicyclo(3.1.0)hexane-6-endo-carboxaldehyde (53) produces a 52% yield of hydrocarbons composed of cis-bicyclo(3.2.0)heptene-6 (54) and cyclopentene (55).



(53) (54) (55)

Thus, if the carbenoid carbon of the cyclopropylcarbene system is outside the second ring, then the usual ring expansion and fragmentation reaction occur. The difference in behavior of these two intermediates may simply be due to the more strained structure of a bicyclo(2.2.0)hexene (56) than that of the bicyclo(3.2.0)heptene-6 (54).

V INSERTION

The insertion of $\overset{\alpha}{\wedge}$carbenic or cationic center into a carbon-hydrogen bond represents one of the most interesting and important

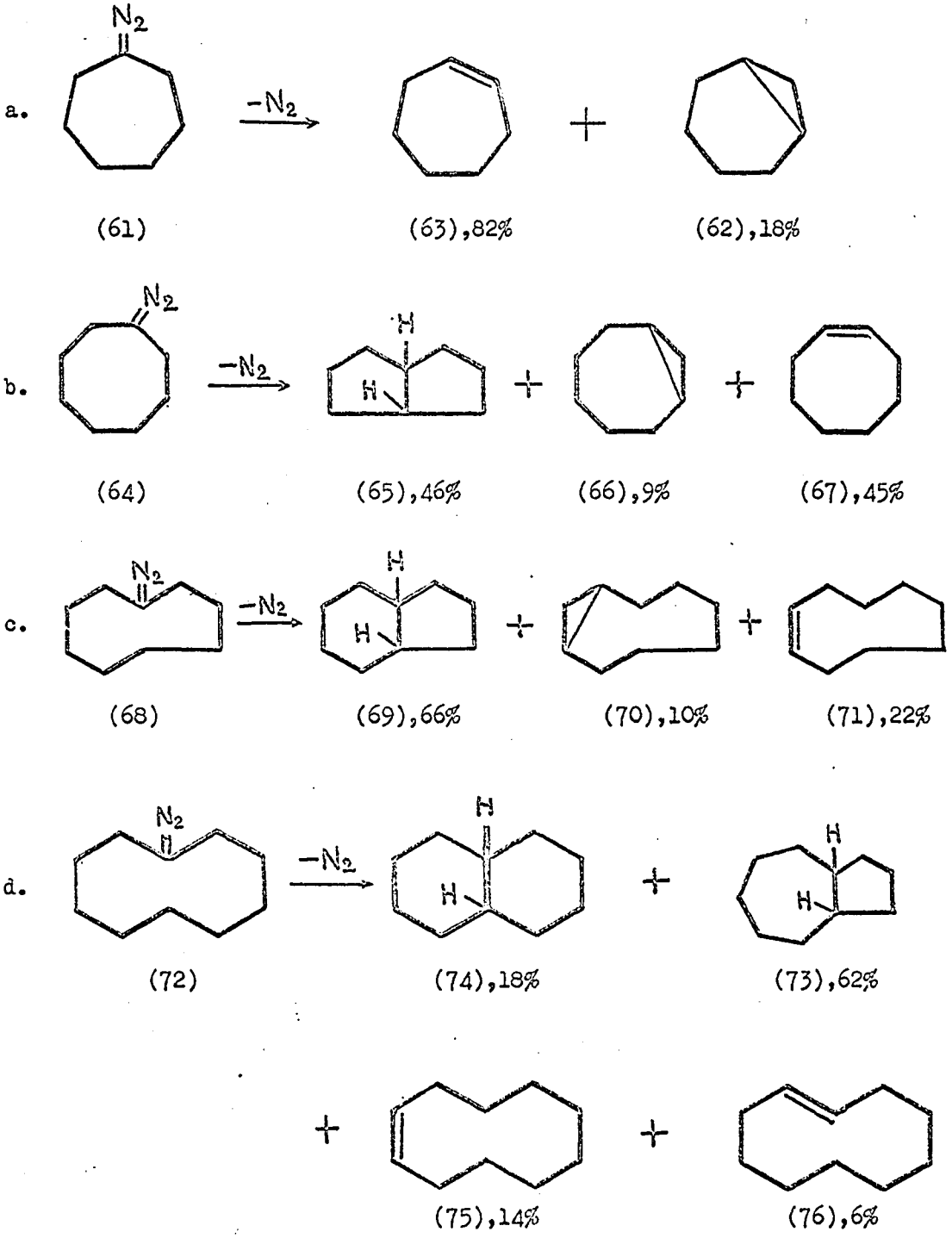
types of reaction in the decomposition of diazo-compounds. Early in 1920, Meerwein and van Emster reported the formation of tricyclene (23) when diazocamphane (22) decomposes.[17,18] 2-Diazonorbornane (57) was also found to convert to nortricyclene (58) in almost quantitative yield.

(57) (58)

A recent example for this type of reaction is the formation of bicyclo(1.1.0)butane (47) from cyclopropanecarboxaldehyde p-tosylhydrazone (30) reacting with sodium methoxide in protic solvent.[19] The reaction was suggested to proceed by cationic processes involving intramolecular reaction of cyclopropylcarbonium (59) or cyclopropylmethyldiazonium (60) intermediates.[16]

The decomposition of homologous C_5 through C_{10} diazocycloalkanes has been studied in order to determine the kind and extent of transannular insertion reaction which simple cyclic carbenes gives.[10] The reaction is characterized by extensive 1,3-, 1,5- and 1,6- transannular insertion along with rearrangement of α-hydrogen. The absence of 1,4-insertion products was simply explained by unfavorable stereochemistry during decomposition.

Figure 2


a.
N_2
$-N_2$
(61)
(63),82%
(62),18%
b.
N_2
$-N_2$
H
H
(64)
(65),46%
(66),9%
(67),45%
c.
N_2
$-N_2$
H
H
(68)
(69),66%
(70),10%
(71),22%
d.
N_2
$-N_2$
H
H
H
H
(72)
(74),18%
(73),62%
(75),14%
(76),6%

Decomposition of diazocycloheptane (61) yielded bicyclo(4.1.0)-heptane (62) (18%) by 1,3-transannular insertion and cycloheptene (63) (82%) by 1,2-rearrangement of hydrogen (Figure 2a)

Thermolysis of diazocyclooctane (64) gave cis-bicyclo(3.3.0)-octane (65) (46%), bicyclo(5.1.0)octane (66) (9%) and cis-cyclooctene (67) (45%) (Figure 2b).

Diazocyclononane (68) yielded cis-hydrindane(69) (66%), bicyclo(6.1.0)nonane (70) (10%) and cis-cyclononene (71) (22%) (Figure 2c).

Diazocyclodecane (72) gave cis-bicyclo(5.3.0)decane (73) (62%) and cis-decalin (74) (18%) by transannular insertion and cis-cyclodecene (75) (14%) and trans-cyclodecene (76) (6%) by hydrogen rearrangement (Figure 2d).

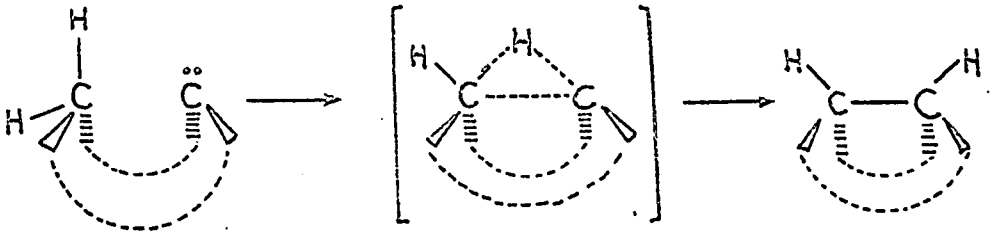


Figure 3

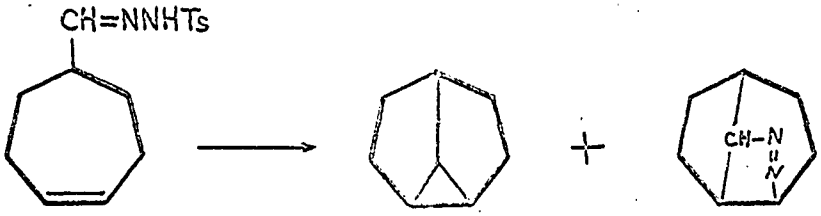
In all cases the insertion processes are stereoselective in that only cis-bicyclic hydrocarbons are formed. This stereospecificity was explained as a necessary consequence of transfer of axial hydrogen in ring system and is consistent with the principle that carbenic in-

sertions occur with retention of configuration (Figure 3).[20]

A study has been made of the effect of ring size on the reactions of cycloalkylcarbenes formed by the action of sodium metal on cycloalkylcarbinyl chlorides(77) (from cyclopropyl to cyclohexyl).[21] Bicyclic hydrocarbons containing fused cyclopropane rings, presumably formed through intramolecular insertions of cycloalkylcarbenes into C-H bonds, were found in the products of all reactions except those with cyclopropylmethyl chloride (78). A maximum yield of insertion product (bicycloalkane) relative to isomeric olefins was found with cyclopentylmethyl chloride (79) due to the favorable coplanar arrangement of the bivalent carbon, the ring carbon to which it is attached, and the C-H bond. In the small rings, ring expansion is competitive as the C-H bond on the adjacent carbon is less accessible to the bivalent intermediate. The decrease in insertion by the carbene from cyclohexylmethyl chloride (80) may be ascribed to the strain introduced in attaining a near eclipsed conformation.

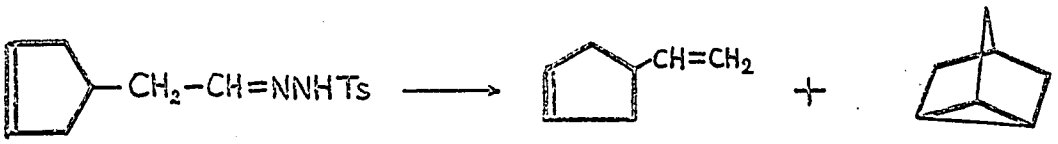
The insertion of bivalent carbon intermediates into unsaturated centers is also very well known and has been demonstrated to be of great preparative value. Some unsaturated carbenes have been reported to undergo facile ring closure by intramolecular addition, yielding bridged compounds. For example, 4-cycloheptenecarboxaldehyde p-tosylhydrazone (81) was decomposed to give tricyclo(5.1.0.0)octane (82) by intramolecular carbene addition as well as 3,4-diazatricyclo(3.3.2.0)-

dec-3-ene (83) by 1,3-dipolar addition of the diazomethane.[22]



(81) (82) (83)

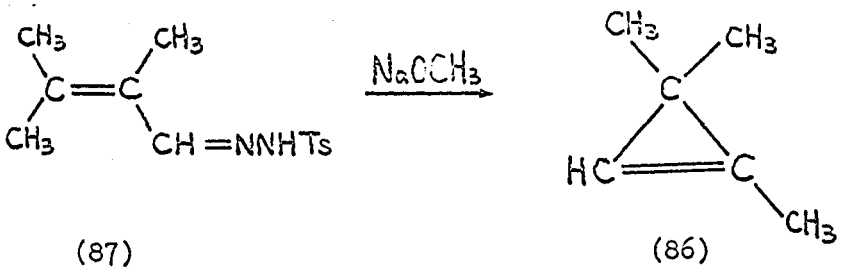
In a similar way, base-induced decomposition of the tosylhydrazone of 3-cyclopentenylacetaldehyde (84) gives 4-vinylcyclopentene (85) as major product (30% yield) along with nortricyclene (58) as a minor reaction product (3% yield).



(84) (85) (58)

The decomposition of tosylhydrazones of a number of α,β-unsaturated aldehydes and ketones has been investigated and proven to be a convenient way of synthesis of some alkyl-substituted cyclopropenes.[23] As an example of the reaction, 1,3,3-trimethylcyclopropene (86) was obtained in 72% yield when the tosylhydrazone of α,β-dimethylcrotonaldehyde (87) was added to a suspension of sodium methoxide in

refluxing diglyme (ca.160°).



(87) (86)

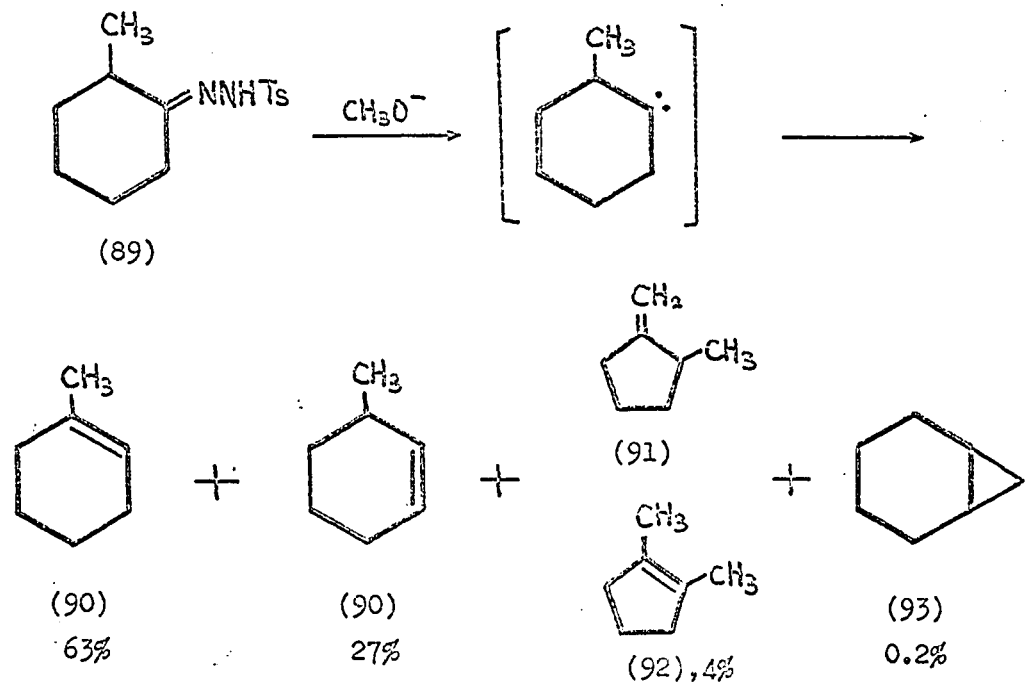
The yields were found to vary from excellent to poor depending mainly on the degree of β-substitution of the tosylhydrazone. Tosylhydrazones of α,β-unsaturated aldehydes and ketones appear to give good yields of cyclopropenes when the β-carbon atom is fully substituted with alkyl groups. The presence of one hydrogen atom at the β-position suffices to diminish the cyclopropene yield substantially, and no cyclopropene from tosylhydrazones with two hydrogens at the β-position has been obtained so far. The probable reaction sequence in forming cyclopropene is: tosylhydrazone ⟶ diazoalkene ⟶ alkenylcarbene ⟶ cyclopropene.

VI HYDROGEN MIGRATION

Usually $\overset{\alpha}{\wedge}$diazo-compound decomposes to give olefin by hydrogen migration. The original well-known Bamford and Stevens reaction[4] described that p-toluenesulphonylhydrazones of aliphatic and alicyclic ketones can be converted into olefins by treatment with alkali. This can be shown by the finding that diazocyclopentane and diazocyclohexane

decompose thermally to cyclopentene (55) (100%) and cyclohexene (88) (100%) respectively, but is contrasted with the conversion of 2-diazocamphane (22) and 2-diazonorbornane (57) to tricyclene (23) and nortricyclene (58), respectively, as major products. These results were described as the differences in carbenic reactions of 6-membered ringsin their chair and rigid-boat forms.[10]

In a similar way, decomposition of 2-methylcyclohexanone tosylhydrazone (89) with sodium methoxide in N-methylpyrrolidone led to a mixture of hydrocarbon products in 54-64% yield consisting of 90% of methylcyclohexenes (90) by hydrogen migration, 4% of 2-methylmethylenecyclopentane (91) together with its thermally produced isomer, 1,2-dimethylcyclopentene (92), by alkyl migration and 0.2% of norcarane (93) as an insertion product.[24]

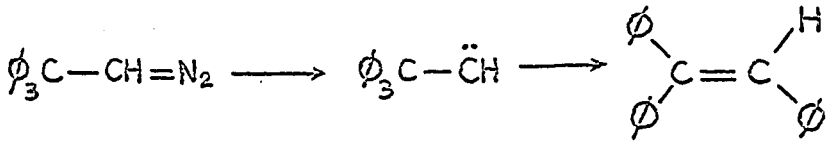


These observed yields indicate a reaction preference in this carbene of hydrogen migration >> alkyl migration ~ insertion. The preference for hydrogen migration compared to insertion has been observed in other alicycles[10], as well as commonly in acyclic substances.[7]

VII CARBON-SKELETON REARRANGEMENT

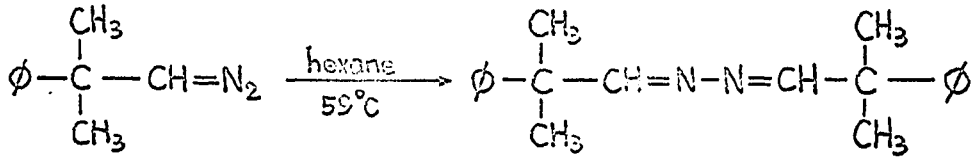
Carbon-skeleton rearrangement of a carbene is equivalent to intramolecular insertion of the carbenic center across a carbon-carbon bond and is useful in the synthesis of some terpenoid systems.[25] This reaction ordinarily involves the migration of alkyl and phenyl groups.

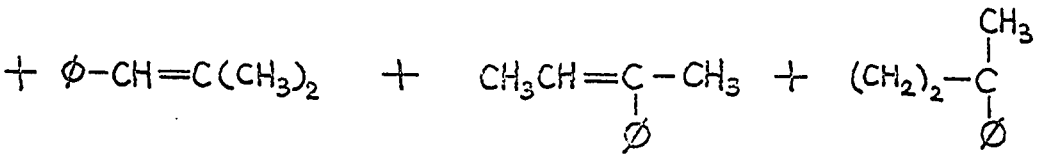
Hellerman and Garner[26] reported that thermal decomposition of 1-diazo-2,2,2-triphenylethane (94) gives triphenylethylene (95), and it is apparent that phenyl migration occurs in triphenylmethylcarbene (96) systems.



(94) (96) (95)

In studying the rearrangement in the neophyl (2-methyl-2-phenylpropyl) (97) system which proceeds via a carbene intermediate, Philip and Keating[27] found that the phenyl/methyl migration aptitude in this rearrangement is about 10 : 1.



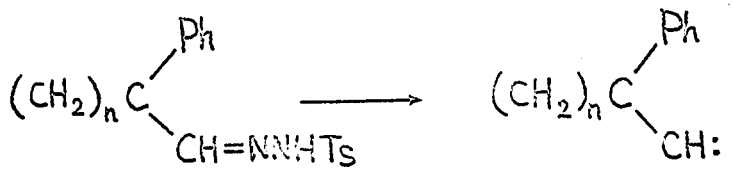


49% 8% 43%

This can be contrasted with the lack of methyl migration in radical rearrangements[28-32], and the 3000-300 : 1 phenyl/methyl migration aptitudes characteristic of normal carbonium ion rearrangements.[31] This result is consistent with the postulate that the carbenic intermediate is a highly reactive electrophilic species.[33] A tentative order of migration aptitudes, hydrogen > phenyl > methyl was therefore suggested by these workers for carbene rearrangements.

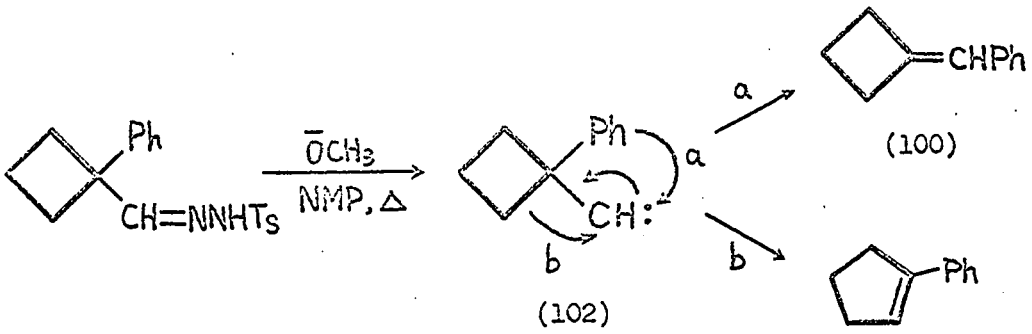
The ring size effects in the neophyl carbene rearrangement were further studied by the decomposition of 1-phenylcycloalkanecarboxaldehyde p-tosylhydrazone (98) with sodium methoxide in N-methyl-2-pyrrolidone at 180°.[34] 1-Phenylcycloalkylcarbenes (99) were postulated intermediates and the ring sizes studied were the three- through six-membered.

These reactive intermediates rearrange to mixtures of hydrocarbons in good yields, with varying degrees of phenyl migration and



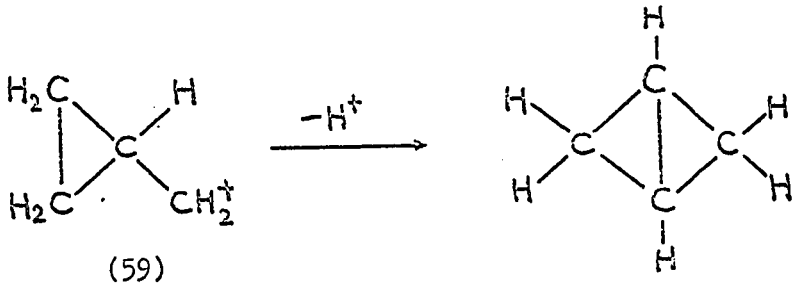
(98) (99)

alkyl migration (ring expansion). The ring size determines the relative amount of phenyl migration (i.e. the neophyl rearrangement), from none in the cyclopropyl compound to some 41% in the cyclohexyl case with a gradual increase in each succeeding ring size. For example, phenylmethylenecyclobutane (100) and 1-phenylcyclopentene (101) are formed from 1-phenylcyclobutylcarbene (102) by phenyl and alkyl migrations, respectively.



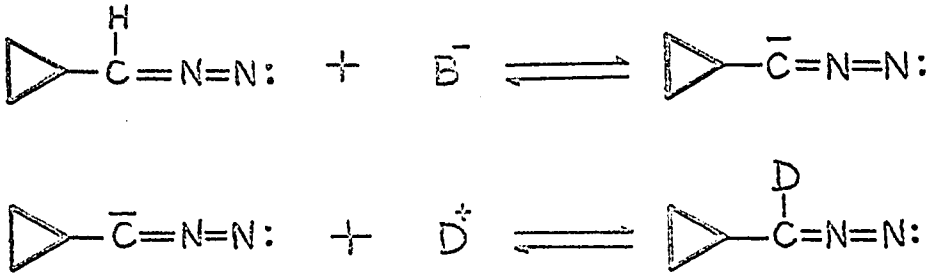
(102) (100) (101)

One of the most interesting and important facts about the thermal decomposition of p-tosylhydrazones is the drastic solvent dependence of the reaction. The importance of experimental conditions on the paths and the apparent carbenic and cationic mechanisms of the base-catalyzed decomposition reaction of cyclopropanecarboxaldehyde p-tosylhydrazone (30) has been demonstrated by many workers.[9,18,19,35] In the absence of a proton source, such as an alcohol, the decomposition of the sodium salt of cyclopropanecarboxaldehyde p-tosylhydrazone yields cyclobutene (38) by ring expansion and 1,3-butadiene (35) by reorganization as principal products; bicyclo(1.1.0)butane (47) is nearly negligible in aprotic conditions. Whereas in the presence of weak proton donors such as alcohol, water, ethylene glycol, parent tosylhydrazone, p-toluenesulfinic acid, or incompletely neutralized solvents, the decomposition results primarily in formation of bicyclo(1.1.0)butane. It has thus been suggested that bicyclo(1.1.0)butane (47) is not formed primarily by carbenic decomposition of the tosylhydrazone but rather by cationic processes involving intramolecular reaction of cyclopropylcarbonium (59) or cyclopropylmethyldiazonium (60) intermediates.[16]

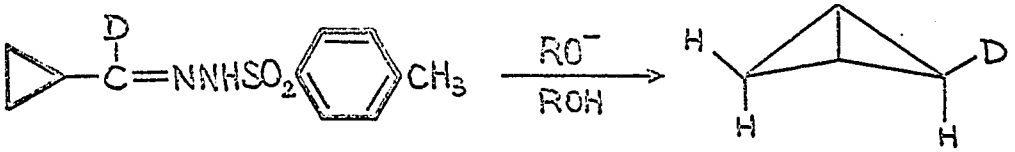


(59) (47)

This reaction has been further investigated using a deuterium-labeled substrate and a deuterium-containing solvent.[36] Deuterium exchange was observed in the diazo-compound produced in the presence of an excess of base.

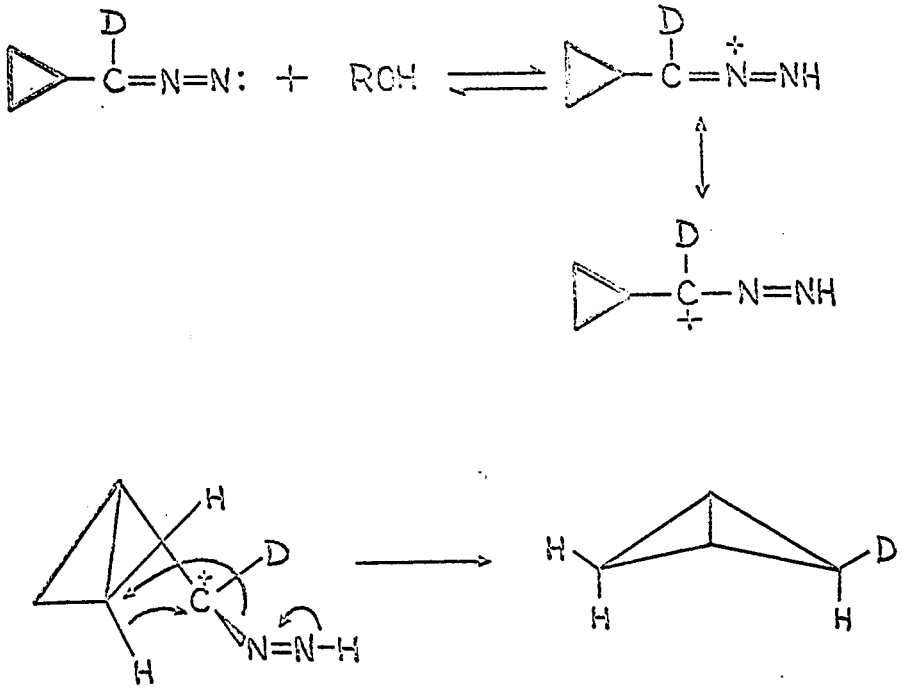


The reaction of (30-d) in the presence of a limited amount of base and that of the unlabeled tosylhydrazone with an excess of base in ethylene glycol-d_2 gave the same product (47-d) which contained 92% of one deuterium.



(30-d) (47-d)

The reaction cannot involve the cyclopropylcarbinyl cation or any ion derived from it produced by protonation at carbon by solvent for otherwise additional deuterium would have been introduced when the reaction was carried out in ROD. The mechanism shown below suggests an intramolecular transfer of a proton from one carbon to another during ring closure.

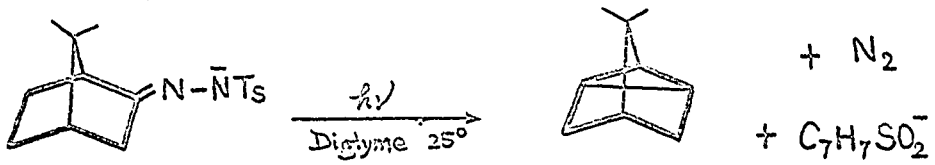


The possible role of hydrogen bonded bivalent intermediates in the decomposition of cyclopropanecarboxaldehyde p-tosylhydrazone is suggested by Shechter and Friedman[16] in a foot-note, but no evidence is cited.

The photochemical decomposition of tosylhydrazone salts parallels closely the thermal process. A similar solvent dependence effect has been found in the photolysis of the potassium salt of a p-tosylhydrazone.[37]

Irradiation of camphor p-tosylhydrazone potassium salt (13') under aprotic conditions gives high yields of tricyclene (23), the pro-

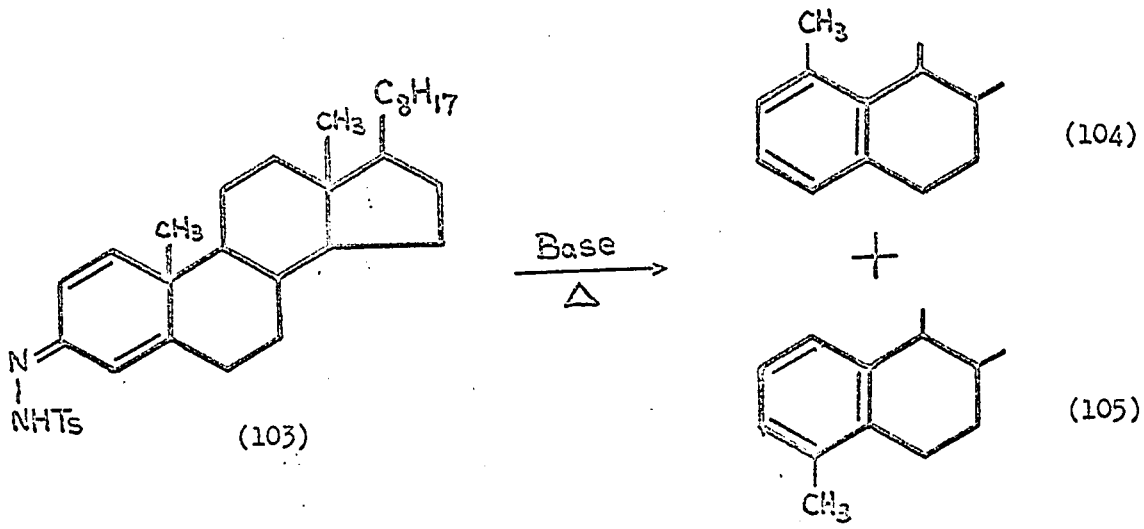
duct formed by carbenoid decomposition. As the concentration of available



(13') (23)

protons increases, the amount of tricyclene decreases and the amounts of camphene (15) and alcohols or ethers, the products formed by cationoid decomposition increase. Such a result is in line with the results obtained by thermal decomposition of the tosylhydrazones.

The effect of bases on the pyrolytic reaction of p-tosylhydrazones is still unknown. It was found that changing of bases could alter the product composition in the carbenoid decomposition of cholesta-1,4-dien-3-one p-tosylhydrazone (103).[38] The reaction gave 15-30% yield of 1-methyl-19-norcholesta-1,3,5(10)-triene (104) and 4-methyl-19-norcholesta-1,3,5(10)-triene (105) as major products.



(103) (104) (105)

Table 2[38]

Base	Yield%	% Composition of 1-methyl isomer	% Composition of 4-methyl isomer
LiH	20	66	34
$LiNH_2$	17	65	35
$NaOCH_3$	21	63	37
$KOCH_3$	15	44	56
CaH_2	22.5	33	67
K-t-butoxide	33	20	80

The results are summarized in Table 2. The 1-methyl isomer (104) was the principal product when the p-tosylhydrazone (103) was decomposed by lithium hydride, lithiumamide, or sodium methoxide; whereas the formation of the 4-isomer (105) was favored by the use of potassium t-butoxide or calcium hydride as base.

The mechanism suggested is shown in Figure 4, but the detail of the influence of bases on the product distribution is not clear.

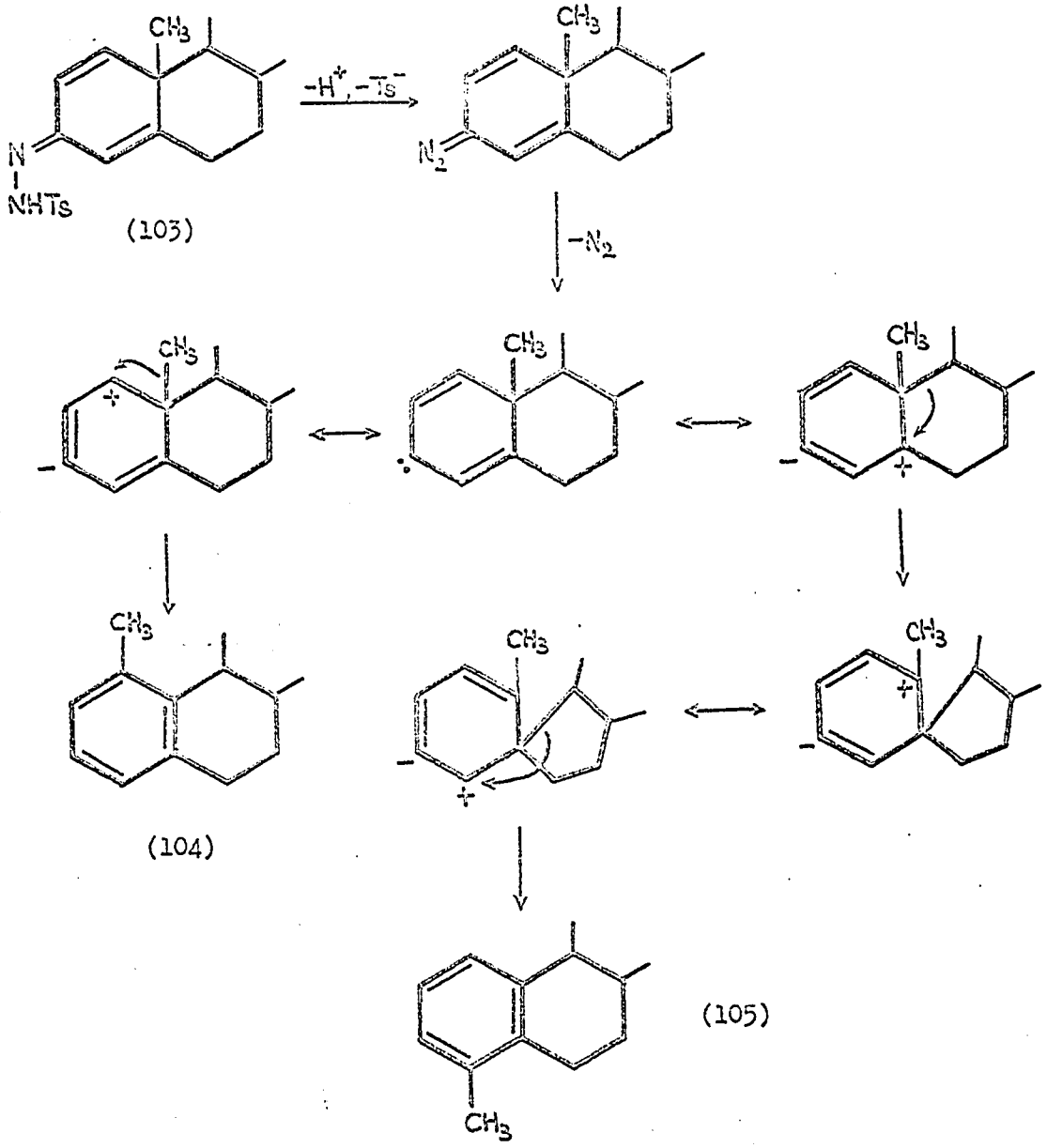
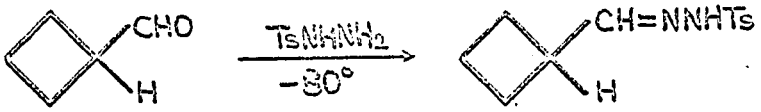


Figure 4

RESULTS AND DISCUSSION

The required starting material, cyclobutanecarboxaldehyde p-tosylhydrazone (2) was prepared by the following sequence of reactions, starting with 1,1-cyclobutanedicarboxylic acid (106):

(106) (121)



(107) (2)

All compounds in this series were characterized.

An unusual technique was employed here in the preparation of the tosylhydrazone from cyclobutanecarboxaldehyde (107). A slight excess of cyclobutanecarboxaldehyde was allowed to react with p-toluenesulphonylhydrazine at -80° without solvent, taking care to exclude moisture. All other attempts in making the desired tosylhydrazone (2) in many solvents under a great number of different reaction conditions proved unsuccessful.

The thermal decomposition of cyclobutanecarboxaldehyde p-tosyl-

hydrazone (2) with bases in different solvents at 195° over a period of 90 minutes was observed.

This reaction gave five principal products: cyclopentene (55) by ring expansion, methylenecyclobutane (108) by hydrogen migration, bicyclo(2.1.0)pentane (109) by insertion, methylcyclobutane (110) by hydride transfer and 2-methyl-1-butene (27) by ring opening along with ethylene and acetylene by fragmentation.

The percentage composition of the isolated mixtures of hydrocarbon products varied with the choice of solvent and base. The mixtures were analyzed by analytical scale vpc using a column packed with 30% di-2-ethylhexyl sebacate on 60/80 Chromosorb P.▲ (Figure 5). Each fraction was separated and collected by preparative scale vpc and its structure analyzed by comparison of its n.m.r. and infrared spectra with those of an authentic sample.

The results from some of the typical runs are summarized in Table 3. Bicyclo(1.1.1)pentane (1), which was expected to be one of the reaction products by insertion, was not detected in the reaction products mixture from this thermal decomposition of cyclobutanecarboxaldehyde-p-tosylhydrazone (2) under either protic or aprotic conditions. This highly strained bicyclic system was still unknown at the time this project was started but was successfully prepared by Wiberg et al.[1] by the reaction of 3-bromocyclobutane-1-methyl bromide (3) with sodium

▲ Available from Johns-Manville Co.

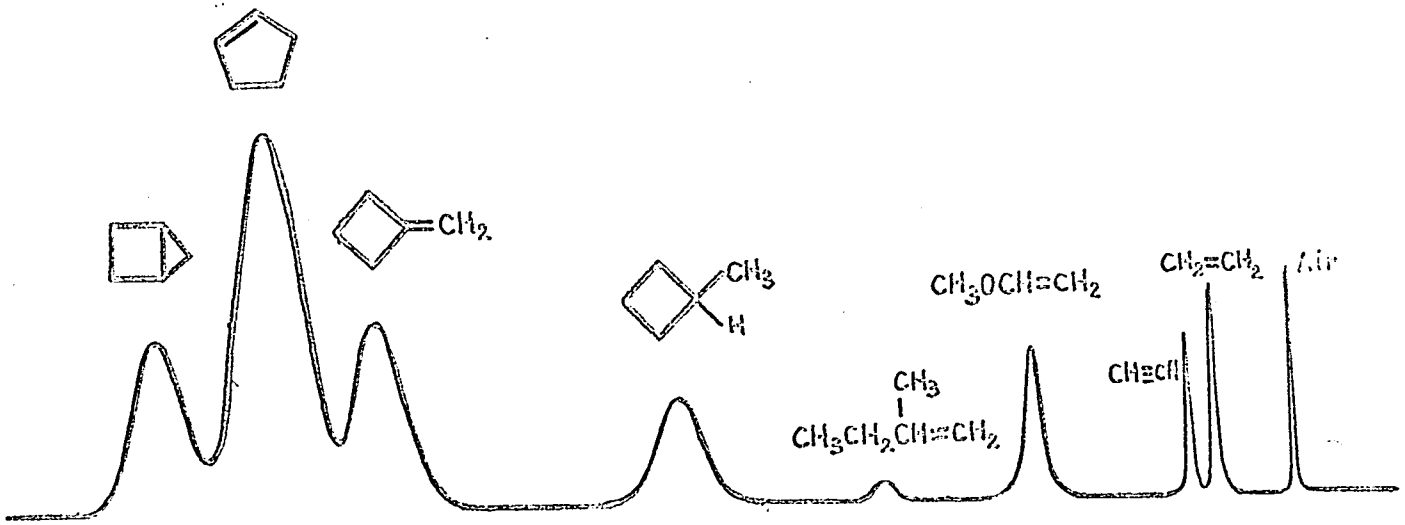
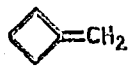
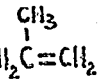


Figure 5 VPC spectrum of the reaction product mixture from thermal decomposition of cyclobutanecarboxaldehyde p-tosylhydrazone

Table 3

BASES	SOLVENTS & CATALYSTS	% COMPOSITION OF PRINCIPAL HYDROCARBONS				
						
NaH & n-heptanol	Dry diglyme	13.6	17.7	56.5	12.2	0
$NaOC_7H_{15}$	Dry diglyme	10.0	30.0	37.2	22.6	0.2
NaH	Mesitylene	15.5	29.9	40.7	9.1	4.8
NaH & n-heptanol	Dry diglyme with 20% Tsl... H_2	1.3	15.8	71.5	11.4	0
NaH & n-heptanol	Wet diglyme, contains 2% H_2O	4.0	17.8	63.0	15.2	0
NaH & pentaerythritol	Dry diglyme	2.5	19.3	69.5	7.6	1.1
NaH	m-Cresol	5.3	1.3	91.9	0	1.5

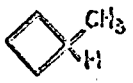
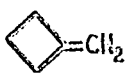
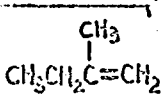
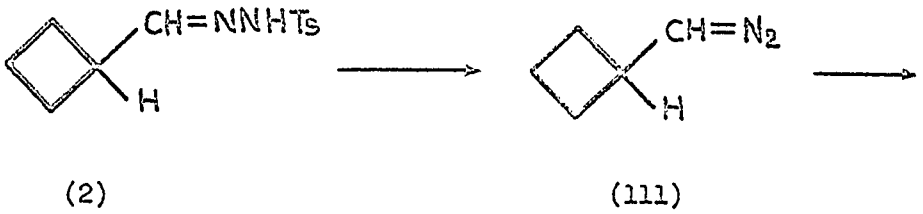
BASES	SOLVENTS & CATALYSTS	% COMPOSITION OF PRINCIPAL HYDROCARBONS				
						
NaH	Ethylene glycol	2.1	3.8	92.5	0	0.9
$NaOCH_2CH_2OH$	Ethylene glycol	0.4	7.3	92.2	0	0.1
NaH	Ethylene glycol, contains 5% H_2O	2.4	2.8	94.0	0	0.4
NaH & n-heptanol	Dry diglyme, CuCl catalyst	1.9	24.0	71.5	0	2.6
NaH & n-heptanol	Dry diglyme, $CuSO_4$ catalyst	4.6	29.1	61.5	0	4.8
NaH & n-heptanol	Dry diglyme, $NiCl_2$ catalyst	10.4	13.6	71.9	0	4.1

Table 3 (continued)

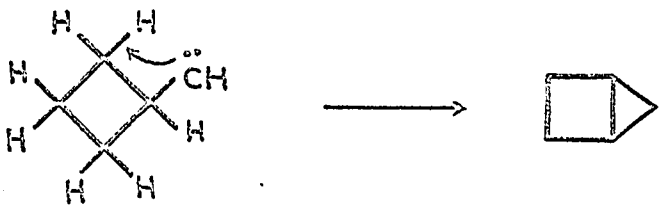
during the course of our work. The absence of bicyclo(1.1.1)pentane as one of the products in this [illegible] is considered to be in agreement with the finding that [illegible] insertion products were not obtainable from simple cyclic carbenes produced by the decomposition of diazocycloalkanes.[10]

Decomposition of cyclobutanecarboxaldehyde p-tosylhydrazone in either protic or aprotic solvents thus yields cyclopentene as a principal product ; good yields of methylenecyclobutane, methylcyclobutane and bicyclo(2.1.0)pentane are also obtained under conditions which avoid cationic processes. In solvents with proton-donor capacity, conversion of the parent tosylhydrazone (2) to cyclopentene is greatly enhanced and the yields of the methyl- and methylene-cyclobutane decrease significantly. Of greater significance is that the intramolecular insertion product, bicyclo(2.1.0)pentane is eliminated completely when the reaction is run under highly protic conditions(see ethylene glycol and m-cresol).

It is thus probable that bicyclo(2.1.0)pentane (109) is formed primarily by carbenic decomposition of cyclobutyldiazomethane (111) involving intramolecular insertion of cyclobutylcarbene (112) into one of its four equivalent β carbon-hydrogen bonds.

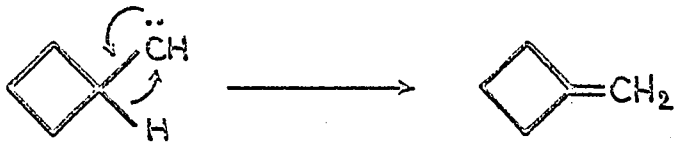


(2) (111)



(112) (109)

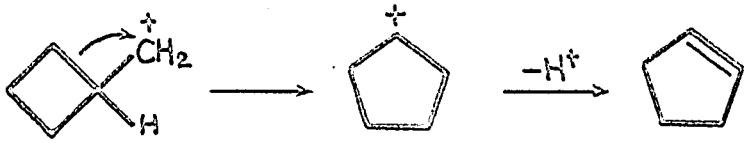
Similarly, methylenecyclobutane (108) appears to be derived mainly from cyclobutylcarbene (112) simply by hydrogen migration.



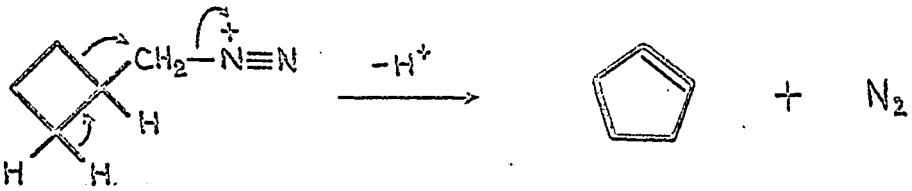
(112) (108)

The formation of cyclopentene (55) as principal product in both protic and aprotic solvents suggests that such ring expansion may take place by alkyl migration in both cyclobutylcarbene (112) and cyclobutylcarbonium (113) (or cyclobutylmethyldiazonium) (114) intermediates.

(112) (55)



(113) (55)



(114) (55)

The cationic processes is more favourable, however, as reflected by the higher yield of cyclopentene in ethylene glycol than in diglyme (diethylene glycol dimethyl ether, an aprotic solvent).

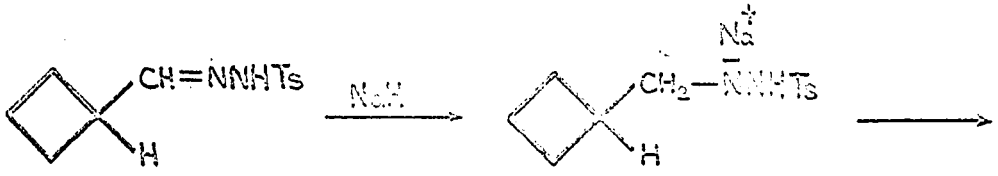
It is surprising that the saturated product, methylcyclobutane (110), is formed in this reaction under every experimental condition. It has been established that the treatment of tosylhydrazones (4) with reducing hydrides results in the reduction of a carbonyl to a CH_2 or acid to CH_3 group. Substituted tosylhydrazides (5) have been proven as the intermediate compounds.[2]

$$TsNHN{=}CHR \xrightarrow{\text{Reducing hydride}} TsNHNH\text{-}CH_2R \longrightarrow TsH + N_2 + RCH_3$$

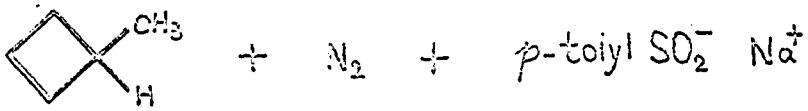
(4) (5)

It was also proposed recently that the carbon-nitrogen double bond of the tosylhydrazone is vulnerable to attack by sodium hydride.[39]

These findings account for the formation of methylcyclobutane (110) in certain cases when sodium hydride was used as base.



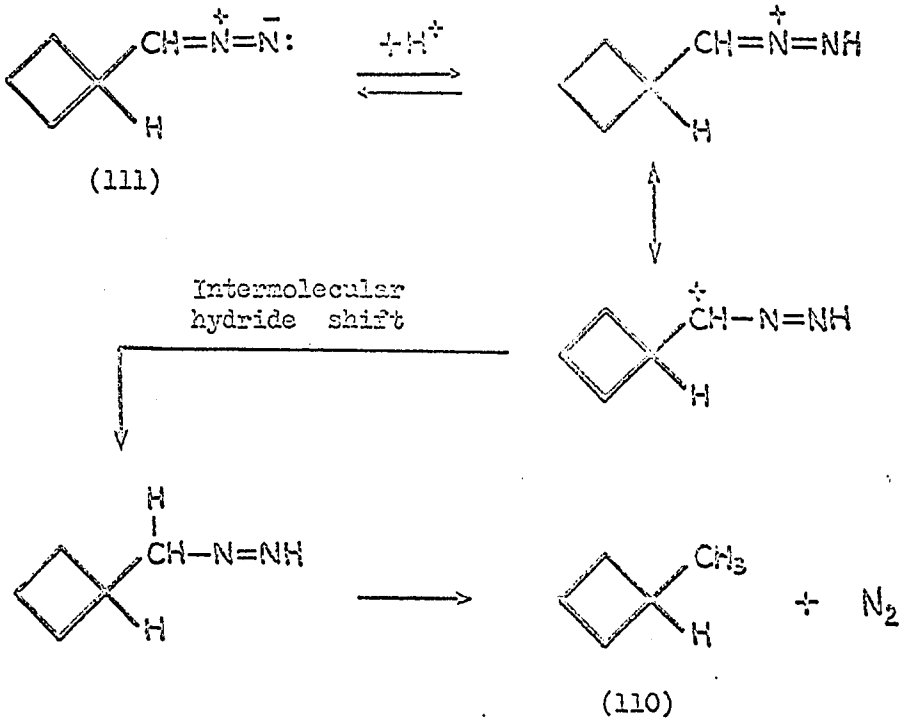
(2)



(110)

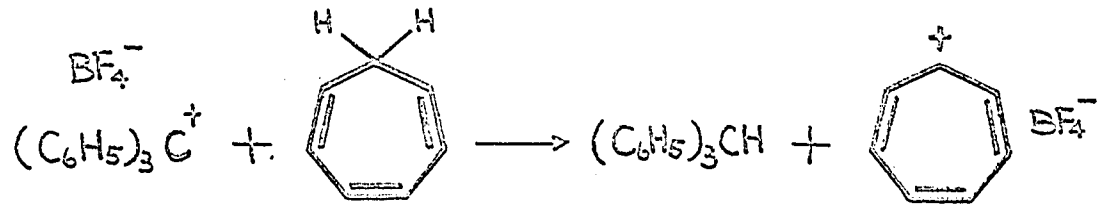
This mechanism, however, can not explain the experimental data in the cases when other bases such as sodium ethylene glycolate or sodium n-heptoxide were used.

It seems quite possible that when the reaction is carried out in proton-donor solvents, the mechanism probably involves protonation at either nitrogen or carbon of the diazo-compound (111), followed by an intermolecular hydride shift.



(111) (110)

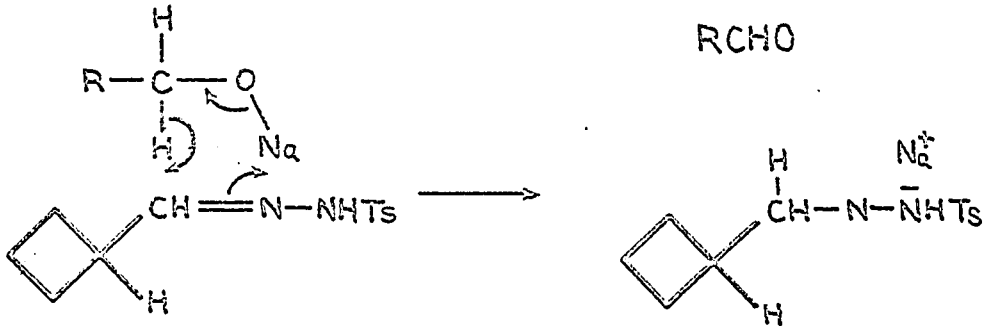
Many examples of such intermolecular hydride transfer are known.[40] A carbonium ion can usually abstract hydride from a hydrocarbon, particularly if this leads to a more stable carbonium ion. For instance, tropylium ion (115) may be obtained by treating cycloheptatriene (116) with triphenylmethyl cation (117).[41]



(117) (116) (115)

The hydride source in the methylcyclobutane formation has not been elucidated. It seems unlikely that the protic solvents are the hydride source because the yields of methylcyclobutane are decreased in highly protic conditions.

A possible mechanism for the formation of methylcyclobutane (110) as a reduction product, especially in protic solvents, may involve the hydride shift from the sodium salt of the alcohol to the p-tosylhydrazone of cyclobutanecarboxaldehyde (2) via the cyclic intermediate (118) and cannot be excluded.



(118)

An aliphatic aldehyde would then be formed as a biproduct. This proposed mechanism is supported by the appearance of a carbonyl absorption at 1670 cm^{-1} in the infrared spectrum of the crude reaction products mixture from pyrolysis of cyclobutanecarboxaldehyde p-tosylhydrazone with sodium n-heptoxide. The aldehyde was unfortunately not identified.

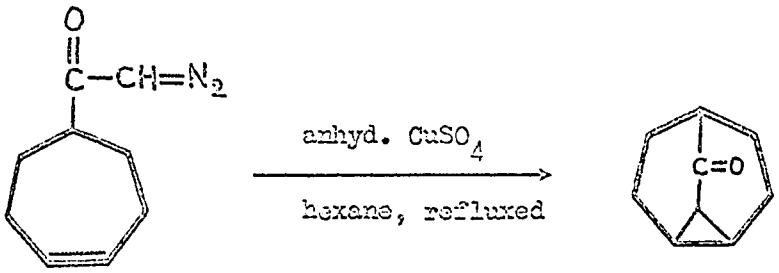
The ring rupture product, 2-methyl-1-butene (27), constitutes only a minor fraction in the hydrocarbon product mixture. It may be

formed either directly from the decomposition of the tosylhydrazone or by isomerization of other products. The assignment of structure to this fraction is tentative, since a clear n.m.r. spectrum is not available due to the insufficient sample.

In all cases in this pyrolytic reaction, these five major products: methylcyclobutane (110), methylenecyclobutane (108), cyclopentene (55), bicyclo(2.1.0)pentane (109) and 2-methyl-1-butene (27) were always accompanied by ethylene and acetylene by fragmentation as indicated by vapor phase chromatography (Figure 5).

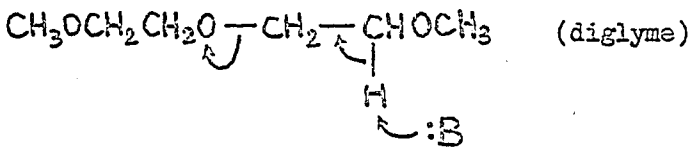
The products formed in the pyrolysis reaction, and their relative amounts were unaffected by the rate of heating used.

It is interesting to note that the presence of anhydrous metal salts as catalysts results in abolition of the intramolecular insertion product, bicyclo(2.1.0)pentane (109). The compositions of other hydrocarbons are not altered appreciably. This result is in sharp contrast with use of anhydrous cupric sulfate to catalyze the supposed formation of carbenes from diazo-compounds.[42] For instance, it was reported that 55% yield of tricyclo(3.3.1.$0^{2,8}$)nonan-9-one (119) was obtained by cupric sulfate catalyzed cyclization of 4-cyclohepten-1-yldiazomethyl ketone (120).



(120) (119)

In most runs, the base used for these reactions was sodium n-heptoxide formed by mixing equimolar amounts of sodium hydride and n-heptanol. Sodium methoxide gave essentially the same results except methanol was also obtained as one of the major components of the hydrocarbon product mixture and made separation of the products difficult. When sodium hydride alone was used, an additional very volatile product was obtained which was found to be methoxyethylene (121), $CH_3OCH=CH_2$, by examining its n.m.r. signals (1-proton quartet at 3.56τ, 2-protons multiplet at 6.08τ, 3-protons singlet at 6.52τ). This product is formed by β-elimination in diglyme by the attack of the strong base, sodium hydride.

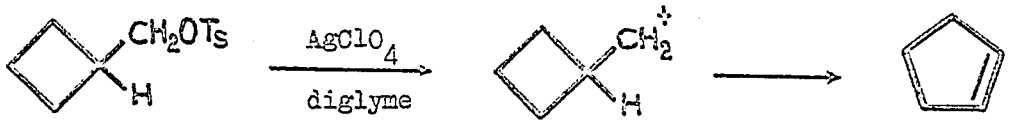


(diglyme)

The effect of varying bases on the product composition in the thermal decomposition of cyclobutanecarboxaldehyde p-tosylhydrazone (2) is not clear. Dannenberg and Gross[38] reported that changing of bases altered the product composition significantly in the decomposition of cholesta-1,4-dien-3-one p-tosylhydrazone (103). But no detail of the

mechanism was ever proposed. When sodium n-heptoxide was used in the decomposition of cyclobutanecarboxaldehyde p-tosylhydrazone, the product composition deviated appreciably from that when equimolar amounts of sodium hydride and n-heptanol were used. The difference is not very reliable, however, because the decomposition reaction with sodium n-heptoxide as base was done only once while all the other reactions were run at least three times until consistent results were obtained. The difficulty in reproducing the results is due to the complexity of the reaction and the experimental difficulty in operating these pyrolysis reactions.

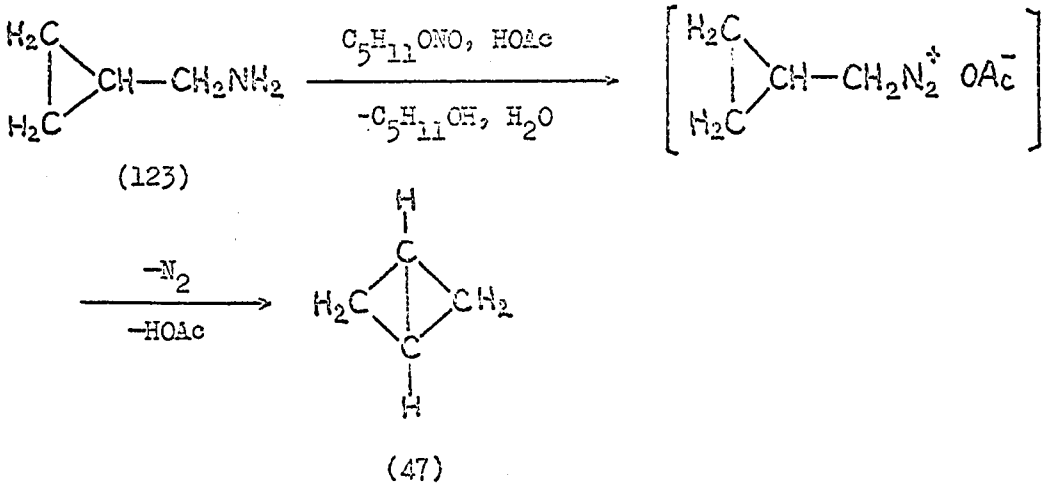
Since cyclopentene (55) is apparently derived from intramolecular decomposition of cyclobutylmethyldiazonium intermediate (114) involving a cyclobutylcarbonium ion (113), a study has also been made of the intramolecular reaction of the cyclobutylcarbonium ion (113) as generated from the treatment of cyclobutylmethyl p-tosylate (122) by silver perchlorate. In diglyme as solvent, this reaction indeed gave cyclopentene (55) as the only C_5 product.



(122) (113) (55)

This result is in agreement with the finding by Friedman and Logullo[35,43] that aprotic diazotization of cyclopropylcarbinylamine (123) by amyl nitrite and acetic acid in chloroform gave the intramolecu-

lar product, bicyclo(1.1.0)butane (47), while the cationic decomposition of sodium cyclopropanecarboxaldehyde p-tosylhydrazone in proton-donor solvents.



(123)

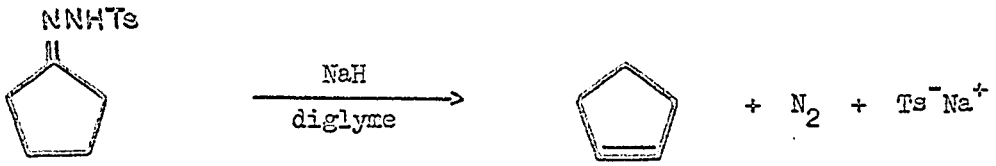
(47)

Other products formed by the reaction of cyclobutylmethyl p-tosylate with silver perchlorate are: dimethyl ether (21.6%) which gives a single n.m.r. signal at 6.76τ, acetaldehyde (12.3%) whose n.m.r. spectrum consists of a doublet at 7.88τ and a quartet at 0.30τ, methyl formate (4.3%) which shows two sharp n.m.r. signals at 6.35τ and 2.14τ, and 23.6% of an unidentified fraction. The dimethyl ether, acetaldehyde and methyl formate arose via oxidation of the diglyme by the perchlorate anion and were obtained from a blank reaction of silver perchlorate with diglyme alone.

Reaction of cyclobutylmethyl p-tosylate in caproic acid also gave cyclopentene as a principal product (80.5%) along with 12.4% of n-pentane formed by decarboxylation of the solvent, caproic acid, and

7.1% of 2-methyl-1-butene (27).

The thermal decomposition of cyclopentanone p-tosylhydrazone (124) with sodium hydride in diglyme has also been done in order to compare the reaction products with those of the same reaction of cyclobutanecarboxaldehyde p-tosylhydrazone (2). This reaction gave cyclopentene (55) exclusively in almost quantitative yield. This is in agreement with the experimental finding by Friedman and Shechter[10] that diazocyclopentane (125) decomposes thermally to cyclopentene (55) (100%).



(124) (55)

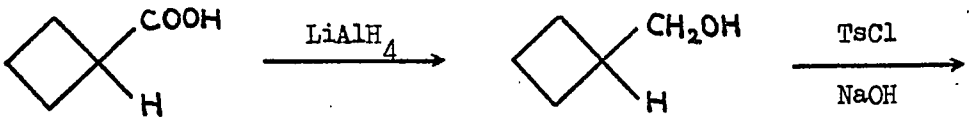
It is interesting to note that some of the volatile hydrocarbon product mixture from the decomposition of cyclobutanecarboxaldehyde p-tosylhydrazone (2) polymerized rapidly to give a white precipitate shortly after removal from the dry ice bath. The white polymer had a high vapor pressure and gave a melting poing spreading over a very wide range (20° to over 330°) (λ_{max} 3500, 2900, 1620, 1525, 1450, 1400, 1120, 1035, 830, and 720 cm^{-1}). No evidence on the structure of the monomer was obtained. The possibility that this monomer arises from the hydride transfer reaction cannot be excluded.

The hydrocarbon product mixture was separated by preparative

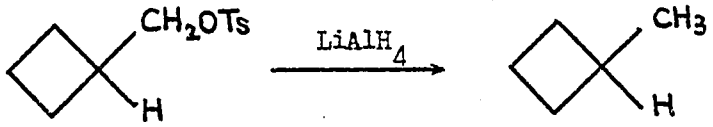
scale vpc at 0°C using a column packed with 30% di-2-ethylhexyl sebacate on 60/80 Chromosorb P. Each fraction was identified by its n.m.r. and infrared spectra.

The n.m.r. spectrum of the methylcyclobutane (110) fraction shows a doublet at 8.94τ corresponding to a methyl group split by an adjacent ring proton and a grouping of resonances centered at 8.05τ arising from the cyclobutyl ring protons, and is in agreement with the assigned structure (Figure 6).

The structure of methylcyclobutane is confirmed by comparison of its gaseous phase infrared (1 atm.) and n.m.r. spectra as well as retention time in vapor phase chromatogram with those of an independently prepared sample from reduction of the p-toluenesulphonic ester of cyclobutyl carbinol (122) with lithium aluminum hydride.



(126) (127)



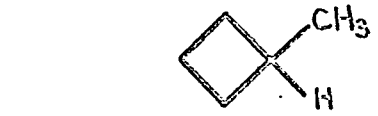
(122) (110)

The methylenecyclobutane(108) fraction shows three groupings of n.m.r. signals centered at 7.98τ(2 protons), 7.32τ(4 protons) and 5.35τ

(2 protons) which agree exactly with those published in Varian NMR Catalogue[44] (Figure 7).

The n.m.r. spectrum of the bicyclo(2.1.0)pentane (109) fraction has three groupings of resonances centered at τ = 9.52 (2 protons), 8.63 (4 protons) and 7.93 (2 protons) corresponding to cyclopropyl, cyclobutyl and bridgehead hydrogens, respectively, and is in agreement exactly with that reported by Chesick[45] (Figure 8).

The identity of the cyclopentene fraction was confirmed by comparison of its n.m.r. and infrared spectra as well as retention time in vapor phase chromatogram with those of an authentic sample.



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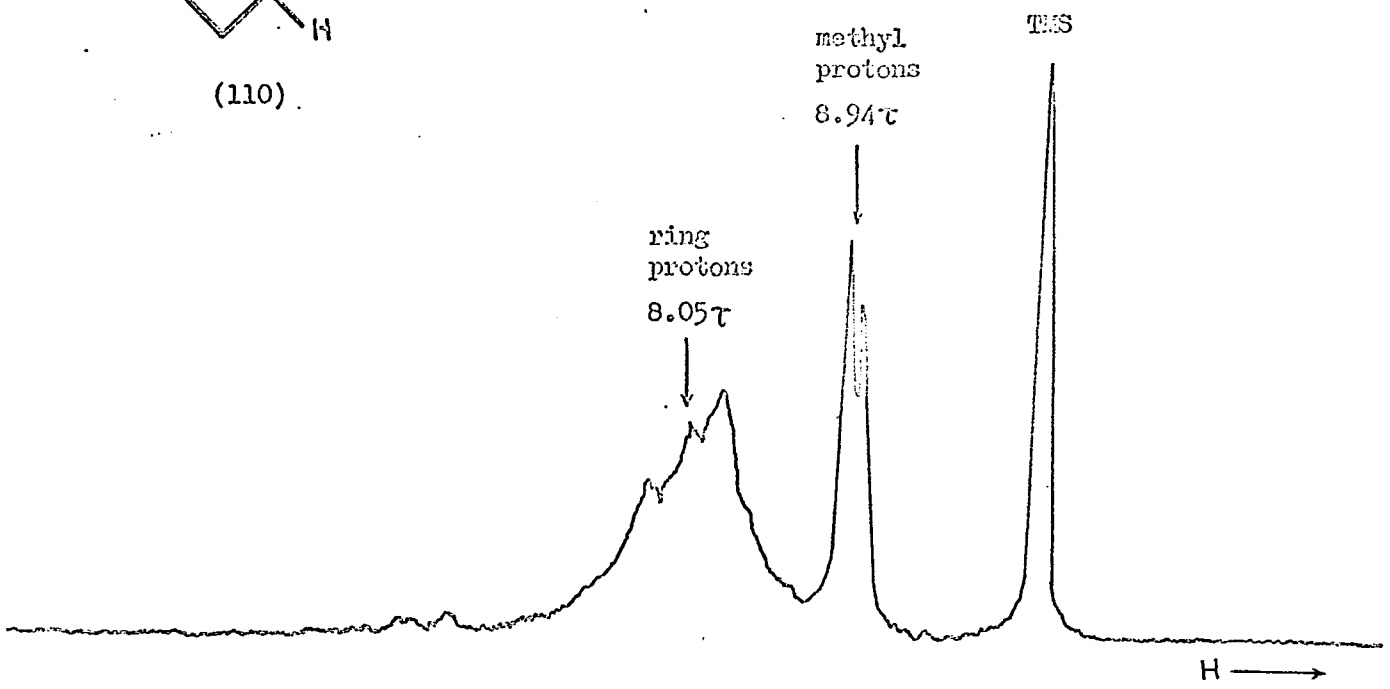
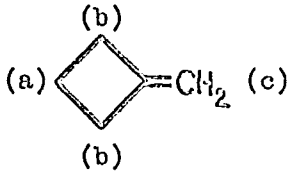


Figure 6.— n.m.r. spectrum of methylcyclobutane

TMS = Tetramethyl silane



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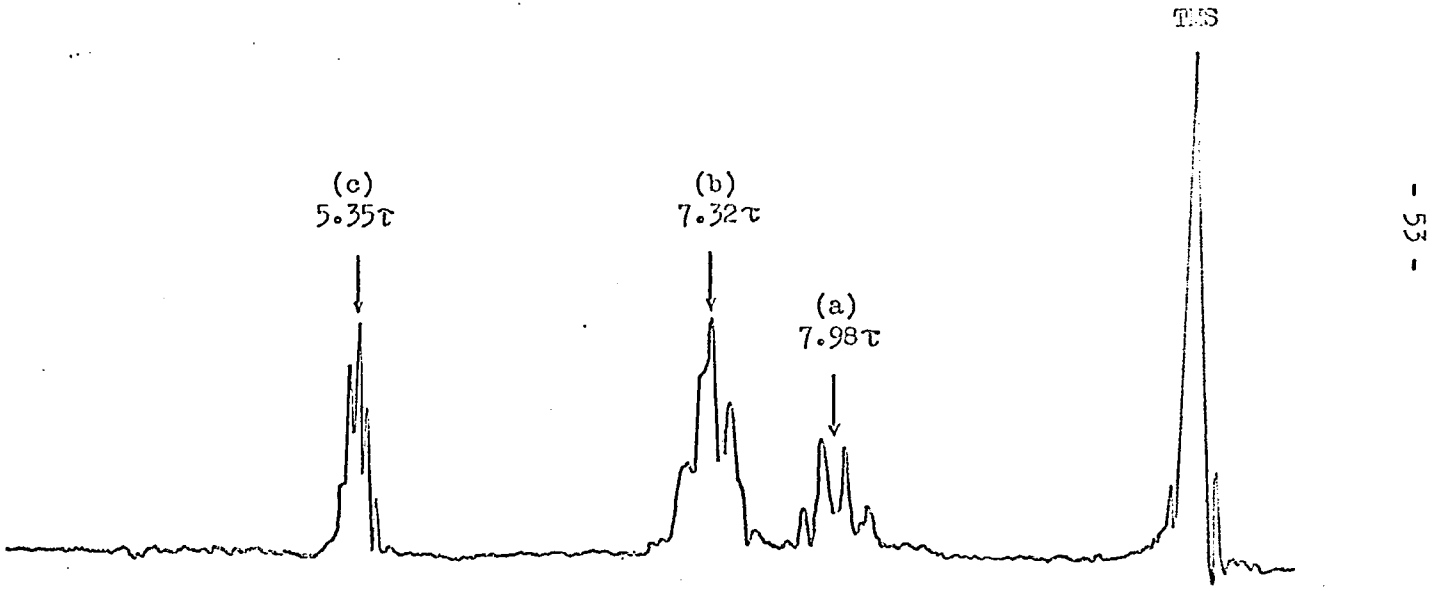
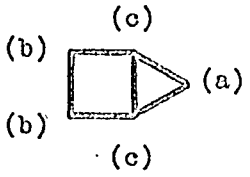


Figure 7.— n.m.r. spectrum of methylenecyclobutane



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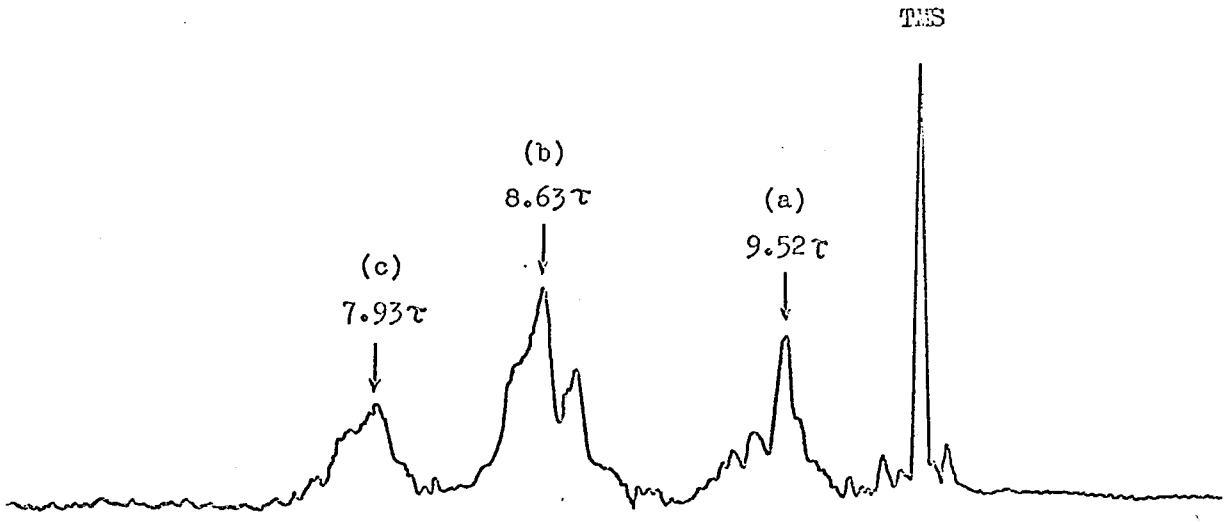


Figure 8.— n.m.r. spectrum of bicyclo(2.1.0.)pentane

EXPERIMENTAL

All melting points are uncorrected for stem exposure.

Infrared spectra were recorded on a Perkin-Elmer Model 137 "Infracord" Spectrophotometer.

Ultraviolet spectra were measured in 1 cm cells on a Beckman DK-2 Spectrophotometer.

Nuclear magnetic resonance spectra were obtained using a Varian Model V-4302 Spectrometer operating at 60 Mc/sec. Tetramethylsilane was used as an internal reference, and all spectra were recorded at room temperature.

Microanalyses were performed by Midwest Microlab, Inc., Indianapolis, Indiana, U.S.A., and by Alfred Bernhardt, 433 Mülheim (Ruhr), Höhenweg 17, West Germany.

Vapor phase chromatograms were recorded on a Perkin-Elmer Model 154 Vapor Fractometer with helium as the carrier gas.

MATERIAL.— All commercially available chemicals were carefully purified by standard methods. Special care was given to the drying of the solvents, utilizing lithium aluminum hydride as the drying agent and distilling under nitrogen atmosphere for the ethers.

APPARATUS.— The apparatus used to run the decomposition reaction of cyclobutanecarboxaldehyde p-tosylhydrazone (2) and cyclopentanone

p-tosylhydrazone (124) with bases and also the reaction of cyclobutylmethyl p-tosylate (122) with silver perchlorate is sketched in Figure 9.

CYCLOBUTANECARBOXYLIC ACID (126)[46,47].— Cyclobutanecarboxylic acid was prepared by decarboxylation of 1,1-cyclobutanedicarboxylic acid (106) carried out in a distilling flask at 160-170° until no more carbon dioxide was evolved (about two hours). The dark coloured liquid was distilled by raising the temperature to give 97.5% yield of cyclobutanecarboxylic acid, b.p. 195° (lit. b.p. 195°).[48]

CYCLOBUTANECARBONALDEHYDE (107)[49].— A mixture of 50 g. of cyclobutanecarboxylic acid (126) and 82 g. of 84% formic acid was passed dropwise at 380° through a stainless steel tube carrying manganous oxide (MnO) as catalyst at a rate of 15 ml of mixture per hour. The reaction product collected in a trap at ice-salt temperature was extracted with ether. The ethereal solution was washed with saturated sodium bicarbonate solution, water, and dried over anhydrous sodium sulfate, and the ether distilled off. The yield of cyclobutanecarboxaldehyde (107), b.p. 115-120°, was 12.5 g. (29.8% yield). On repeated distillation, the pure aldehyde boiled at 116-118° (lit. b.p. 116-117°)[50]; 2,4-dinitrophenylhydrazone m.p. 152-154°, golden needle crystals (lit. m.p. 153-154°)[49]; strong aldehyde absorption occured in the infrared spectrum at 2700 (C-H) and 1710 cm^{-1} (C=O).

The aldehyde could easily be oxidized to cyclobutanecarboxylic

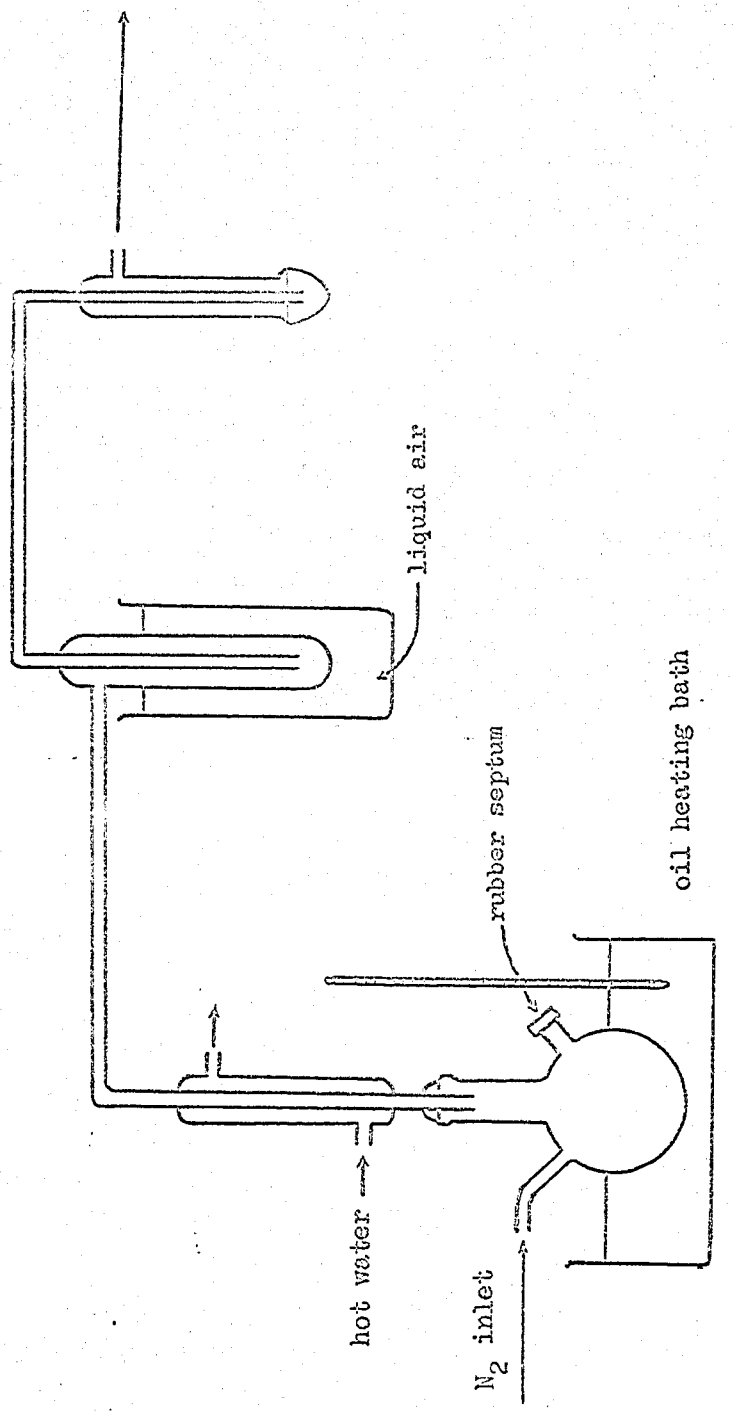
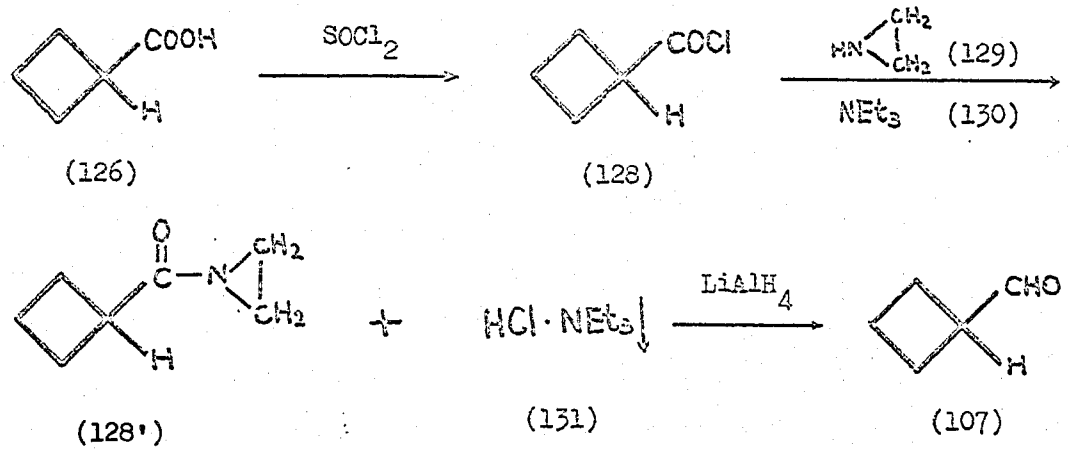

liquid air
rubber septum
oil heating bath
magnetic stirrer
hot water
N_2 inlet

Figure 9

acid (126) by air after standing at room temperature over-night, and polymerized to a trimer slowly in a sealed tube.

The manganous oxide catalyst absorbed on the porous surface of boiling chip packing in the stainless steel combustion tube was freshly made by decomposition under nitrogen atmosphere of manganese hydroxide at 500° which was formed as a precipitate by mixing equimolar amounts of 50% manganese nitrate solution and concentrated ammonium hydroxide inside the tube. A serious explosion occured once and another procedure for making manganous oxide was employed by decomposition of manganous carbonate at 330° in the same apparatus.

Cyclobutanecarboxaldehyde (107) was also prepared by reduction of the corresponding aziridine (128') with lithium aluminum hydride.[51]



CYCLOBUTANECARBONYL CHLORIDE (128)[47,52].— To 27.2 g. of cyclobutanecarboxylic acid (126) was added 55.0 g. of thionyl chloride (b.p. 75-6°), and the mixture was refluxed for 1.5 hours. The product

was distilled to give 27.0g. (84.5% yield) of cyclobutanecarbonyl chloride, b.p. 130-140° (lit. b.p. 137-139°).

REDUCTION OF CYCLOBUTANECARBONYL CHLORIDE (128)[51].— Cyclobutanecarbonyl chloride (23.7 g., 0.2 mole) was added over a period of one hour to a stirred solution of ethylenimine (129) (8.8 g., 0.2 mole) and triethylamine (130) (20.0 g., 0.2 mole) in 100 ml of anhydrous diethyl ether with cooling by an ice-salt mixture. The reaction mixture was stirred for an additional 0.5 hour and precipitated triethylamine hydrochloride (131) was filtered off and washed with 100ml of diethyl ether. The combined ether solution was cooled to 0°C and a slurry of 2.0 g. of lithium aluminum hydride (0.05 mole, 95% purity) in 100 ml of diethyl ether was added to the stirred solution over a period of 0.5 hour. After an additional hour, cold 5N sulfuric acid was added, the ether layer was separated, and the aqueous layer extracted. The combined ether extracts were washed with water, sodium bicarbonate solution, water again, and dried over anhydrous sodium sulfate. Ether was removed by evaporation under reduced pressure. Distillation yielded 4.0 g. of cyclobutanecarboxaldehyde (23.8% yield).

CYCLOBUTANECARBOXALDEHYDE p-TOSYLHYDRAZONE (2).— Cyclobutanecarboxaldehyde (5% excess) was added dropwise onto p-toluenesulphonylhydrazine (132) fine powder at -80° with vigorous stirring. Precaution was made to prevent condensation of moisture into the reaction mixture by passing through dry N_2 and putting on a rubber stopper rapidly.

The mixture was then stirred at room temperature with occasional cooling until a fine dry solid was obtained. The excess aldehyde (107) and water thus formed were removed under high vacuum ($\sim 1\times10^{-5}$mm) at room temperature and the cyclobutanecarboxaldehyde p-tosylhydrazone (2) was stored at -30°. The hydrazone (2) was heat sensitive and could not be further purified by crystallization; m.p. 70-72° (decomp.).

The infrared spectrum exhibited absorptions characteristic of a tosylhydrazone (N-H 3200 cm^{-1}, C=N 1590 cm^{-1}, $-SO_2-$ 1320 and 1155 cm^{-1}).

The n.m.r. spectrum (60 Mc; in CH_3OH) gave absorptions at 2.39τ (quartet, 4 protons), 2.62τ (singlet, one proton), 5.42τ (singlet, one proton), 7.62τ (singlet, 3 protons), and aliphatic protons in the region of 7.80 to 8.07τ (multiplet, 7 protons). These data agreed very well with those from the n.m.r. spectrum of cyclopentanone p-tosylhydrazone (124).

CYCLOPENTANONE p-TOSYLHYDRAZONE (124).— Cyclopentanone p-tosylhydrazone was prepared according to the method described by DePuy and Froemsdorf.[53] The p-toluenesulfonylhydrazine (132), 50 g., was dissolved in 700 ml of 1N HCl and an equimolar amount of the cyclopentanone (133) (22.5 g.) added with stirring. After standing for one hour the reaction mixture was filtered, and the product recrystallized from an ethanol-water mixture to give 56 g. (77.2% yield) of white crystalline hydrazone, m.p. 180-181° (lit. m.p. 180-181°)[10].

The n.m.r. spectrum gave absorptions at 2.40τ (quartet, 4 pro-

tons), 2.74 (singlet, one proton), 7.55 (singlet, 3 protons) and two groupings of resonances centered at 7.73 and 8.17 (multiplet, 8 protons) arising from the alicyclic ring protons.

PYROLYSIS OF CYCLOBUTANECARBOXALDEHYDE p-TOSYLHYDRAZONE (2).— The apparatus used is shown in Figure 9. In a typical run, a mixture of 2.52 g. (10 m.mole) of cyclobutanecarboxaldehyde p-tosylhydrazone and 0.47 g. of sodium hydride (11 m.mole, conc. 56%) was placed in a 50 ml three neck flask equipped with a reflux condenser, nitrogen inlet and serum cap. Into the flask, 15 ml of diglyme was injected by syringe through the serum cap, followed by 5.5 ml of a 2 molar solution of n-heptanol in diglyme (11 m.mole). The reaction mixture was stirred with a magnetic stirrer and heated gradually by means of an oil bath up to 195°. Hot tap water was passed through the condenser in order to separate the volatile reaction products from high boiling solvent. Pure nitrogen was passing through at a slow rate to sweep out the volatile hydrocarbons into the liquid air trap. After the reaction was completed (one hour), the volatile hydrocarbon product mixture was collected from the trap by distillation under vacuum and stored at -80° with dry ice.

Explosion of the light orange coloured hydrocarbon product mixture in a n.m.r. sample tube occured probably due to the decomposition of the diazo-compound at room temperature.

In the cases when metal salt was used as a catalyst, one gram of the anhydrous metal salt was mixed with the tosylhydrazone before injecting the solvent. The same procedure was employed for the runs in the

presence of p-tosylhydrazine or pentaerythritol, $C(CH_2OH)_4$, (134).

PYROLYSIS OF CYCLOBUTANECARBOXALDEHYDE p-TOSYLHYDRAZONE (124).— The thermal decomposition of cyclobutanecarboxaldehyde p-tosylhydrazone (124) with sodium hydride in diglyme was carried out in the same way as that of the cyclobutanecarboxaldehyde p-tosylhydrazone (2).

CYCLOBUTYLCARBINOL (127).— A solution of 10 g. of cyclobutanecarboxylic acid (126) (0.1 mole) in 50 ml of anhydrous diethyl ether was added dropwise through a dropping funnel over a period of two hours into a slurry of 6.0 g. of lithium aluminum hydride (95% purity, 0.15 mole) in 200 ml of anhydrous diethyl ether in a 500 ml three neck flask equipped with a reflux condenser under nitrogen atmosphere. The reaction mixture was stirred for 18 hours at room temperature. Cold 5N sulfuric acid was added. The ether layer was separated and the aqueous layer extracted. The combined ether extracts were dried over anhydrous sodium sulfate. Distillation of the ether solution gave 6.9 g. of cyclobutylcarbinol boiling constantly at 145° (lit. b.p. 142°/750mm).[54] The yield was 80%. The infrared spectrum showed strong hydroxyl absorption at 3300 cm^{-1}.

CYCLOBUTYLMETHYL p-TOLUENESULPHONATE (122)[55].— To a stirred mixture of 12.9 g. of cyclobutylcarbinol (127) (0.15 mole) and 32.5 g. of p-toluenesulfonyl chloride (135) (0.17 mole), was added dropwise 60 ml of 5N NaOH solution (0.3 mole). The temperature was kept below 15°

by cooling with running water. After the addition was finished, the reaction mixture was stirred at room temperature overnight. The reaction mixture was extracted with ether. The ether layer was washed with water twice and dried over anhydrous sodium sulfate. The solution was filtered and ether was removed by evaporation under reduced pressure. The ester was obtained as a light yellow oil, 28 g., 78% yield. The infrared spectrum exhibited characteristic sulfonyl bands at 1360 and 1175 cm^{-1}.

Attempt to purify the cyclobutylmethyl p-tosylate by vacuum distillation resulted in an explosion.

METHYLCYCLOBUTANE (110).— Methylcyclobutane was made by reduction of cyclobutylmethyl p-tosylate (122) with lithium aluminum hydride. The same equipment setup as that for the pyrolysis reaction of tosylhydrazone was used.

Into a slurry of 1.2 g. of lithium aluminum hydride (30 m.mole) in 30 ml of dry diglyme, was injected slowly 4.8 g. (20 m.mole) of the tosyl ester (122) (crude reaction product without distillation, volatile impurities were removed by evacuation under high vacuum). The reaction mixture was stirred at room temperature under nitrogen atmosphere for one hour, and the temperature was then raised up slowly to 185°. The volatile product collected consisted of only one component as shown by vapor phase chromatogram.

Structure was confirmed by n.m.r. and infrared spectra.

TREATMENT OF CYCLOBUTYLMETHYL p-TOSYLATE (122) WITH SILVER PERCHLORATE.— The apparatus used for the reaction of cyclobutylmethyl p-tosylate with silver perchlorate was the same as that for pyrolysis of the tosylhydrazone (Figure 9).

Dry diglyme and caproic acid ($n\text{-}C_5H_{11}COOH$, b.p. 205°) were used as solvents in this reaction. In a typical run, a solution of 2.4 g. (10 m.mole) of cyclobutylmethyl p-tosylate (122) in 15 ml of dry diglyme was injected very slowly into a stirred solution of 3 g. of anhydrous silver perchlorate (14 m.mole, dried at 70° overnight under high vacuum) in 20 ml of diglyme. After the addition had been completed (0.5 hour), the clear colourless reaction mixture was stirred at room temperature for an additional 30 minutes, and the temperature was then raised slowly by means of a heating oil bath up to 185° (1.5 hour). The reaction mixture started turning a dark brown color at the temperature of 90°. Approximate 3 ml of colourless volatile hydrocarbon product mixture was collected.

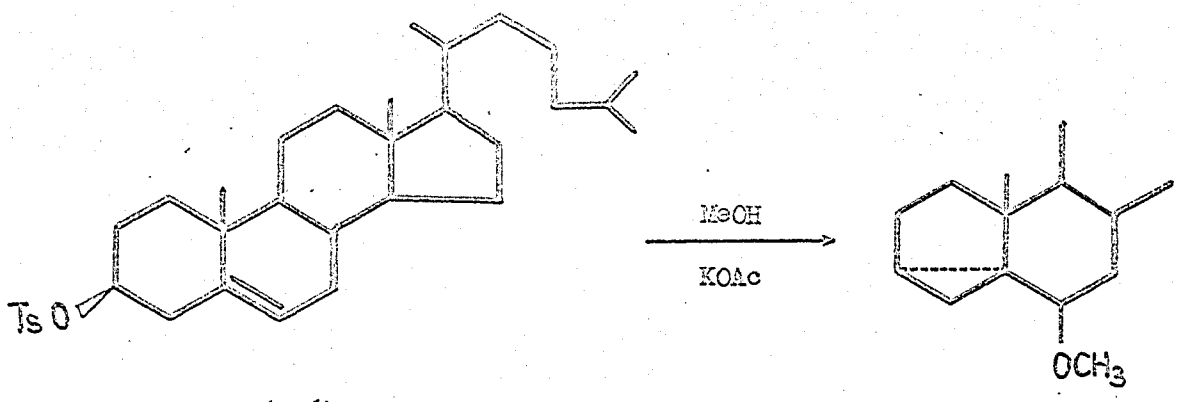
The product mixture was analyzed and separated by vapor phase chromatography using a 15 ft. long column packed with 30% di-2-ethylhexyl sebacate on 60/80 Chromosorb P.

PART II

THE REACTION OF SILVER TETRAFLUOROBORATE WITH ORGANIC CHLORIDES

INTRODUCTION

The participation in a nucleophilic displacement reaction by a β-γ double bond was first observed by Stoll in 1939 when he found that β-cholesteryl p-toluenesulfonate (136) on treatment with potassium acetate in methanol gave rise to i-cholesteryl methyl ether (137) which possessed a cyclopropyl ring.[56]

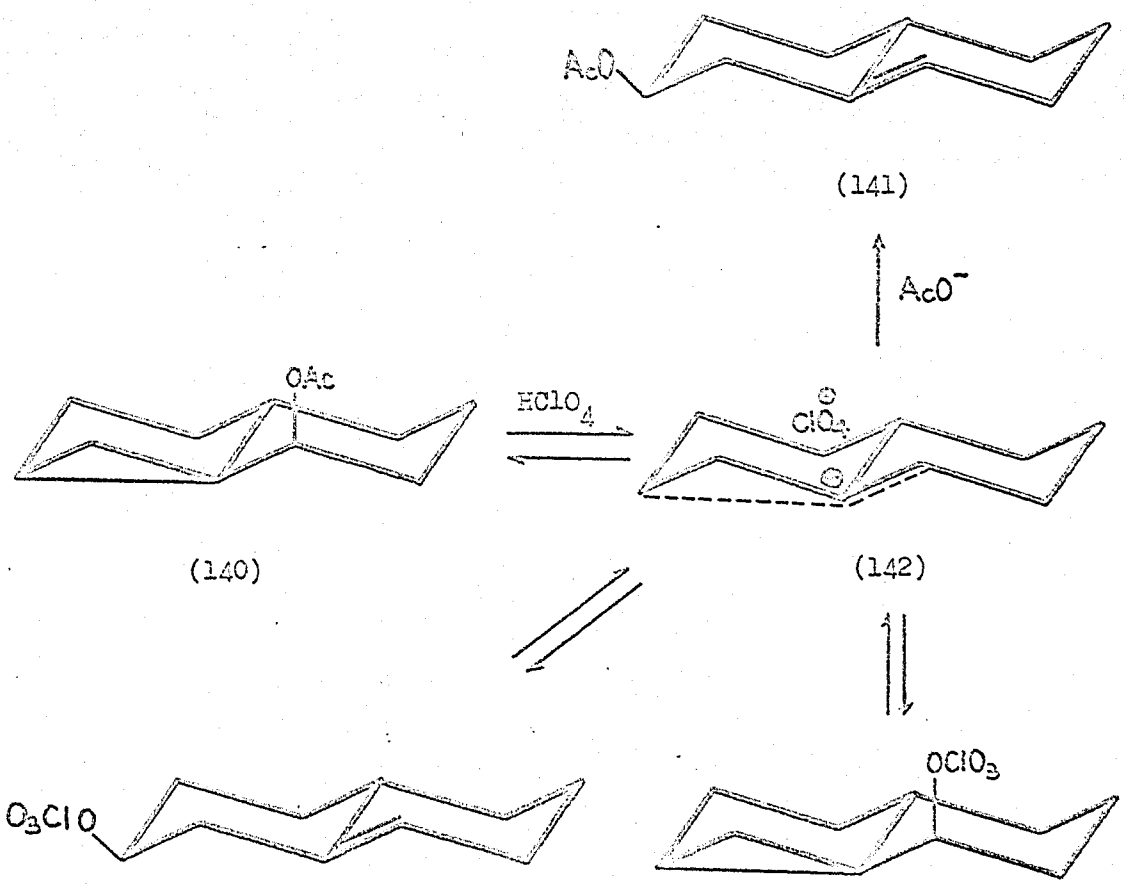


(136) (137)

Cholesteryl chloride (138) also gave rise to i-steroid under like reaction conditions.[57]

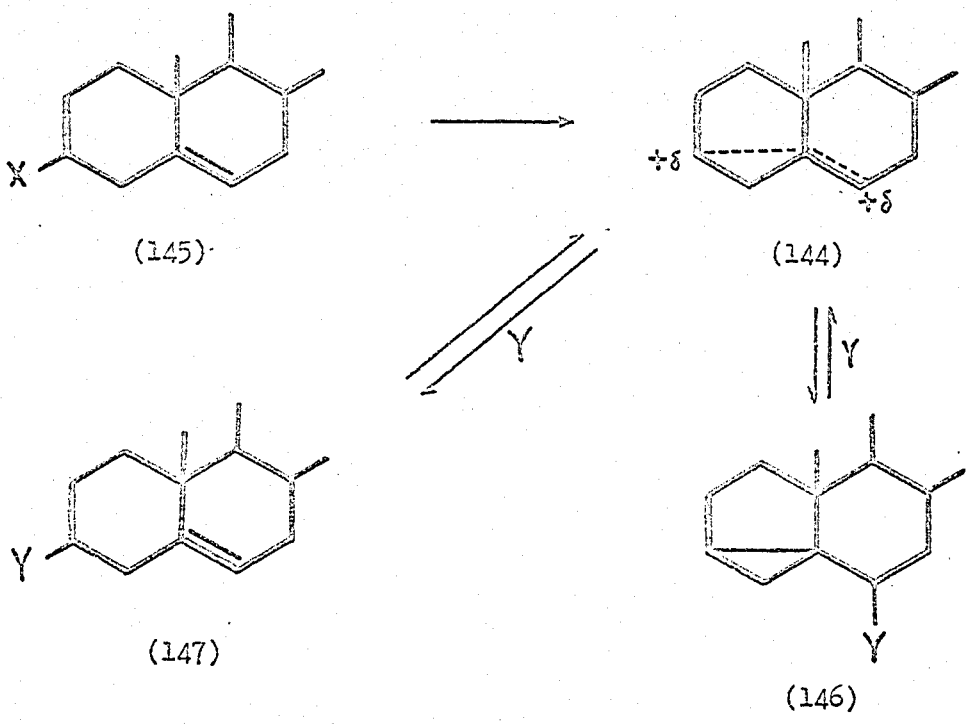
Shoppee[58] pointed out that the retention of configuration in nucleophilic displacements at C_3 in Δ^5-cholestene derivatives and similar systems suggests that a properly situated ethylenic linkage may display neighboring-group participation in replacement reactions.

Extensive kinetic studies have been made of the reactivity of such a "homoallylic" system. Cholesteryl tosylate (136), for example, was found to solvolyze about 100 times as rapidly as does cyclohexyl tosylate (139).[59] The $HClO_4$-catalyzed isomerization of i-cholesteryl acetate (140) in acetic acid solvent to the thermodynamically favored cholesteryl isomer (141) was reported to be first order in $\Sigma HClO_4$, and an intermediate carbonium perchlorate ion pair (142) was proposed.[60]



Acetolysis of cholesteryl iodide (143) in the presence of added acetate has been found to involve a unimolecular heterolysis[61], confirming the view[30] that the rearrangement, accomplished with retention of configuration, involves the i-cholesteryl cation.

This , and other evidence, indicates that a resonance-stabilized carbonium ion of the type (144) is an intermediate in the reaction of certain cholesteryl compounds (145).[62-69]



(145) (144) (147) (146)

X = Cl, OTs; Y = OCH_3, OAc.

The i-cholesteryl derivative (146) is formed as a kinetically controlled product. Under certain conditions, the normal cholesteryl

derivative (147) is also formed as a thermodynamically controlled product via the same intermediate (144)

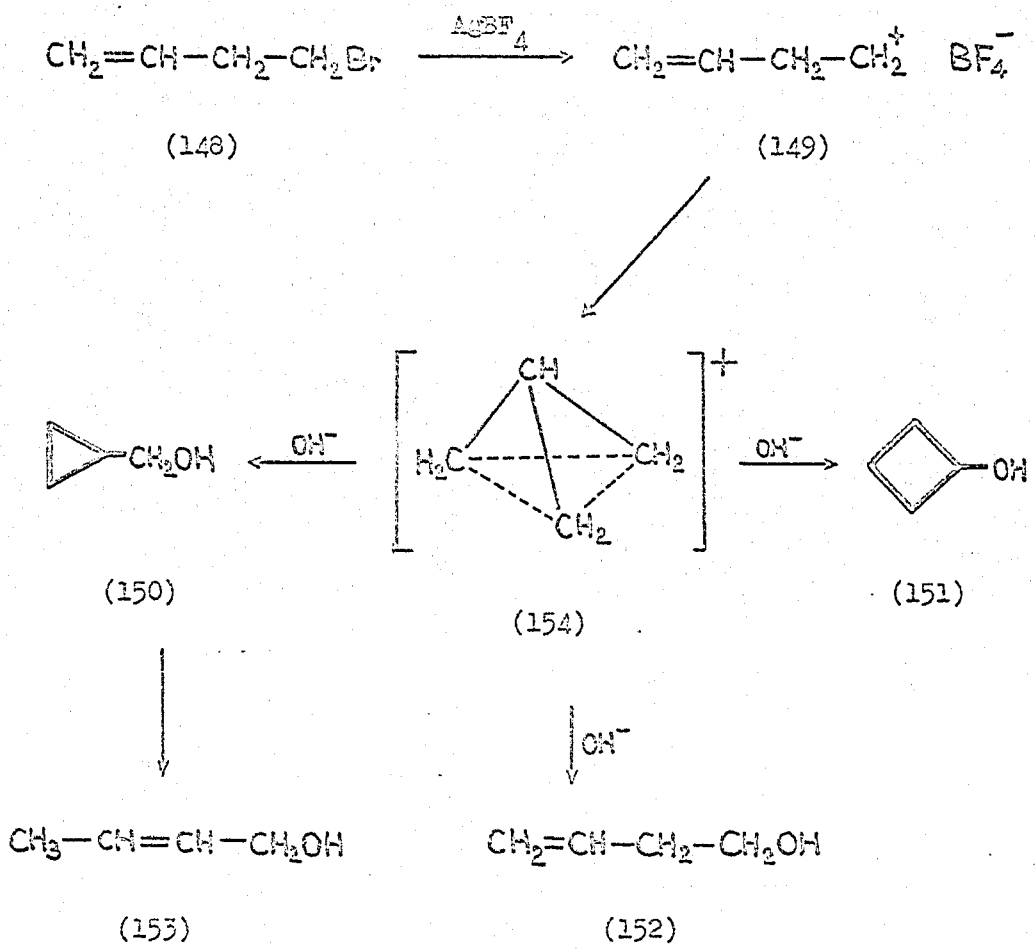
The formation of i-ethers in solvolytic reactions of cholesteryl halides and tosylates with alcohols under buffered conditions, and the ready rearrangement of the kinetically formed i-ethers to the thermodynamically more stable 3β-ethers under acid conditions strongly suggest such a mechanism.

A similar participation of a β-γ double bond in a simple aliphatic system has been recently reported by Hanack and Schneider.[70] In studying the rearrangements of the carbonium ions as a function of reaction time and temperature, 1-bromo-3-butene (148) in nitromethane or dichloromethane was treated with silver tetrafluoroborate to give a proposed tetrafluoroborate intermediate (149). Hydrolysis of the reaction mixture with an excess of sodium bicarbonate solution gave four alcohols: cyclopropylcarbinol (150), cyclobutanol (151), 3-buten-1-ol (152), and 2-buten-1-ol (153). The proportions of these products were reported to depended on the time and temperature.

A possible route may involve the formation of a nonclassical bicyclobutonium ion intermediate (154) which is attacked by hydroxyl ion to give rise to cyclopropylcarbinol (150), cyclobutanol (151) and 3-buten-1-ol (152). Hanack and Schneider[70] proposed that 2-buten-1-ol (153) is formed by ring rupture from cyclopropylcarbinol (150).

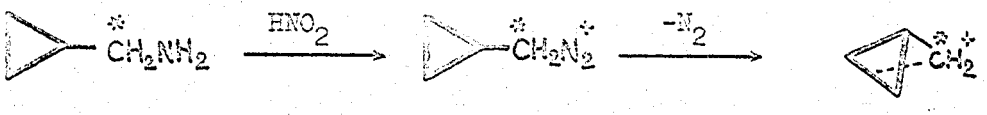
1-Bromo-3-pentene (155) was treated in the same way and gave a

similar result.

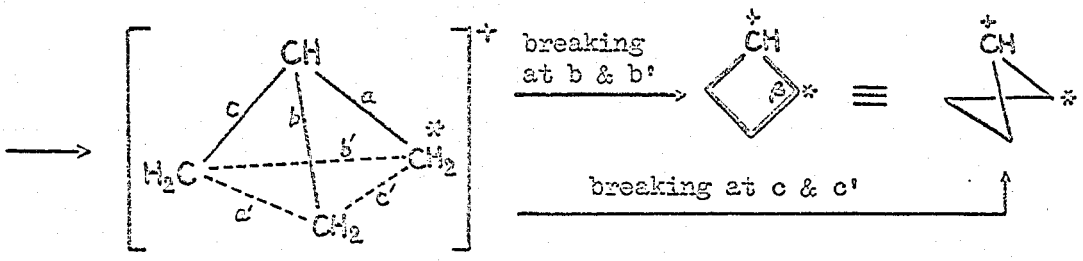


A similar nonclassical carbonium ion intermediate (154) has been proposed by Roberts[71-73] in order to explain the mechanisms for the hydrolysis of cyclopropylcarbinyl benzenesulfonate (156) or of the corresponding chloride (78), or the deamination of aminomethylcyclopropane (123). These reactions also yield mixtures of cyclopropylcarbinol (150), cyclobutanol (151) and 3-buten-1-ol (152).

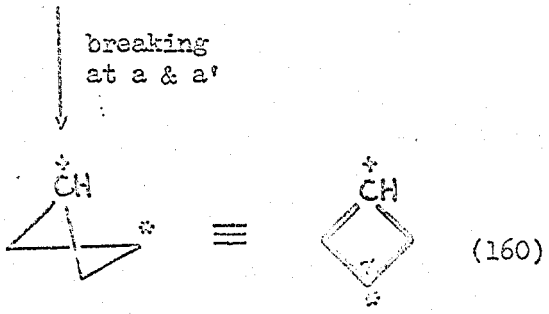
This proposal was based on the finding that if the aminomethylcyclopropane is labeled at C_α with C^{14} (157), one third of the labeled carbon in the resulting cyclobutanol (161) lies in the γ position, none in the α position, and two thirds in the β position. This points to the intervention of an intermediate (158) in which the two carbons which ultimately become β-carbons, and the single carbon which ultimately becomes a γ-carbon, are geometrically equivalent. Such an



(157) (159)



(158)



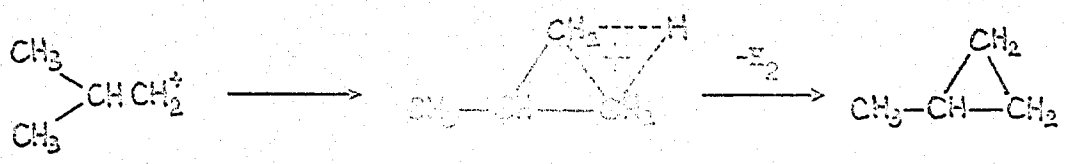
(160)

intermediate (158) could be [illegible] by the attraction of the $-CH_2^+$ group of the cyclopropylcarbinyl cation (159) to the electron-rich portion of the carbon-carbon bond [illegible]. Redistribution of these two bonding electrons in the regions between the three methylene groups results in partial bonding. Conversion of this very strained intermediate to the cyclobutyl cation (160) requires breakage of one of the "full" bonds (a, b or c) and one of the "one-third" bonds (a', b' or c').

In studying the intra- and intermolecular reactions of poorly solvated cations, Friedman et al.[74] reported that diazotization of aliphatic amines in aprotic media yields carbonium ion species that are markedly different from those formed in protic media in that skeletal rearrangements and double-bond migration are minimized, and cyclopropane formation is significantly increased. For example, a 14-16% yield of the insertion product methylcyclopropane (161) was obtained by aprotic diazotization of isobutylamine (162). Whereas it has long been known that the reaction of isobutyl iodide (163) with silver acetate in acetic acid gave predominantly tert-butyl acetate (164) by way of a rearrangement of the tertiary hydrogen atom.[75] Friedman suggested that in proton-donor solvents the cationic species are stabilized by solvation and thus rearrangement to thermodynamically more stable intermediates occurs, whereas under aprotic conditions products are derived from kinetic rather than thermodynamic factors.

"Internal solvation" occurs in the poorly solvated cations to

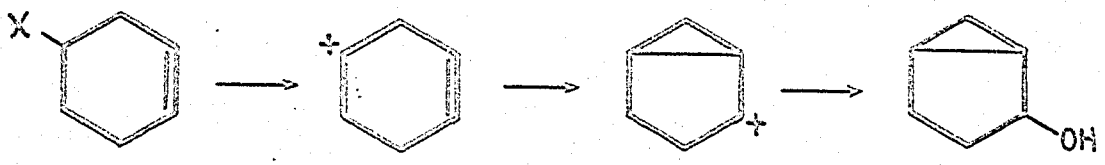
yield the more stable protonated cyclopropane intermediate (165). Cyclopropanes could then readily by simple loss of $H^{\oplus}_{a}$ proton.



(165) (161)

The formation of bicyclo(1.1.0)butane by aprotic diazotization of cyclopropylcarbinyl amine (123) or cyclobutylamine (166) are other examples of intramolecular carbonium ion insertion.[35]

In analogy to the formation of i-ether in solvolytic reactions of cholesteryl halides (167) and tosylate (136) with alcohol under buffered conditions, a similar neighboring-group participation by a β-γ double bond was observed by Hanack and Keberle[76] in that bicyclo(3.1.0) hexan-2-ol (168) was reported to be formed by deamination of Δ^3-cyclohexenylamine (169) or by acetolysis of Δ^3-cyclohexenyl p-tosylate.

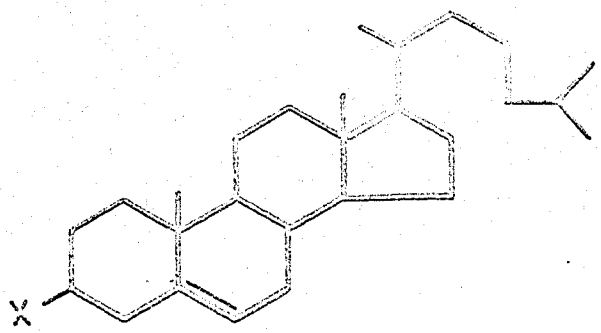


X = NH_2 (169)

X = OTs (170)

(168)

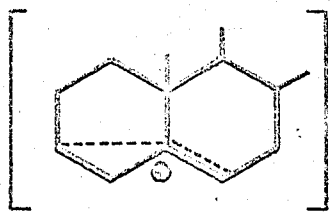
Based on these findings, as a prelude to attempting to form a carbocyclic ring by intramolecular carbonium ion insertion, we used a steroid molecule as a model compound to study the carbonium ion produced by the treatment with silver tetrafluoroborate. Under aprotic conditions, one of the expected products from cholesteryl chloride (138) or tosylate (136) would be 3,5-cyclocholest-6-ene (171).



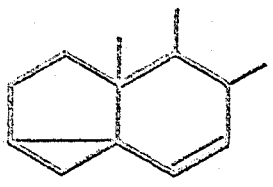
$AgBF_4$ →

X = OTs (136)

X = Cl (138)



$-H^+$ →



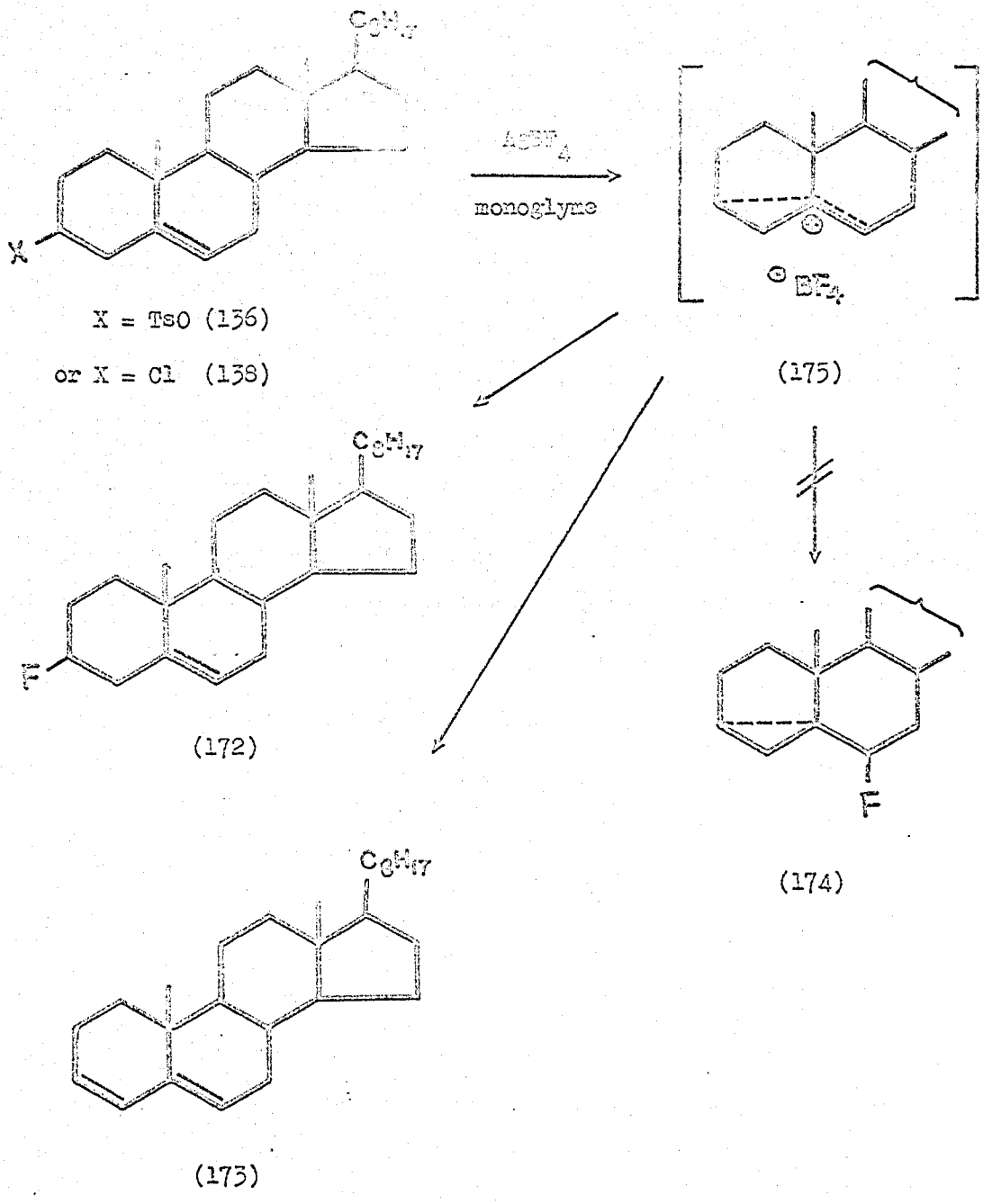
(171)

RESULTS AND DISCUSSION

The treatment of cholesteryl chloride (138) or cholesteryl tosylate (136) in ethylene glycol dimethyl ether (aprotic solvent) with $AgBF_4$ gave identical results with formation of cholesteryl fluoride (172) (23% yield) and cholesta-3,5-diene (173) (56% yield) as principal products. The expected product, 3,5-cyclocholest-6-ene (171), was not obtained (Figure 10).

The formation of cholesta-3,5-diene (173) instead of 3,5-cyclocholest-6-ene (171) suggested the preference of the cholesteryl cation to react by proton expulsion from C_4 rather than from C_7. This result is in agreement with the finding that acetolysis of cholesteryl iodide (143) in the presence of added acetate at 93.8° gives 10% yield of cholesta-3,5-diene (173).[61] The 3β-fluorocholest-5-ene (172) was formed with retention of configuration at C_3. Its formation may simply involve a nucleophilic attack at C_3 of the homoallylic bridged cation by a fluoride ion. The i-cholesteryl fluoride (174) which might be formed by nucleophilic attack at C_6 was not obtained. The formation of the 3β-fluoride and the diene suggests that reaction conditions (or mechanism) are such that they lead to the thermodynamic products.

The first step in the reaction sequence is probably the formation of an ion pair[*] consisting of the homoallylic cation and the tetrafluoroborate anion (175). This ion pair, unlike that proposed by



X = TsO (136)

or X = Cl (138)

(175)

(172)

(174)

(173)

Figure 10

Winstein[60] (142) for the perchloric acid catalyzed rearrangement of the i-cholesteryl acetate (140), cannot form a stable covalent ester. The isolated and identified products indicate that there are several pathways this ion pair may follow: (a) proton loss from C_4 to give directly the cholesta-3,5-diene (173), (b) formation of the 3,5-cyclocholest-6-ene (171) followed by acid catalyzed ring opening to the diene (173), (c) formation of the 3β-$OCH_2CH_2OCH_3$ derivative (for the monoglyme case) followed by the BF_3 catalyzed elimination to give the diene[77], and (d) breaking down of the BF_4^- ion to give a covalent fluoride (172). It is interesting to note that only the 3β-fluoro compound was isolated.

The possibility that cholesteryl fluoride (172) is formed from the carbonium tetrafluoroborate ion pair (175) is in sharp contrast with Freedman's observation[78] on n.m.r. evidence that conversion from tetraphenylcyclobutenium bis(tetrafluoroborate) (176) to the monofluorocation (177) does not occur. The dication (176) was obtained by the treatment of 3,4-dibromotetraphenylcyclobutene (178) in methylene chloride solution with two moles of silver tetrafluoroborate.

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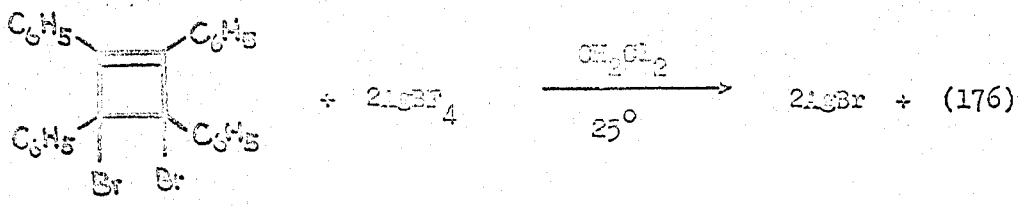
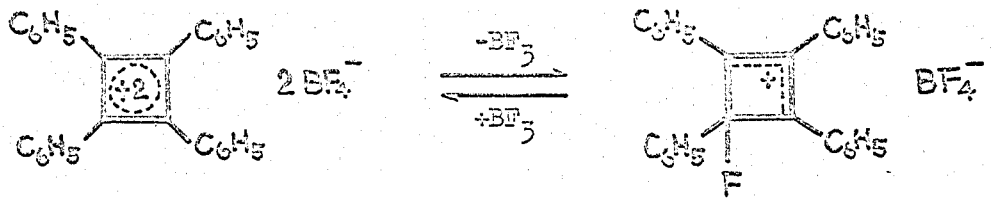
* The term "ion pair" is used for simplicity, and no implications are intended as regards exact electronic structure of the carbonium ion and the variety of ion pairs involved.[60]

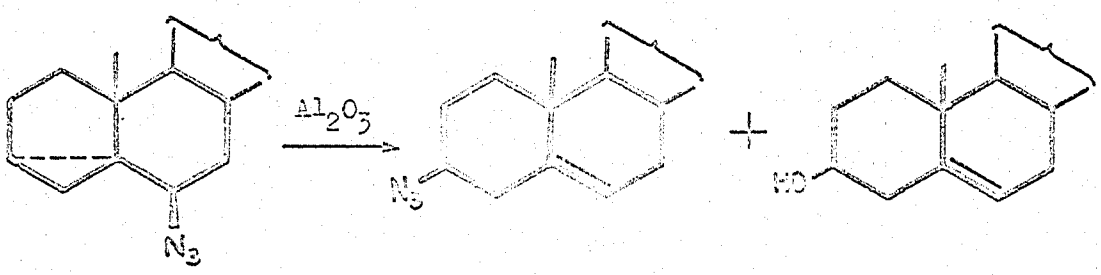


(178)



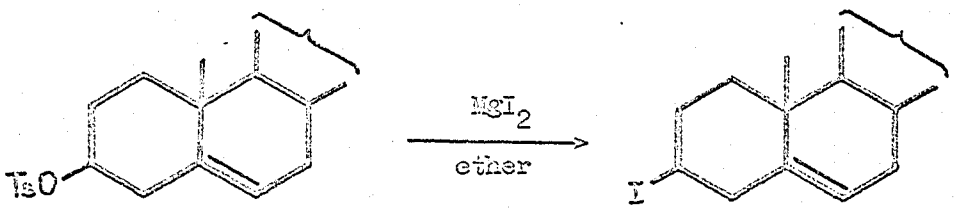
(176) (177)

The reaction products mixture was separated and purified by thick layer chromatography on silica gel. It was found that cholesteryl fluoride (172) was converted to cholesta-3,5-diene (173) in a 79% yield on chromatography over aluminum oxide. A similar rearrangement was observed by Jones[79] that prolonged contact with neutral aluminum oxide converted 3α,5-cyclo-6β-azidocholestane (179) into a mixture of 3β-azidocholest-5-ene (180) and cholesterol (181).

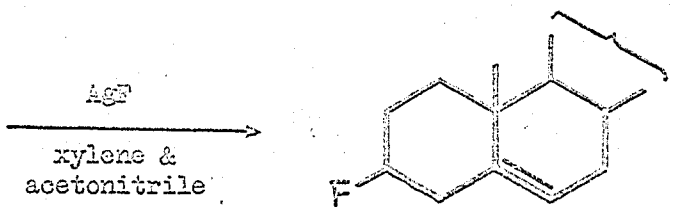


(179) (180) (181)

Cholesteryl fluoride (172) was also prepared in 64% yield by the treatment of cholesteryl tosylate (136) with anhydrous silver fluoride in a 1 : 1 mixture of dry xylene and acetonitrile for comparison purposes[80]

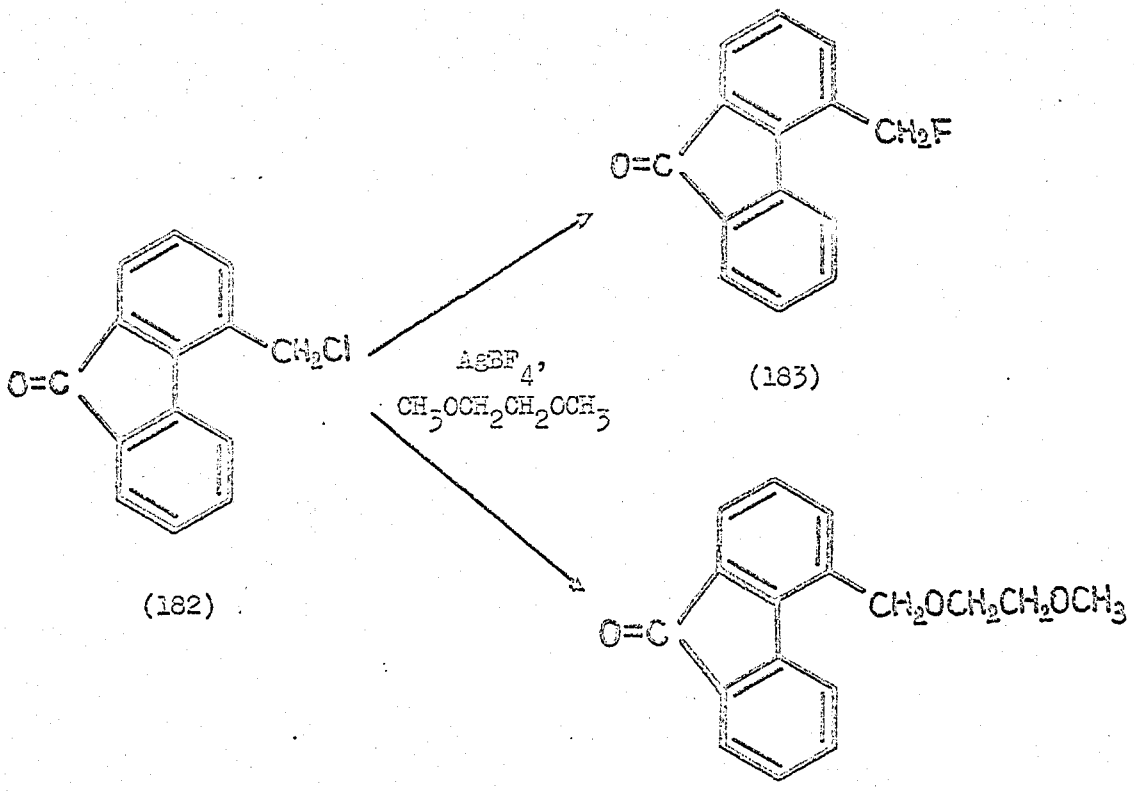


(136) (143)



(172)

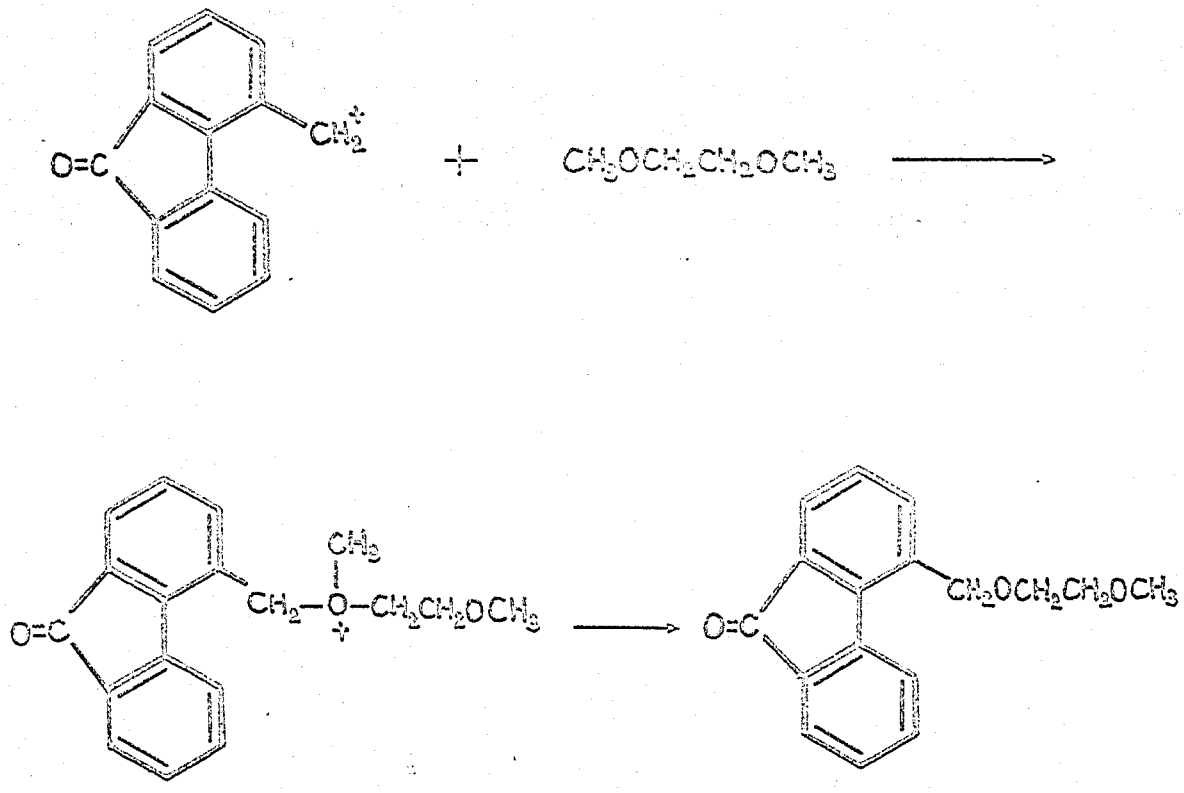
In an attempt to test the generality of the reaction between organic chlorides and silver tetrafluoroborate to give the corresponding fluorides, 4-chloromethylfluorenone (182) was treated similarly with silver tetrafluoroborate in monoglyme (ethylene glycol dimethyl ether). 4-Fluoromethylfluorenone (183) was obtained (42% yield) as well as 4-(β-methoxyethoxy)methyl-fluorenone (184) (44% yield). The latter was formed from the reaction of the carbonium ion intermediate with solvent, monoglyme, and is in agreement with the



(182) (183) (184)

result reported by Friedman et al[81] that alkylation of solvent occurs when the poorly solvated alkyl cations are generated by aprotic diazotization of aliphatic amines in aromatic solvents (such as benzene and toluene) or in ethers(such as diglyme).

The reaction appears to involve an oxonium ion intermediate (185).



(185) (184)

With further investigation, the treatment of organic chlorides or tosylates with [illegible] may prove to be a convenient way to synthesize [illegible].

EXPERIMENTAL

CHOLESTERYL CHLORIDE (138).—— Cholesteryl chloride was prepared by the method of Daughensbaugh and Allison.[82,83]

To 30 g. of cholesterol (131) and 6 ml of pyridine, 60 ml of thionyl chloride was added rapidly. The reaction mixture was kept cool with running water and then refluxed for one hour. Sulfur dioxide was liberated. The mixture was cooled, poured into water and then extracted with ether. The ethereal solution was dried over anhydrous sodium carbonate. When the solvent was removed under reduced pressure a semi-crystalline product remained. This was dissolved in acetone, treated with activated charcoal (Norit A) and recrystallized from acetone. The cholesteryl chloride was obtained in 45% yield, 14 g., m.p. 94-95° (lit. m.p. 95-96°). The reaction was repeated without the addition of pyridine with identical results.

CHOLESTERYL p-TOLUENESULFONATE (136)[84,85].—— To a solution of 58.2 g. of dry cholesterol (181) in 70 ml of dry pyridine, 58.2 g. of p-toluenesulfonyl chloride (135) was added. Within five minutes a white crystalline precipitate began to form. After the mixture had stood over-night, the reaction mass was dissolved in chloroform, the chloroform solution washed with 2% hydrochloric acid solution, then water and finally dried over sodium sulfate. Removal of the chloroform by distillation gave a tarry residue which crystallized after ether was

added at ice-salt temperature. The product was filtered and washed with ether; yield 65.2 g. (80.7%); m.p. 131-132° (lit. m.p. 131.5-132.5°).

REACTION OF CHOLESTERYL CHLORIDE (138) WITH SILVER TETRAFLUOROBORATE.—— Reaction were done either in diglyme (diethylene glycol dimethyl ether) or monoglyme (ethylene glycol dimethyl ether) as solvents. Identical results were obtained.

After dissolving 2.00 g. of anhydrous silver tetrafluoroborate in 20 ml of dry monoglyme, a solution of 1.00 g. of cholesteryl chloride (138) in 10 ml of dry monoglyme was added. The mixture was stirred at 70° under nitrogen atmosphere for 30 minutes. Temperature was then raised up to the refluxing temperature of monoglyme (85°C) and stirring was continued for another 30 minutes. The mixture was cooled, filtered to removed the silver chloride precipitate formed (0.346 g., 98.8% yield), and diluted with ether. The ethereal solution was washed with water several times to remove monoglyme and finally dried over anhydrous sodium sulfate. After removing ether under reduced pressure, 0.937 g. of white solid was obtained which consisted of two components as indicated by thin layer chromatography. Separation by thick layer chromatography on silica gel gave 0.509 g. (56.0% yield) of cholesta-3,5-diene (173) and 0.218 g. (23.3% yield) of 3β-fluorocholest-5-ene (172). The analytical sample of cholesta-3,5-diene

(173) obtained was recrystallized from ethanol and showed m.p. 79-80° (lit. m.p. 79.5-81.0°), λ [illegible] ε 19800 (lit. ϵ_{236}, 21100).[86,87]

Anal. Calcd. for [illegible]: C, 87.39; H, 12.03. Found: C, 87.27; H, 11.86; and C, 87.[illegible]; H, 11.[illegible].

The pure sample of 3β-fluorocholest-5-ene (172) was obtained by recrystallization from ethanol and showed m.p. 96-96.5° (lit. m.p. 94-96°)[88]; $\lambda_{max}^{cyclohexane}$ 205 mμ, ε 1600. The infrared spectrum showed strong C-F absorption at 1010 cm^{-1}.

Anal. Calcd. for $C_{27}H_{45}F$: C, 83.36; H, 11.67; mol. wt., 388.64. Found: C, 82.92; H, 11.59; mol. wt., 388 (mass spec.).

The assignment of the structure as 3β-fluorocholest-5-ene (172) has been confirmed by comparison of its n.m.r. and infrared spectra with that of an independently prepared sample by the method of Jacobsen and Jensen.[80]

REACTION OF CHOLESTERYL p-TOSYLATE (136) WITH SILVER TETRAFLUOROBORATE.—— This reaction was run in the same way as that with cholesteryl chloride (138). Identical results were obtained.

3β-IODOCHOLEST-5-ENE (143)[85,80].—— To a colorless solution of magnesium iodide, prepared from 17.50 g. of iodine and 1.65 g. of magnesium in 400 ml of anhydrous ether, was gradually added a solution

of 7.5 g. of cholesteryl p-tosylate (136) in 50 ml of anhydrous ether; here a yellowish-white precipitate of sodium p-tosylate began to separate immediately. After boiling for three hours, the mixture was poured into water. The ether layer was washed with water (tested with silver nitrate) and dried over anhydrous sodium sulfate. Removal of the ether under reduced pressure and recrystallization from ethanol gave a crystalline precipitate with melting point 106-107.5° (lit. m.p. 107-108°).[82,89]

3β-FLUOROCHOLEST-5-ENE (172).— 3β-Fluorocholest-5-ene was prepared by the method of Jacobsen and Jensen.[80]

To a solution of 2.0 g. of 3β-iodocholest-5-ene (143) in 35 ml of a 1:1 mixture of dry xylene and acetonitrile was added 3.0 g. of anhydrous silver fluoride. A precipitate of silver iodide formed immediately. The reaction mixture was stirred at room temperature for 15 minutes and filtered to remove the excess silver fluoride and silver iodide. The clear solution was washed with water and dried over anhydrous sodium sulfate. Evaporation of the solvent under reduced pressure gave 1.62 g. of crude reaction product. Purification by silica gel thick layer chromatography gave 0.982 g. (62.4% yield) of 3β-fluorocholest-5-ene (172). All the physical constants are identical with that of the product obtained from the reaction of cholesteryl chloride (138) or cholesteryl p-tosylate (136) with silver tetrafluoroborate.

CHROMATOGRAPHY OF 3β-FLUOROCHOLEST-5-ENE (172).— In an at-

tempt to separate the crude product mixture from the reaction of cholesteryl chloride (138) with silver tetrafluoroborate by chromatography on aluminum oxide, conversion of 3β-fluorocholest-5-ene (172) to cholesta-3,5-diene (173) was observed.

In a quantitative experiment in order to determine the percentage of conversion, 0.0648 g. of pure 3β-fluorocholest-5-ene (172) was chromatographed on a three inch long aluminum oxide column. Elution with light petroleum ether (30-60°) gave 0.0487 g. of cholesta-3,5-diene (173). The yield of conversion was thus 79.2%.

REACTION OF 4-CHLOROMETHYLFLUORENONE (182) WITH SILVER TETRAFLUOROBORATE.—— 4-Chloromethylfluorenone[**] (m.p. 167-8°; 1.00 g.) in 20 ml of dry monoglyme was treated with a solution of 4.00 g. of silver tetrafluoroborate in 10 ml of dry monoglyme under nitrogen atmosphere at 70° for one hour. The mixture was filtered to remove the silver chloride precipitate (0.56 g., 89.5% yield), diluted with diethyl ether, and extracted with water to remove monoglyme and excess silver tetrafluoroborate. The ethereal solution was dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure and the collected residue, after drying under vacuum, weighed 1.00 g. The crude

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**The author is indebted to Mr. R. Chevalier for supplying this chemical.

product mixture was chromatographed on silica gel. Elution with benzene gave 0.395 g. of 4-fluoromethylfluorenone (183) (42.6% yield), m.p. 119.5-120.5° after recrystallization from 95% ethanol; elution with ether gave 0.524 g. (44.7% yield) of yellow oil which was identified as 4-(β-methoxyethoxy)methyl-fluorenone (184).

The infrared spectrum of the 4-fluoromethylfluorenone fraction showed a characteristic C-F absorption at 1010 cm^{-1} and C=O absorption at 1720 cm^{-1}; the n.m.r. spectrum consisted of two sharp peaks at 4.04 and 4.85τ (2 protons) and a complex multiplet centered at 2.58τ (7 protons).

Anal. Calcd. for $C_{14}H_9FO$: C, 79.20; H, 4.23; F, 8.96; mol. wt., 212.06. Found: C, 75.88; H, 4.23; F, 8.66; mol. wt., 212 (mass spec.).

The infrared spectrum of 4-(β-methoxyethoxy)methyl-fluorenone (184) showed an intense broad ether absorption at 1100 cm^{-1} and a characteristic carbonyl band at 1720 cm^{-1}. The n.m.r. spectrum in carbon tetrachloride consisted of a group of resonances centered at 2.66τ (7 protons), a sharp singlet at 5.37τ (2 protons), a complex multiplet centered at 6.43τ (4 protons) and a sharp singlet at 6.71τ (3 protons).

CLAIMS TO ORIGINAL RESEARCH

(1) Cyclobutanecarboxaldehyde p-tosylhydrazone was synthesized and its n.m.r. spectrum reported.

(2) The base induced thermal decomposition of cyclobutanecarboxaldehyde p-tosylhydrazone was studied. Intermolecular hydride shift with the formation of methylcyclobutane was first observed in this type of reaction, and a product dependence on solvent was observed.

(3) The reaction of cyclobutylcarbonium ion produced by the treatment of cyclobutylmethyl p-tosylate with silver perchlorate was investigated. Cyclopentene was found only product.

(4) A new method for the preparation of organic fluorides from the corresponding chlorides by treatment with silver tetrafluoroborate was discovered. Cholesteryl fluoride and 4-fluoromethylfluorenone were conveniently prepared by this method.

(5) Dehydrofluorination of cholesteryl fluoride to cholesta-3,5-diene in a aluminum oxide chromatographic column was observed.

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