SYNTHESIS AND SOLVOLYTIC REACTIVITIES
OF
UNSATURATED CYCLOBUTYL BROMIDES

Thesis by

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ABSTRACT

In order to study the effect of unsaturation electrons at the 3-position of a cyclobutyl carbonium ion, 3-methylenecyclobutyl bromide and 1-methyl-1-bromocyclobut-2-ene have been synthesized and their rates of solvolysis in aqueous ethanol determined and correlated with the solvolytic rates of a series of analogous bromides.

The synthesis of 3-methylenecyclobutanol, the precursor of 3-methylenecyclobutyl bromide, was accomplished by two independent schemes, both utilizing the cycloaddition reaction of allene and an activated olefin. Allene and vinyl benzoate afforded small yields of 3-methylenecyclobutyl benzoate, which liberated the alcohol on reduction. 3-Methylenecyclobutanecarbonitrile, obtained in good yield from allene and acrylonitrile by a published procedure, was converted to 3-methylenecyclobutylamine by hydrolysis followed by Curtius degradation. 3-Methylenecyclobutanol was obtained from the amine by nitrous acid deamination. 3-Methyl-3-bromocyclobutene was synthesized by dehydrobromination of 3-methylenecyclobutyl bromide, followed by low-temperature addition of one mole of hydrogen bromide.

The rate of solvolysis of 3-methylenecyclobutyl bromide in aqueous ethanol was found to be appreciably slower than the value predicted from simple molecular orbital theory by assigning a small resonance integral between the 1- and 3-positions in the carbonium ion intermediate. It is concluded that "homoallylic

resonance" is hindered in this system because the planar structure requires inefficient π-type overlap of the p-orbitals at the 1- and 3-positions, instead of the σ-type orbital overlap which contributes to the startling rate enhancement observed elsewhere in the solvolysis of anti-7-norbornenyl derivatives, for example. Cross-ring interaction is considered to be of some importance in the methylcyclobutenyl carbonium ion, although the solvolysis rate data in this case permit a wide range of interpretation.

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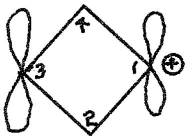
I. INTRODUCTION

The purpose of the present work was to determine the extent of π-type interaction between electrons centered on the 3-position of a cyclobutyl carbonium ion with the vacant p-orbital at the 1-position.



Historically, the problem is of particular interest in view of the attempts by Roberts and co-workers (1-4) to gain evidence for cross-ring interactions in other 1,3-unsaturated cyclobutane systems, and studies of the solvolysis rates of non-planar homoallylic derivatives, due largely to Winstein (5-10) and Roberts (11-14). Since much of the former involves synthetic methods used in the present work, it will be discussed first.

1,3-Interactions in the Cyclobutane Ring

Most of the recent work on the syntheses and properties of unsaturated small-ring compounds has been inspired by predictions derived from quantum mechanical calculations, usually involving the simple molecular orbital (LCAO) treatment (4,15). The experimental results obtained have often been ambiguous because of the lack of precise data on the magnitude of those factors which tend to cancel any excess energy gained from electron delocalization; the most important of these (16) are σ-bond strain and non-bonded atomic repulsions.

Molecular orbital calculations for the cyclobutadienylcarbinyl cation, radical, and anion (15) indicate a delocalization energy of 1.59 β (about 31 kcal.) for these species, a fact which led to the synthesis and study of the reactions of methylenecyclobutene by Applequist and Roberts (1). It was hoped that by removal of a proton, hydrogen atom, or hydride ion from the 4-position of this compound, a stable cyclobutadienylcarbinyl intermediate could be formed. Although polymerization studies presented no clear-cut evidence for an intermediate of unusual stability, the experimental results were consistent with the assignment of a small resonance integral between the 1- and 3-positions in the diene. In addition, methylenecyclobutene reacted rapidly with only one mole of bromine in carbon tetrachloride to give an initial product containing no exocyclic double bonds. It therefore seemed likely that attack of the bromonium ion occurred at the exomethylene carbon, in spite of the greater angle strain of the resulting cationic intermediate relative to the intermediate derived from attack on the ring. It was considered unlikely that hydrogen hyperconjugation involving the 4-position could adequately explain the results, since 4,4-dimethylmethylenecyclobutene apparently added bromine in the same manner.

Stabilization of an intermediate cation by 1,3-interaction has also been invoked to explain the straightforward behavior of 1,3-dimethylenecyclobutane on bromination, in contrast to the complex nature of the reaction of bromine with methylenecyclobutane (99). The former compound, reported by Caserio, Parker, Piccolini, and

Roberts in 1958 (2) and later obtained as a minor product from the direct dimerization of allene (17), rapidly added one mole of bromine to give 1-bromo-1-bromomethyl-3-methylenecyclobutane by simple 1,2-addition. The product was not isomerized by treatment with zinc bromide, and the original diene could be regenerated by debromination with zinc dust. Bromination of methylenecyclobutane gave, in addition to the expected 1,2-addition product, dibromides resulting from ring contraction and ring opening (99).

No evidence for cross-ring interaction in 1,3-dimethylenecyclobutane itself could be obtained from the ultraviolet spectrum. Furthermore, it has been pointed out (2) that the "normal" bromination behavior of this compound could have been due entirely to destabilization by the exomethylene double bond of the nonclassical intermediate which was postulated to explain the rearrangement of methylenecyclobutane with bromine.

Searching for a more polar molecule, which would be superior to the hydrocarbon as a test for cross-ring interaction, Caserio and Roberts reported the synthesis of 3-methylenecyclobutanone in 1958 (3). Due to experimental difficulties, the ketone was obtained only admixed with its conjugated isomer, 1-methylcyclobuten-3-one, a fact which prevented a precise evaluation of possible electronic interaction between the double bond and the carbonyl group. Evidence suggesting that such interaction was not important, however, was found in the relative rates of hydrolysis of the diethyl ketals of 3-methylenecyclobutanone and its hydrogenation product, 3-methylcyclobutanone. The fact that the unsaturated ketal hydrolyzed more slowly than the saturated analog by a factor of at least 20 tended to rule out any significant degree of participation of the exomethylene double bond in the rate-determining ionization step of the hydrolysis.

Delocalization of negative charge by 1,3-π-interaction has been invoked to explain the unusual acidity of 1-phenyl-2-hydroxycyclobuten-3-one (18) and 1-phenyl-2-hydroxycyclobutenedione (19) with respect to the 5- and 6-ring analogs (20). In order for this argument to be valid, such interactions must be considerably less important in the undissociated enols; nonetheless, this effect has also been suggested (4) as a major factor contributing to the stability of phenylcyclobutenedione (21). Perhaps a more startling case is 1,2-dihydroxycyclobutenedione (22) which decomposes at 293° and is an acid of strength comparable to sulfuric acid. Even if the dianion is assumed to be completely symmetrical, its remarkable stability is more easily rationalized by considering resonance forms involving 1,3-π-bonding.

Smutny (19) and Manatt (4) calculated the delocalization energies (DE's) of a number of unsaturated cyclobutane derivatives by the simple LCAO molecular orbital method, and found that the assignment of small (0.2-0.5 β) 1,3-resonance integrals generally increased the DE's of the systems by 0.8-15 kcal., depending on the magnitude of the assigned exchange integral. Manatt's calculations included the cyclobutenyl and 3-methylenecyclobutyl cations, and indicated that 1,3-interactions would stabilize these species by 41 and 0.8 kcal./mole, respectively if $\beta_{13} = 0.2\beta$;

or 10.9 and 4.7 kcal./mole if $\beta_{13} = 0.5\beta$. In an attempt to find experimental verification for these predictions, Manatt studied the acid-catalyzed hydrolysis of 4-nitrobenzoate esters of 3-phenylcyclobut-2-enol and 3-phenyl-2-chlorocyclobut-2-enol (4), but the results were inconclusive because of acyl-oxygen cleavage of the esters. Attempts to prepare arylsulfonate esters of the sensitive cyclobutenols were unsuccessful.

It is seen that concrete evidence for electron delocalization by 1,3-π-interaction in cyclobutanes has yet to be uncovered. Even in the case of the α-diketones mentioned above, for which the argument is most convincing, other phenomena can be mentioned which could explain their unusual stability and acidity.

Experimental Methods

The cycloaddition reaction of alkenes to give cyclobutane compounds has in the last few years all but rendered classical methods obsolete for the synthesis of four-membered rings. Although a significant part of the present work was concerned with this reaction, it has recently been reviewed elsewhere (23), and will be discussed only briefly here.

Manatt's synthesis of 3-phenylcyclobut-2-enol (4), as well as the preparation of several other substituted phenylcyclobutenes (24) started with unsym-difluorodichloroethylene as the "primary addend" (23); however, the fluorinated ethylenes were found (25) to be poorly suited to the synthesis of simple cyclobutene systems without vinylic halogen or phenyl substituents. The synthesis of 3-methylenecyclobutyl derivatives from allene and substituted alkenes developed by Cripps (26) was used as the starting point in the preparation of 1,3-dimethylenecyclobutane (2) and 3-methylenecyclobutanone (3). Good yields were obtained with allene and acrylonitrile; however, conversion of the resulting adduct to 3-methylenecyclobutanone, for example, required many steps and was difficult to carry out on a preparative scale. Accordingly, part of the present research was devoted to exploratory experiments with less active "secondary addends" (23) such as vinyl esters and halides which, if they formed adducts with allene, would lead more directly to 3-methylenecyclobutanone and 3-methylenecyclobutanol. Except for the isolation of small amounts of 3-methylenecyclobutyl benzoate from the reaction of vinyl benzoate and allene, these attempts were mainly unsuccessful (see page 76). The fact that vinyl benzoate forms an adduct and vinyl acetate does not (27), is probably best explained by the inductive effect of the phenyl group (23).

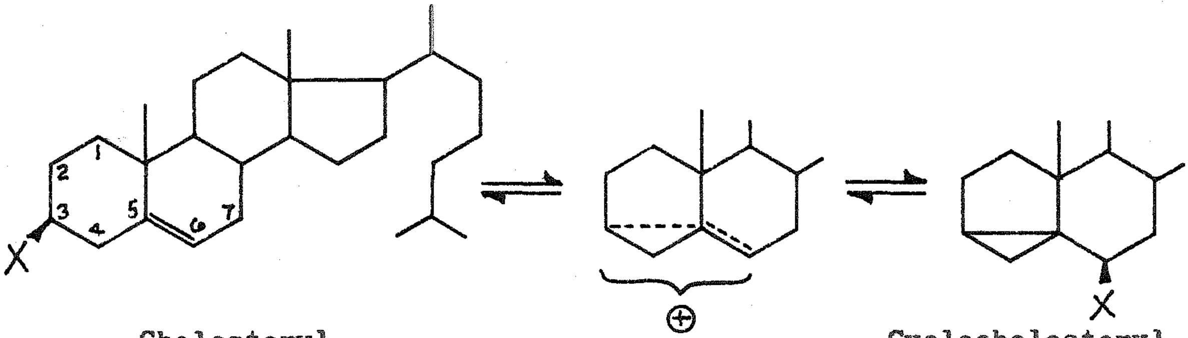
The best synthesis of 3-methylenecyclobutyl bromide used in the present work was achieved by published procedures (1,2) with only minor revisions; it will be discussed in detail in the next section. Perhaps the most noteworthy step was the conversion of 3-methylenecyclobutylamine (1) to 3-methylenecyclobutanol in 78% yield by nitrous acid deamination; this result is in striking contrast to the behavior of 3-methylcyclobutylamine noted by Silver (28). Deamination of the latter amine produced only 5% of the corresponding alcohol, the major products being cyclopropylmethylcarbinol and allylmethylcarbinol. Here again, the straightforward behavior of the unsaturated amine may be ascribed to destabilization of the proposed non-classical cationic intermediate by the exomethylene double bond (see page 3).

Homoallylic Interactions in Non-Planar Systems

In contrast with the cyclobutane systems discussed above, 1,3-electronic interactions in non-planar systems, such as derivatives of cholesterol and *anti*-7-norbornenol, are well established.

The phenomenon of participation of neighboring unsaturation electrons with a developing cationic center has generally been merged with that of neighboring-carbon participation (more specifically, participation of carbon-carbon σ-bond electrons) in previous discussions of non-classical ions (9,29). Admittedly, due to inevitable uncertainties in the geometry and hybridization of the transition state, the distinction is not always clear-cut. For example, participation of β-aryl substituents in solvolytic reactions, especially those resulting in aryl migration, can be included in both classes. Because of the obvious limitations of simple cyclobutane systems, it is to some advantage to restrict the discussion here to cases in which the straightest parallels can be drawn to the solvolyses of 3-methylenecyclobutyl and methylcyclobutenyl bromides. A more extensive discussion of electron delocalization in carbonium ion reactions is given in recent, consecutive papers by Roberts (14) and Winstein (9).

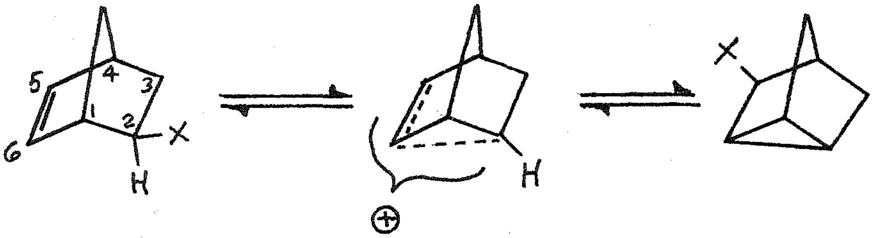
Winstein and Rowland Adams (5) first proposed in 1948 a mesomeric cation involving interaction of homoallylic *p*-orbitals to account for the accelerated rate and retention of configuration in the acetolysis of cholesteryl derivatives. This system has since been the subject of thorough investigations, including solvolytic studies of the "homoallylic isomer," 3,5-cyclocholestan-6-β-yl (*cyclo*-cholesteryl) (9), and the determination of substituent effects in the solvolysis of 6-arylcholesteryl derivatives (30), leaving no reasonable doubt that orbital overlap between the 3- and 5-positions is important.



Cholesteryl

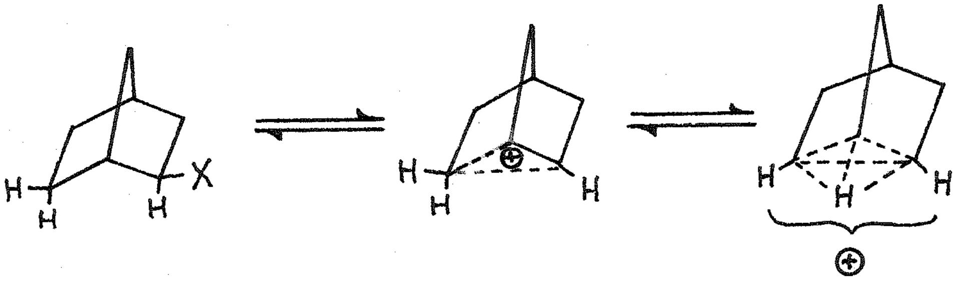
*Cyclo*cholesteryl

Another striking example of neighboring π-electron participation occurs in the solvolysis of *exo*-dehydronorbornyl halides and *p*-bromobenzenesulfonates, reported independently by Roberts (11) and Winstein (6) in 1950. In acetolysis, the *exo*-brosylate was found (6) to be 7000 times faster than the *endo* isomer, and even faster than *exo*-norbornyl brosylate, which itself is very reactive because of extensive σ-bond electron delocalization.



Exo-dehydronorbornyl

Nortricyclyl



Exo-norbornyl

Both dehydronorbornyl and cholesteryl derivatives readily undergo "homoallylic rearrangement" (6) to cyclopropane-bridged structures (see above); although a significant increase in angle strain accompanies the cholesteryl-*cyclo*-cholesteryl transformation* (9), the energy difference is not sufficient to prohibit the formation of a σ-bond between the 3- and 5-positions under favorable conditions. A case which clearly illustrates the ability of neighboring π-electrons to stabilize a carbonium ion although actual σ-bond formation is apparently prohibited is the solvolysis of *anti*-7-norbornenyl derivatives, reported by Winstein, Woodward, *et. al.* (7), and also studied carefully by Roberts and his co-workers (12). *Anti*-7-norbornenyl tosylate was found to undergo acetolysis at a rate approximately 10^{11} times that of the saturated analog, 7-norbornyl tosylate, and 25 times that of *exo*-dehydronorborn-2-yl tosylate. The reaction proceeded with complete retention

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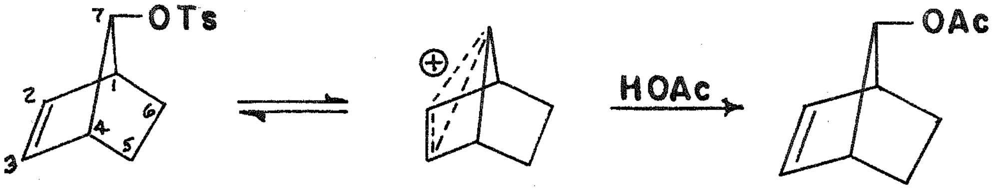
*This is not true of the dehydronorbornyl-nortricyclyl transformation, which apparently involves a slight *decrease* in ground-state free energy (9) because the 5,6-double bond is appreciably strained to begin with.

of configuration, and no rearranged product was detected*(8).



Attack of solvent at C-2 or C-3 of the intermediate carbocation would have to come from the hindered endo side; however, the fact that such attack does not occur is probably better explained by noting that the resulting product would contain a bicyclopentane structure, which is known (31,32) to be very highly strained. It is clear that σ-bond formation resulting from homoallylic rearrangement in the solvolysis of cyclobutenyl or 3-methylenecyclobutyl derivatives would be extremely unlikely, since such an

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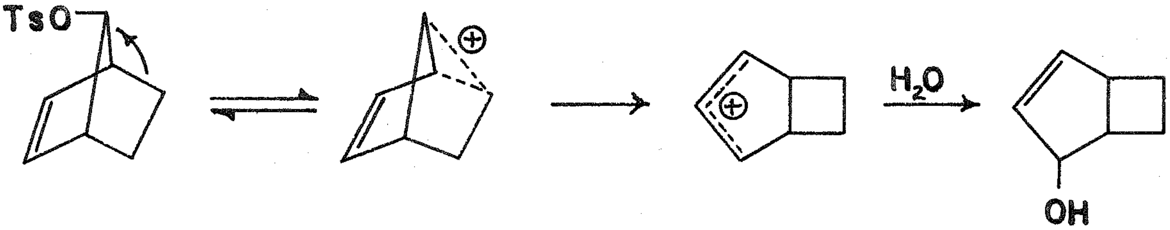
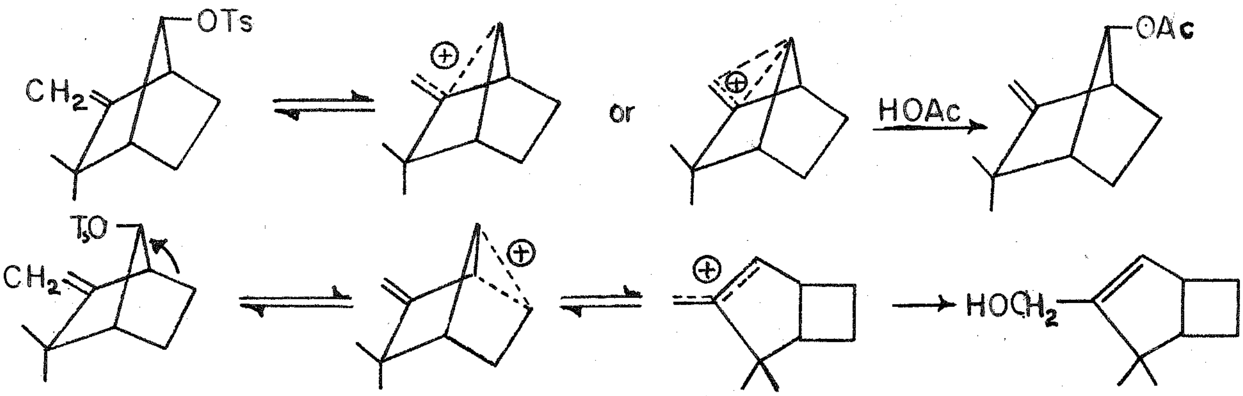
*It is interesting that although syn-7-norbornenyl tosylate cannot be compared in reactivity with the anti-isomer, it still undergoes acetolysis 10^4 times as rapidly as the 7-norbornyl derivative (9). Products studies have shown, however, that in this case, σ-bond participation resulting in ring contraction must be occurring, the driving force being the formation of a symmetrical allylic cation.



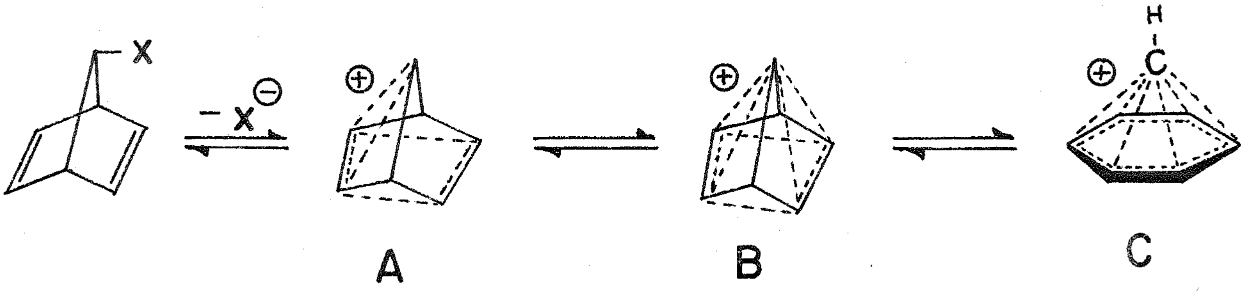
isomerization would result in a bicyclobutane structure which would be expected to have an even higher strain energy (33).

The sensitivity of the solvolysis rates of homoallylic derivatives to changes in molecular geometry was strikingly demonstrated by van Tamelen and Judd (34) in their study of 7-camphenyl tosylates. In contrast to the rate differential of 10^7 for *anti* and *syn*-7-norbornenyl tosylates (see above), *anti*-7-camphenyl tosylate was found to acetolyze *more slowly* than the *syn* epimer by a factor of 2, and only 6 times faster than the very sluggish 7-norbornyl tosylate. The solvolysis products of the 7-camphenyl derivatives corresponded to those observed in the 7-norbornenyl case, an observation which would seem to indicate that participation of the double bond was still occurring in spite of the very different rate behavior. Retention of configuration accompanied the acetolysis of the *anti* epimer, while the *syn* compound rearranged to an allylic structure.



In accounting for the absence of pronounced solvolysis rate acceleration in *anti*-7-camphenyl tosylate, it must be mentioned that in addition to being less favorably situated for π-orbital overlap, the double bond is significantly less strained in the ground state than that of 7-norbornenyl tosylate (12), and there is an inferior degree of alkyl substitution in the non-classical cation. It is likely, especially in view of the solvolysis product configuration, that these latter factors are of considerable importance.

Recently, Winstein and his associates have discovered homoallylic systems which are of interest here because of their great reactivity, although direct comparisons with cyclobutane systems cannot fairly be made. Solvolysis of 7-norbornadienyl chloride (10) occurs at a rate 750 times that of anti-7-norbornenyl chloride (12), which means there is a rate difference of about 10^{14} between 7-norbornadienyl and 7-norbornyl derivatives. The extensive possibilities for π-electron delocalization in the 7-norbornadienyl cation can be easily seen,* and one cannot summarily rule out the possibility of participation of the 1,7- and 4,7-bonding electrons to give rise to an even more symmetrical species with six equivalent carbon atoms (10).



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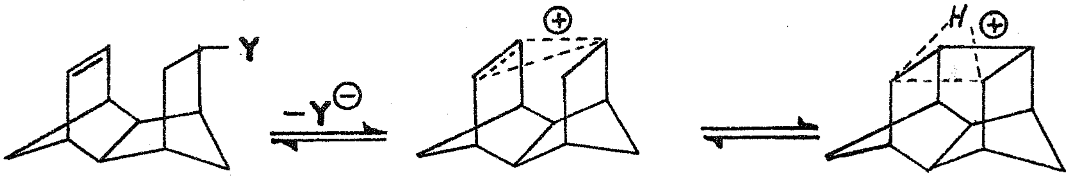
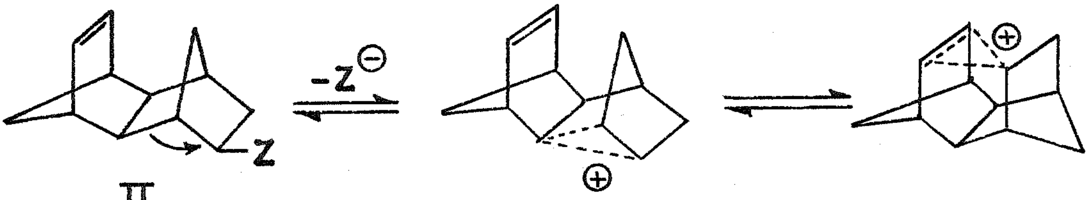
*Woods (29) has performed molecular orbital calculations on non-classical ions A and B, and found that the predicted delocalization energy for A is 8.4 kcal., while that for cation B, using the same structural parameters and resonance integrals, is 17.4 kcal./mole.

A special example of "homoallylic" interaction (35,36) is provided by the solvolysis of I (see below; Y = trifluoroacetate).



I

Although I is not homoallylic in the usual sense, the geometry is favorable for orbital overlap, and the solvolysis rate is enhanced by a factor of 10^4 over the analogous compound with *endo*-*exo* ring fusion (II; Z = *p*-bromobenzenesulfonate),



II

even though II can eventually form the same non-classical ion.

The phenomenon of homoallylic resonance is discussed from a more theoretical standpoint in the next section, in conjunction with the results of the present research on cyclobutane compounds. The much larger field of allylic compounds has been reviewed (37), and since former treatments of allylic systems have generally neglected 1,3-interactions, discussion of this topic will also be deferred to the next section.

II. RESULTS AND DISCUSSION

Synthesis and Properties of 3-Methylenecyclobutyl and Methylcyclobutenyl Derivatives

One objective of the present work was the discovery of new extensions of the cycloaddition reaction (23) which might lead directly to derivatives of 3-methylenecyclobutanol or 3-methylenecyclobutanone. Many small-scale experiments were carried out with allene and ketene diethyl acetal (38), but the only products identified were ethylene and ethyl acetate, resulting from pyrolysis of the acetal (39). Ketene dimethyl acetal was synthesized by the method of McElvain (40), and although this compound showed much greater thermal stability than the diethyl acetal (41), no cycloadduct with allene could be identified. The reactions of allene with vinyl acetate and vinyl chloride were likewise unsuccessful. Cripps, Williams, and Sharkey (26) had observed the formation of an adduct from allene and ketene cyanohydrin acetate (α-acetoxyacrylonitrile), which was assigned the structure 1-cyano-1-acetoxy-3-methylenecyclobutane. Since the conditions used by Bartlett and Tate (42) for hydrolysis of dehydronorcamphor cyanohydrin O-acetate to the corresponding ketone were considered too harsh for the cyclobutane system, it was hoped that acid hydrolysis of the acetoxy group followed by equilibration of the free cyanohydrin with an excess of a suitable aldehyde would liberate 3-methylenecyclobutanone. After an attempt to prepare α-acetoxyacrylonitrile by enol acetylation of pyruvonitrile (43) with isopropenyl acetate (44) was unsuccessful, this compound was synthesized from ketene and hydrogen cyanide by the method of Johnson and Newton (45). The maximum yield of adduct from allene and α-acetoxyacrylonitrile reported by Cripps, et. al. (26) was 20%; the best yield in the present work was only 6%. This fact, combined with the somewhat dangerous and time-consuming nature of both the synthesis of the monomer and the cycloaddition reaction, precluded any further experiments on this system.

The reaction of allene and difluorodichloroethylene resulted in an adduct in yields of 18-24%, which was assigned the structure 1,1-dichloro-2,2-difluoro-3-methylenecyclobutane. The compound gave a satisfactory analysis, and on treatment with methanolic potassium hydroxide, gave rise to potassium chloride and a diene which exhibited a maximum at 242 mμ in the ultraviolet and did not show ether absorptions in the infrared. Prolonged treatment with sodium methoxide liberated fluoride ion, giving rise to a mixture of methyl ethers which was not identified. In spite of the presence of an allylic gem-difluoro group, the compound was inert to hot, concentrated sulfuric acid. Large quantities of tetrachlorotetrafluorocyclobutane were formed in the cycloaddition reaction which, because of azeotrope formation with the allene adduct, could be removed only be preparative vapor-phase chromatography (v.p.c.) or by treatment of the mixture with bromine and purification of the adduct as the dibromide. Low-temperature crystallization from a variety of solvents was attempted, with little success.

Adducts of dichlorodifluoroethylene with several other substituted alkenes, including vinyl acetate, isopropenyl acetate, vinyl chloride, and methyl methacrylate (46), were also prepared. Exploratory attempts to transform these halogenated adducts into simple cyclobutene systems were made with results as are outlined in Figure 1.

Vinyl benzoate, which is readily preparable from vinyl acetate and benzoic acid in the presence of mercuric salts (47), reacted with allene under favorable conditions to give 1-3% yields of 3-methylenecyclobutyl benzoate (X). The structure of X was proved by reduction to 3-methylenecyclobutanol and benzyl alcohol, and by infrared and nuclear magnetic resonance (n.m.r.) spectra. The yields of X were too small for preparative work, and since the crude ester resisted all efforts to crystallize it, purification had to be accomplished by chromatography, which was rather unsatisfactory.

The best synthesis of 3-methylenecyclobutanol (XVI) was accomplished by nitrous acid deamination of the known 3-methylenecyclobutylamine (XV) (1). By the procedure of Caserio (2), allene and acrylonitrile gave 47-55% yields of 3-methylenecyclobutanecarbonitrile, which was hydrolyzed to the acid in 96% yield with aqueous alcoholic sodium hydroxide. Treatment of the acid with thionyl chloride in chloroform as described by Applequist (1) afforded 3-methylenecyclobutanecarbonyl chloride (XIII) in 86% yield. Addition of a slight excess of aqueous sodium azide to an acetone solution of XIII resulted in the separation of the

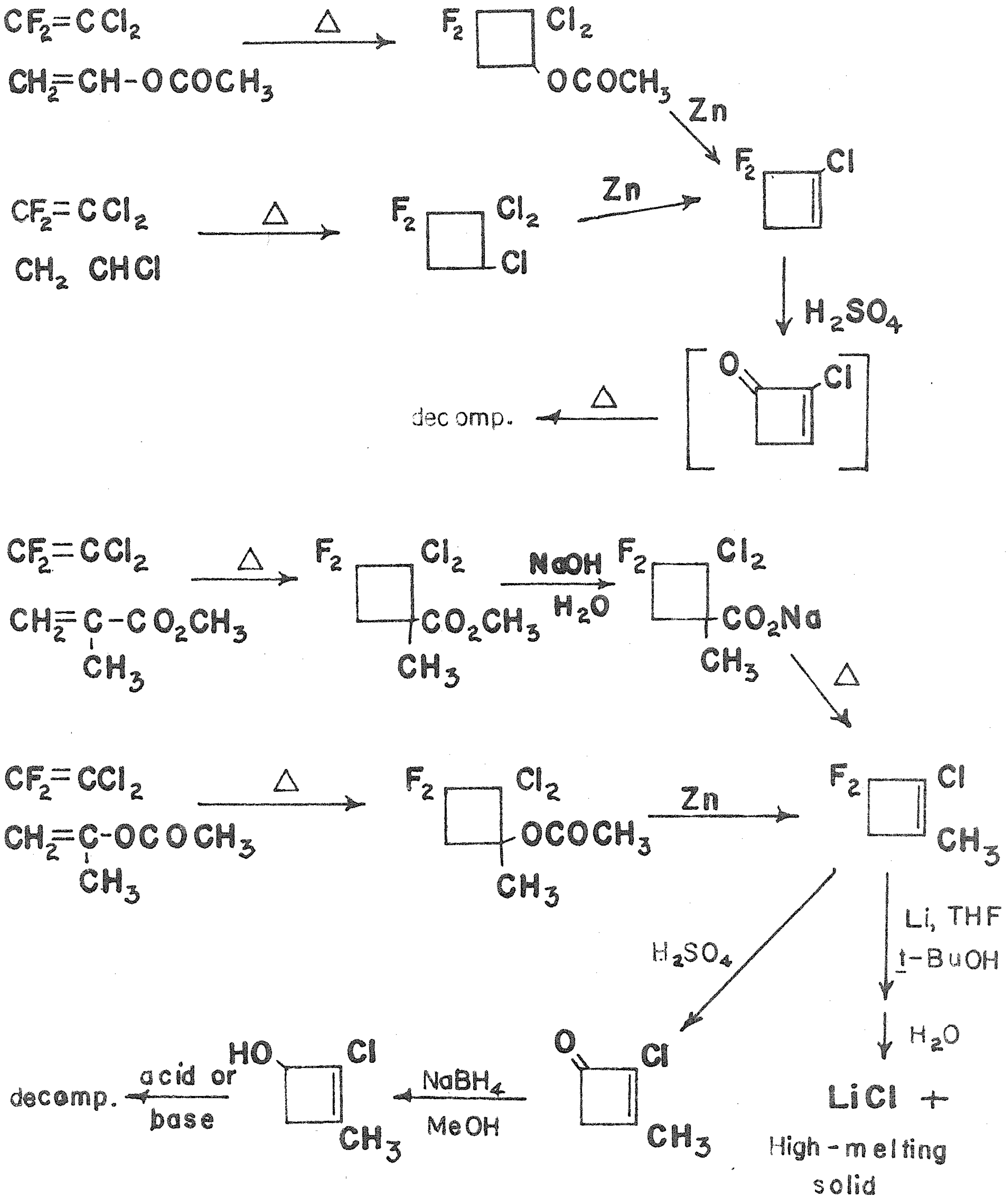
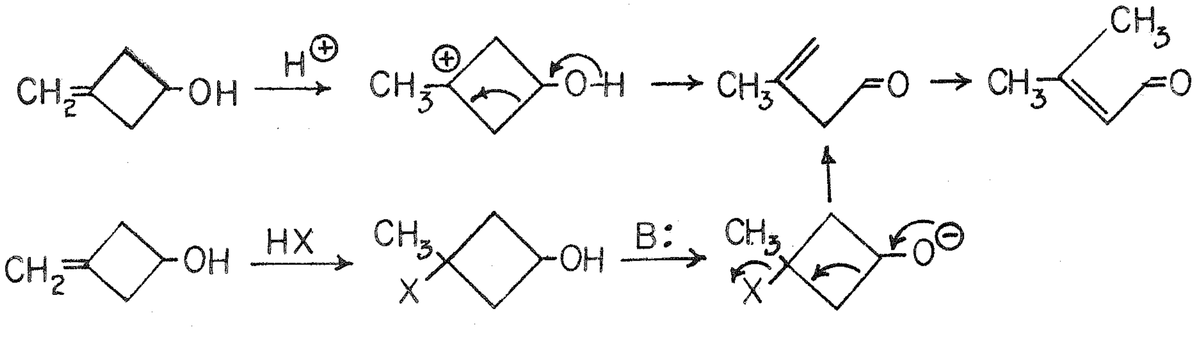

CF2=CCl2
CH2=CH-OCOCH3
Δ
F2 Cl2 OCOCH3
Zn
F2 Cl
CF2=CCl2
CH2 CHCl
Δ
F2 Cl2 Cl
Zn
H2SO4
O Cl
decomp.
Δ
CF2=CCl2
CH2=C-CO2CH3
CH3
Δ
F2 Cl2 CO2CH3 CH3
NaOH
H2O
F2 Cl2 CO2Na CH3
Δ
CF2=CCl2
CH2=C-OCOCH3
CH3
Δ
F2 Cl2 OCOCH3 CH3
Zn
F2 Cl CH3
H2SO4
Li, THF
t-BuOH
H2O
LiCl +
High-melting solid
O Cl CH3
NaBH4
MeOH
HO Cl CH3
acid or
base
decomp.

Figure 1.

corresponding acid azide, which was added immediately to a large excess of boiling ethanol. Evaporation of the solvent provided crude ethyl N-(3-methylenecyclobutyl)-carbamate (XIV) in 86% yield. XIV was hydrolyzed to XV in yields of 47-62% with boiling, methanolic potassium hydroxide.

Treatment of purified XV with nitrous acid in the presence of excess perchloric acid gave rise to 3-methylenecyclobutanol in 78% yield. When the amine perchlorate was treated directly with nitrous acid, without isolation and purification of the free amine, the yield of XVI was only 54%. The structure of XVI was proven by its analysis, comparison of its infrared and n.m.r. spectra with those of the material prepared by reduction of the benzoate (see above), and by conversion to methylenecyclobutene.

Numerous attempts were made to convert XVI to its allylic isomer, 3-methylcyclobut-2-enol, without success. Treatment of XVI with mineral acids under mild conditions had no effect, and stronger acid or prolonged heating induced ring opening and isomerization to β-methylcrotonaldehyde. Dehydrohalogenation of 1-iodo- or 1-bromo-1-methylcyclobutan-3-ol with pyridine or triethylamine also gave rise to β-methylcrotonaldehyde by 1,4-elimination with ring opening.



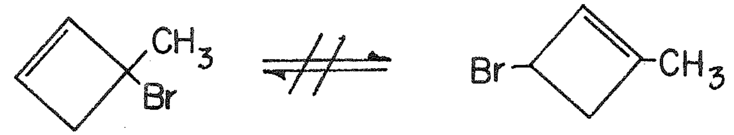
Oxidation of XVI with chromic acid or chromic anhydride-pyridine complex provided only mixtures of oxidation products and recovered starting material.

A single attempt to prepare 3-methylenecyclobutyl bromide (XVII) by treatment of XVI with phosphorus tribromide gave only phosphite ester, which was inert to excess hydrogen bromide. Preparation of the p-toluenesulfonate ester of XVI, which was accomplished in 94% yield using p-toluenesulfonyl chloride in 2,4,6-collidine, followed by prolonged treatment of the crude tosylate with lithium bromide in refluxing acetone, resulted in a 79% yield of crude XVII. This material contained about 10% impurities which could not be removed by distillation; purification had to be accomplished by v.p.c. The pure material gave a correct analysis, and the assigned structure was verified by infrared and n.m.r. spectra, and by dehydrobromination to methylenecyclobutene. Attempted isomerization of XVII with zinc bromide gave only tarry material.

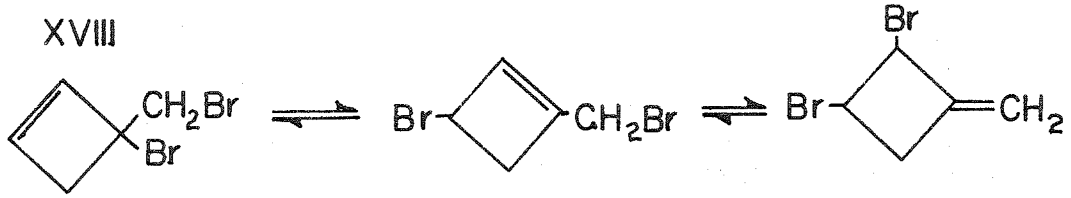
Methylenecyclobutene (1) was obtained in 81% yield by addition of XVII to a solution of sodium methoxide in diethylene glycol at 160-170° under slightly reduced pressure. This dehydrobromination reagent was found by Montgomery (48) to give the best yields of 1-bromocyclobutene from trans-1,2-dibromocyclobutane. Methylenecyclobutene prepared by this method was identical to that obtained by Applequist and Roberts (1) from the pyrolysis of 3-methylenecyclobutyltrimethylammonium hydroxide.

Treatment of methylenecyclobutene with an equimolar quantity of anhydrous hydrogen bromide in pentane at -30° resulted in an

82% yield of a monobromide which was assigned the structure 1-bromo-1-methylcyclobut-2-ene (XVIII) by virtue of its n.m.r. and infrared spectra, chemical tests, and hydrolysis and hydrogenation to 1- and 3-methylcyclobutanol (see Experimental section, page 59). Unlike the other reactive allylic bromides prepared in the present work, XVIII has little tendency to lose hydrogen bromide, and may be stored in an ampoule at 0° for several weeks without appreciable decomposition. The energy barrier for allylic isomerization seems to be exceptionally large, as decomposition occurs before any appreciable isomerization can be observed when XVIII is heated with zinc bromide. This behavior is in contrast to the facile interconversion of isomeric methylenecyclobutene dibromides observed by Applequist and Roberts (1).



XVIII



Hydrolysis of XVIII under acidic or roughly neutral conditions gave a mixture of products which appeared from its n.m.r. spectrum to consist mainly of 1-methylcyclobut-2-enol, 3-methylcyclobut-2-enol, and β-methylcrotonaldehyde, in the approximate ratio 2:1:1. Hydrogenation of the product mixture yielded 1-methylcyclobutanol, cis- and trans-3-methylcyclobutanol, and isovaleraldehyde. No other high-boiling products could be detected by v.p.c., although a small band at 1783 cm^{-1} in the infrared spectrum of the mixture would seem to indicate the presence of a cyclobutanone (see page 61).

The complete synthesis of XVII and XVIII is summarized in Figure 2.

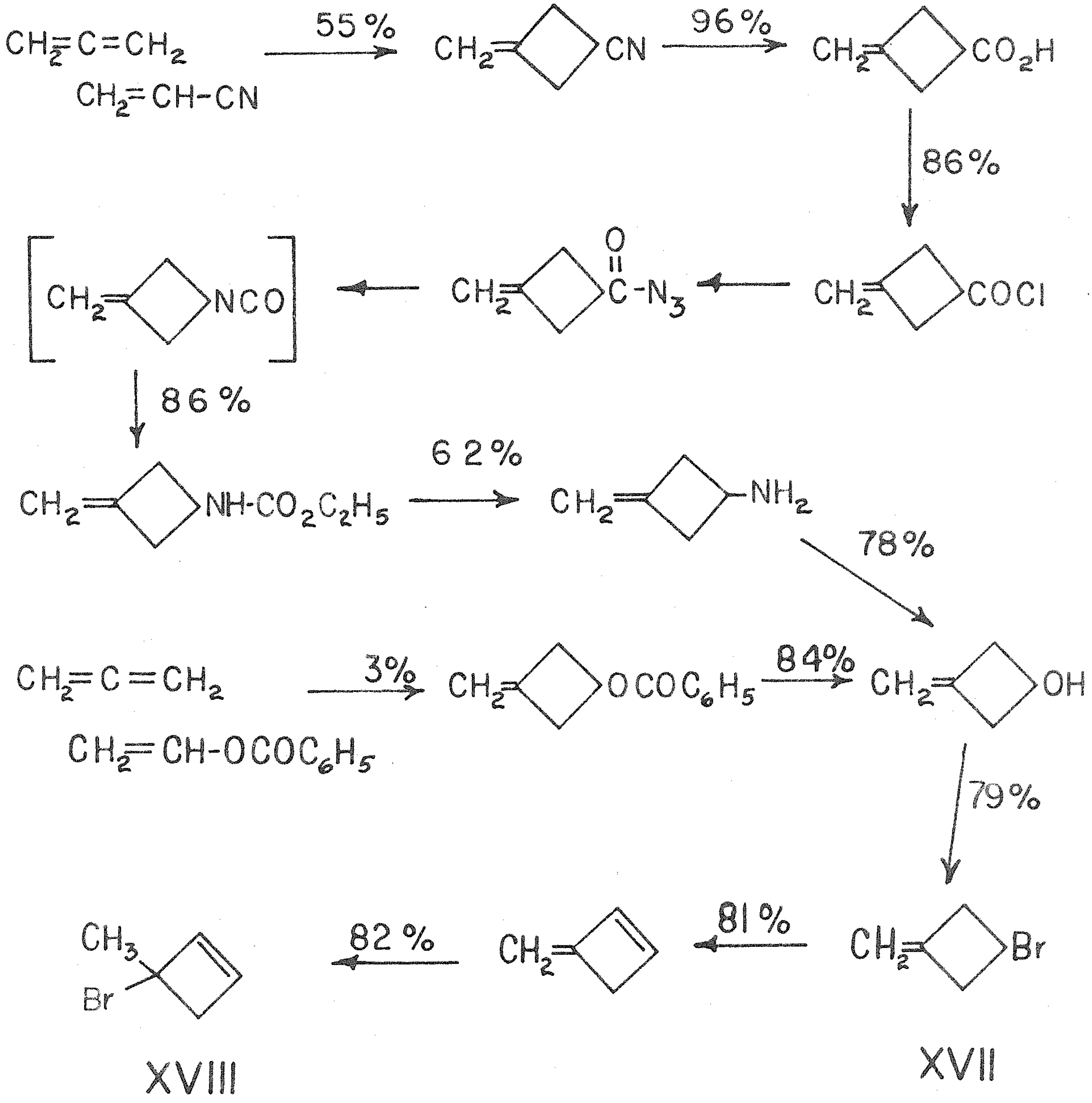


Figure 2.

The syntheses of the other organic bromides used in the solvolytic studies followed published procedures. The open-chain bromides were all obtained by treatment of the corresponding alcohols with phosphorus tribromide. Allylmethylcarbinol (49) was prepared from acetaldehyde and allylmagnesium bromide, 2-penten-4-ol (50) from crotonaldehyde and methylmagnesium iodide. 2-Methyl-2-penten-4-ol (51) was obtained by lithium aluminum hydride reduction of mesityl oxide. 3-Bromocyclopentene (52) was prepared by the addition of hydrogen bromide to cyclopentadiene, and 3-bromocyclohexene (53) was obtained from cyclohexene by allylic bromination with N-bromosuccinimide. An attempt to prepare 2-methylenecyclopentyl bromide by allylic bromination of methylenecyclopentane (54) gave only mixtures of products. Because of their general instability, none of the allylic bromides was analyzed. Purities were established by boiling range, refractive index, and solvolysis titer.

Kinetic Results

The solvents and procedures used in the solvolytic studies are described on page 64, and the results of the kinetic measurements are summarized in Tables I and II, page 25. Although a significant amount of scatter was observed in the experimental points for some individual runs, the only compound which exhibited a reproducible non-first-order trend was 3-methylenecyclobutyl bromide (XVII). The rate constants for the solvolysis of XVII in 50% ethanol were found to decrease by about 35% in the first 10-12% reaction, after which they remained constant. It appears significant that 10-12% coincides with the amount of impurity present in XVII, although it was assumed that because of its low density the impurity was not an isomeric bromide. Since the overall first-order solvolysis rate constant of XVII itself was of primary interest in this work, no attempt was made to seek an explanation for the higher observed initial rate.

Compound XVII was found to solvolyze more slowly than the open-chain analog allylmethylcarbinyl bromide, by factors of 185 at 86° and 155 at 99°. 1-Methyl-1-bromocyclobut-2-ene (XVIII) solvolyzed more slowly than a comparable aliphatic analog, 4-bromo-2-methyl-2-pentene, by a factor of 17,000. Although the aliphatic bromide in the latter case is secondary and the cyclobutenyl bromide tertiary, the degree of alkyl substitution in the allylic system is the same for both molecules, and among other α,γ-substituted allylic halides (55), the actual positioning of the alkyl substituents has a negligible effect on solvolysis rates compared to the number of substituents. The allylic isomers crotyl chloride and α-methylallyl chloride, for example (56), have nearly identical rates of solvolysis in 50% ethanol at 44.6°, and α,α-dimethylallyl chloride solvolyzes faster than the primary isomer, γ,γ-dimethylallyl chloride, by only a factor of 4. The latter pair is more reactive than the former pair, however, by a factor of over 1000.

In spite of the equivalent degree of alkyl substitution in 4-bromo-2-methyl-2-pentene and 1-methyl-1-bromocyclobutene, consideration of inductive and especially of hydrogen hyperconjugative effects leads to the conclusion that α,γ-dimethylallyl bromide is probably a better model for comparison with the cyclobutenyl system. (The reasons for this are discussed later in this section.) Although α,γ-dimethylallyl bromide still solvolyzes faster than XVIII, the difference in rate in this case is only a factor of 15, instead of 10^4.

The other allylic bromides studied in the present work (cyclopentenyl and cyclohexenyl) have the same degree of alkyl substitution as α,γ-dimethylallyl, but strain and conformational effects make direct comparisons with XVIII more complex. The solvolysis rates of cyclopentenyl bromide, α,γ-dimethylallyl bromide, and cyclohexenyl bromide in 80% ethanol decrease in the order named, in qualitative agreement with the corresponding saturated chlorides cyclopentyl (57), isopropyl (58), and cyclohexyl (59). The solvolysis rates of allylic halides seem to be more sensitive to changes in ring size than those of the saturated halides, however: The relative rates in 80% ethanol are 18:2:1, respectively, for the saturated chlorides at 85°, and 1300:6:1 respectively, for the allylic bromides at 0°.

TABLE I.

SOLVOLYSIS DATA FOR HOMOALLYLIC BROMIDES IN 50% AQUEOUS ETHANOL

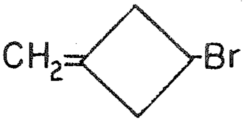
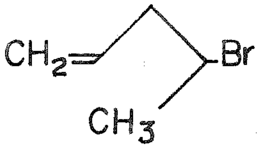
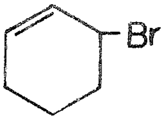
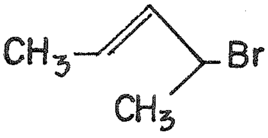
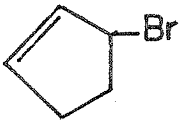
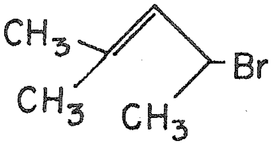
Compound	C_o, moles/liter	Temp., °C	10^5k, sec^{-1}	E^*-, kcal./mole	Rel.Rate at 99°
	0.02710	86.0	0.042	27.6	
	0.02562	99.0	0.16		1.0
	0.01763	78.0	4.0	23.2	
	0.01672	86.0	8.0		
	0.02218	86.0	7.9		
	0.01680	99.0	24.5		160

TABLE II.

SOLVOLYSIS DATA FOR ALLYLIC BROMIDES IN 80% ETHANOL

Compound	C_o, moles/liter	Temp., °C	10^4k, sec^{-1}	E^*-, kcal./mole	Rel.Rate at 0°C
	0.00402	- 5.3±0.2	0.71	21.1	1.0
	0.00724	9.9±0.2	5.65		
	0.00745	10.1±0.2	6.08		
	0.00703	16.1±0.2	14.2		
	0.00555	- 0.2±0.2	3.92	22.0	2.7
	0.00645	- 0.2±0.3	3.90		
	0.00801	10.0±0.2	17.2		
	0.01094	15.0±0.2	33.3		
	0.00709	- 9.1±0.2	6.43	21.3	15
	0.01145	- 9.0±0.2	6.53		
	0.00806	0.1±0.2	23.4		
	0.01140	-46.2±0.5	4.95	18.6	3,500
	0.00635	-46.1±0.5	4.89		
	0.00778	-38.8±0.5	18.9		
	0.00559	-34.8±0.4	33.5		
	0.00449	-64 ±1	1.9	16.8	17,000
	0.00638	-64 ±1	1.7		
	0.00203	-50.5±1	18.1		
	0.00529	-46.2±0.5	43		

Discussion of Kinetic Results

At first glance, the fact that the cyclobutyl bromides studied in this work solvolyze more slowly than any of the appropriate model compounds would seem to indicate that stabilization of carbonium ions by 1,3-interaction does not occur in these systems. Admittedly, this experimental observation lends considerable weight to the statement that such interactions are not of overwhelming importance, at least in comparison with some of the systems mentioned in the Introduction. However, in order to enable one to say anything meaningful about the presence or absence of cross-ring interactions, the sum of the multitudinous other factors which may contribute to differences in free energies of activation for solvolysis must be known to a rather embarrassing degree of accuracy. Although the experimental data available do not permit a precise treatment of the problem, an attempt to gain a rough estimate of the importance of 1,3-interactions may be instructive. The general procedure which will be followed here involves choosing the most appropriate models for comparison with the cyclobutyl compounds, breaking down the net free energy of activation for solvolysis ($\Delta F^{\ddagger}$) into as many components as possible,* and estimating the energy <u>differences</u> between the aliphatic and cyclobutyl cases for each factor independently. The factors considered here are: 1) ionization energy of the carbon-bromine bond, 2) solvation of the carbonium ion, 3) changes

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*The factors contributing to $\Delta F^{\ddagger}$ are assumed in this discussion to operate independently of one another and to be additive (60 in steric strain (B-strain) of non-bonded atoms, 4) changes in angle strain due to rehybridization, 5) inductive effects of alkyl substituents, 6) hydrogen hyperconjugation, 7) carbon-carbon σ-bond participation, 8) 1,4-electronic interactions, 9) 1,3-interactions.

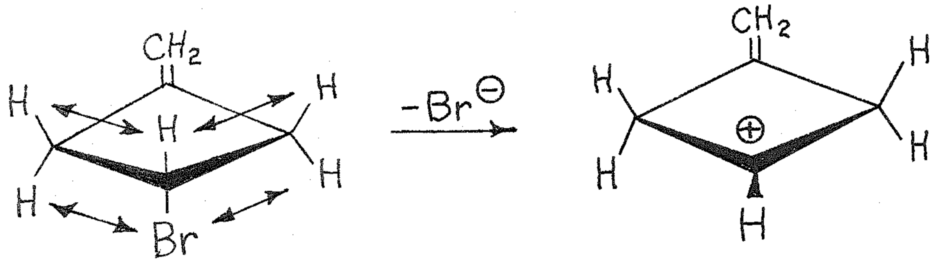
These factors will be discussed individually for the homoallylic systems 3-methylenecyclobutyl and allylmethylcarbinyl, and only those which are appreciably altered will then be considered in the corresponding treatment of the allylic systems.

3-Methylenecyclobutyl Bromide (XVII)

1+2) No precise figures are available for ionic bond dissociation energies of small-ring compounds in solution, although gas-phase dissociation energies suggest that the carbon-bromine bond becomes stronger as ring size decreases (61). The importance of ion-pair solvation in determining dissociation energies for individual compounds in solution is acknowledged (62), and the naive assumption will be made here that any increase in inherent bond ionization energy for 3-methylenecyclobutyl bromide is approximately balanced by increased efficiency of ion solvation due to the smaller steric volume of the ring, relative to the open-chain analog. Whether or not this assumption is valid, factors 1 and 2 are believed to be relatively unimportant by themselves, compared to the variations in energy resulting from other factors.

3) In calculating the change in steric strain between non-bonded atoms for the reaction $R\text{-}X \rightarrow R^{\oplus} + X^{\ominus}$, one may assume

non-bonded repulsions to be equal to zero for both aliphatic and cyclobutyl systems in the transition state,* and for the aliphatic system in the ground-state staggered conformation. The energy decrease resulting from relief of steric repulsions in the ionization of 3-methylenecyclobutyl bromide is then equal to the energy of two adjacent eclipsed hydrogen-hydrogen repulsions plus two similar hydrogen-bromine repulsions, relative to the energy of the staggered conformations.



This energy can be obtained from the measured energy barriers to rotation in substituted ethanes (64) by applying a correction factor for the slightly greater angle between the adjacent C-H and C-Br bonds in the cyclobutyl case. The total calculated repulsion energy for XVII is 3.0 kcal./mole, consisting of 0.6 kcal. for each hydrogen-hydrogen repulsion (65) and 0.9 kcal. for each hydrogen-bromine repulsion (66).

4) The most obvious difference between XVII and its aliphatic analog is the presence in the former of a large σ-bond strain energy due to compression of three $\underline{sp}^3$-carbons and one $\underline{sp}^2$-carbon

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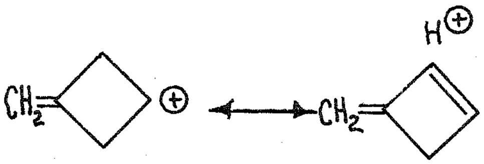
*By the Hammond principle (63), the transition state for solvolysis may be assumed to resemble closely the carbonium ion intermediate, and in this discussion, the slight difference will be ignored.

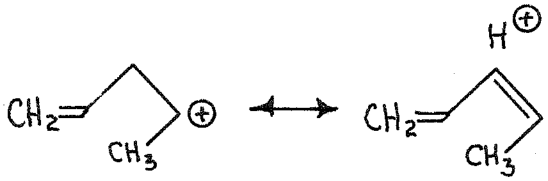
from bond angles of 109.5° and 120°, respectively, to an average 90°. Again, we can assume that no change in σ-bond strain accompanies the ionization of allylmethylcarbinyl bromide, and to a good approximation, the same is true for XVII at C2, C3, and C4. The net strain energy increase for the ionization of XVII is then equal to the increase in strain energy at C1 due to rehybridization from $\underline{sp}^3$- to $\underline{sp}^2$-orbitals (ΔS_{angle}).

Manatt (4) calculated a strain energy increase of 10.5 kcal. for the ionization of cyclobutenyl derivatives, utilizing the bending force constant data given by Westheimer (16) and a C-C-C bond angle of 86° (67). The corresponding value for the cyclobutyl case was 9.2 kcal. However, his treatment did not take into account the change in σ-bond hybridization, which would be expected to change the bending force constant and probably the C-C-C bond angle as well. Snyder (68) arrived at a value of 4.0 kcal./mole for ΔS_{angle} for cyclobutyl derivatives, by an empirical treatment based on heats of hydrogenation. Actually, it is best to consider the 4.0 kcal. as the sum of ΔS_{angle} and all the other factors listed above except non-bonded interactions; the latter was the only category specifically considered by Snyder from a quantitative standpoint. If one assumes that factors 1, 2, and 5-7 are unimportant or cancel one another, or that they have a positive sum (that is, taken together they tend to decrease the rate of XVII relative to allylmethylcarbinyl), then 4.0 kcal. represents an empirical upper limit on ΔS_{angle} for the four-membered ring. Conversely, if one feels justified in assigning a value of greater than 4.0 kcal. for ΔS_{angle}, then the sum of factors 1, 2 and 5-7 must be negative--a conclusion which is intuitively unattractive. Factors 8 and 9 must of course be omitted from this discussion if it is to apply to saturated systems. Snyder's values of ΔS_{angle} and non-bonded interaction energies are in good accord with the observed relative solvolysis rates of 1-methyl-1-chloro- and 1-phenyl-1-bromocycloalkanes (68,69).

Using the known C-C-C bond angles in methylenecyclobutane (70,71) and 1,3-dimethylenecyclobutane (72) and assuming the bending force constants for C-C-C and C-C=C to be approximately equal (73), the calculated value for ΔS_{angle} is 7.3 kcal./mole for 3-methylenecyclobutyl bromide. This will be taken as an upper limit since, by the Coulson-Moffitt picture (74), the actual C_2-C_1-C_4 bond angle is probably slightly greater than the angle formed by straight lines joining the carbon nuclei. It must also be acknowledged that the hybridization at C_1 in the transition state is not pure <u>sp</u>^{2} (74).

5+6) Inductive and hydrogen hyperconjugative effects are of lesser importance in the homoallylic systems than in the allylic systems, and in any case, their relative contributions to carbonium ion stability in general seem to be anyone's guess at present (75-79). The inductive effect of a vinyl group near a reaction center is generally considered to be responsible for the slight decreases in solvolysis rates observed for aliphatic β-vinyl-substituted derivatives relative to their saturated analogs. Although the inductive effect is probably more significant in the cyclobutyl system because it can operate through two methylene groups simultaneously, the magnitude of the effect is unlikely to be large, and this factor can probably be ignored. It can be argued that hydrogen hyperconjugation is less important in the solvolysis of XVII than the aliphatic analog, not only because XVII has one less β-hydrogen, but also because of the possibility of steric inhibition (12) due to the necessity for forming an additional $\underline{sp}^2$ center on the 4-membered ring.





While this sort of steric inhibition of hyperconjugation is not likely to be as pronounced as in the case of the 7-norbornyl cation, for example (12), it cannot escape consideration. On the other hand, it cannot be perfunctorily denied that stabilization of the carbonium ion by hydrogen hyperconjugation may actually be <u>more</u> important in the cyclobutyl system because of the favorable, fixed disposition of all four α-C-H bonds, which approach coplanarity with the vacant <u>p</u>-orbital (76).

Unfortunately, it would be meaningless to assign a precise energy value to hydrogen hyperconjugative effects in the systems under consideration, but a practical upper limit of 1.7 kcal./mole might be set by assuming hyperconjugative stabilization to be zero for the 3-methylenecyclobutyl cation and 0.34 kcal. per β-hydrogen (the value quoted by Taft (80) for the solvolysis of tertiary carbinyl chlorides) for the five β-hydrogen atoms of the allylmethylcarbinyl cation.

7) Because extensive carbon-carbon σ-bond participation occurs in the solvolytic reactions of unsubstituted cyclobutyl derivatives (82), this phenomenon must be kept in mind in a discussion of the reactivities of other four-membered-ring compounds. The fact that deamination of 3-methylenecyclobutylamine, which is assumed to proceed via a carbonium ion intermediate, gave unrearranged 3-methylenecyclobutanol cannot by itself be taken as evidence that anchimeric assistance does not contribute to stabilization of the 3-methylenecyclobutonium ion; however, significant σ-bond participation in the transition state of solvolysis would be expected to be accompanied by a rate enhancement which was not observed. There is no reason to suspect that anchimeric assistance is important in the solvolysis of allylmethylcarbinyl bromide either, and in the absence of precise information regarding other effects which might obscure a slight rate enhancement, the fact that this compound solvolyzes more slowly than isopropyl bromide (83) is considered sufficient to justify ignoring this factor.

8) Winstein (9,81) has pointed out in his discussions of homoallylic resonance that 1,4-interactions should not be neglected, since in the generalized homoallylic cation the C1-C4 distance is no greater than the C1-C3 distance, and the relative orientation of orbitals on C1 and C4 is conducive to effective overlap. However, the planar 3-methylenecyclobutyl carbonium ion is singularly

unadaptable to 1,4-interaction, and again, the absence of rate enhancement in the allylmethylcarbinyl system will be interpreted as evidence against any significant degree of 1,4-electron delocalization there.

9) If one assumes that 1,3-interactions are nonexistent in the allylmethylcarbinyl system (which is a valid assumption if such delocalization requires solvolysis rate enhancement), then the net stabilization of the 3-methylenecyclobutyl carbonium ion due to 1,3-electronic interaction can be taken as the difference between the observed activation energy difference for XVII and allylmethylcarbinyl bromide, given in Table I as 4.4 kcal./mole, and the algebraic sum of factors 1-8 above. Because of the uncertainties in the energy values assigned to factors 1-8, the algebraic sum is best represented in terms of upper and lower limits, as tabulated below:

TABLE III.

ESTIMATED CONTRIBUTIONS OF FACTORS 1-8 TO ACTIVATION ENERGY FOR SOLVOLYSIS OF XVII RELATIVE TO ALLYLMETHYLCARBINYL BROMIDE

Factor	Upper Limit, kcal./mole	Lower Limit, kcal./mole
1	0	0
2		
3	-3.0	-3.0
4	+7.3	+4.0
5	0	0
6	+1.7	0
7	0	0
8	0	0
1-8	+6.0	+1.0

It is seen that taking the average of the upper and lower limits gives a difference in activation energy between XVII and allylmethylcarbinyl of 3.5 kcal./mole, which is close to the observed value of 4.4 kcal./mole, if 1,3-interactions contribute no additional stabilization. The upper limit provides 6.0-4.4 = 1.6 kcal. of extra stabilization for XVII which can be considered the maximum value assignable to 1,3-interaction. However, there is no reason to suspect that the upper limit is more accurate than the lower; in fact, if one considers the relative solvolysis rates of 1-methylcycloalkyl chlorides in 80% ethanol (69) an explanation must be found for the large rate <u>depression</u> of XVII relative to allylmethylcarbinyl. 1-Methylcyclobutyl chloride is slower than <u>t</u>-butyl chloride by a factor of 14 at 25° in 80% ethanol, which amounts to an activation energy difference of only 1.6 kcal./mole; this figure is close to the lower limit given in Table III. The larger solvolysis rate depression of XVII compared to 1-methylcyclobutyl could be due to a combination of factors, including less important non-bonded interactions in the ground state, incursion of some bimolecular (S_N2) displacement (which would probably be more important in the aliphatic system), and lack of anchimeric assistance, which may be operative in 1-methylcyclobutyl chloride (84) though to a lesser extent than in cyclobutyl itself.

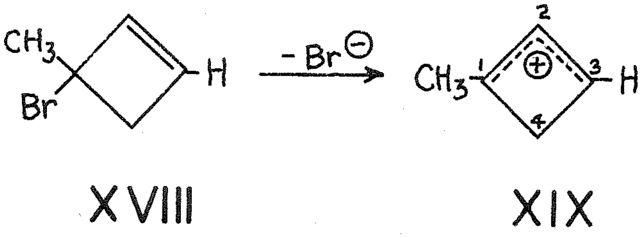
It is concluded that although π-type 1,3-orbital overlap in the 3-methylenecyclobutyl carbonium ion cannot be proven absent, it is of negligible importance in stabilizing the solvolysis transition state.

1-Methylcyclobut-2-enyl Bromide (XVIII)

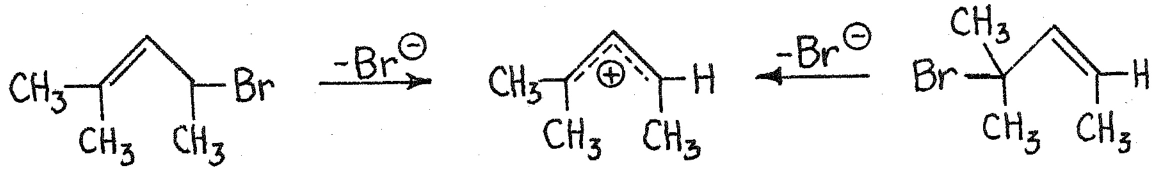
If the factors contributing to relative carbonium ion stabilities in the homoallylic systems are difficult to assess quantitatively, then they can only be considered more so in the allylic systems because of the additional uncertainty in the choice of an appropriate model for comparison with XVIII. For this reason, discussion of the cyclobutenyl system will be shorter and more qualitative.

In comparing the allylic systems with the homoallylic systems, the same considerations with regard to carbon-bromine bond dissociation energy and solvation of the carbonium ion (factors 1 and 2) apply. Relief of non-bonded repulsions (factor 3) is <u>less</u> in the ionization of the allylic system by about 1.2 kcal., because instead of two H-Br and two H-H repulsions, there is one H-Br and one H-CH_3 repulsion (68). Increase in angle strain (factor 4) is slightly <u>greater</u> in the allylic system because the C2-C1-C4 bond angle is more compressed (4); a calculation based on force constant data (16) suggests that the difference is about 1.3 kcal. Since factors 3 and 4 work in opposite directions, the energy differences have the <u>same</u> sign, the sum being +2.5 kcal./mole in favor of the homoallylic system. That is, neglecting 1,3-interactions for the moment, the ionization of 1-methyl-1-bromocyclobut-2-ene (XVIII) should be more endothermic than the ionization of 3-methylenecyclobutyl bromide (XVII) by 2.5 kcal./mole, if each of the compounds is compared to its appropriate aliphatic model. Participation of σ-bond electrons (factor 7) is generally neglected in treatments of allylic systems; solvolysis product studies (see page 59) provide no evidence for this type of delocalization in the systems under consideration here, and it will therefore be ignored. Factor 8 (1,4-interactions) of course does not apply to any allylic compounds. Now, if one can select a model aliphatic allylic system for comparison with XVIII in which inductive and hyperconjugative effects (factors 5 and 6) are considered to be approximately of the same magnitude as those in the cyclobutenyl system, then one can predict that, in the absence of 1,3-interaction, XVIII should solvolyze more slowly than the aliphatic allylic model by a factor of 10^5 at 0°. This figure is derived from the observed difference in solvolysis rates of the homoallylic bromides 3-methylenecyclobutyl (XVII) and allylmethylcarbinyl (a factor of 1000 at 0°) added to the factor of 100 in relative rates which results from the 2.5 kcal./mole of extra activation energy for XVIII, relative to XVII, due to factors 3 and 4.

1-Methylcyclobutenyl bromide (XVIII) ionizes to a "secondary-tertiary" allylic carbonium ion; i.e., the carbon atoms at the ends of the mesomeric cation XIX are respectively secondary and tertiary.

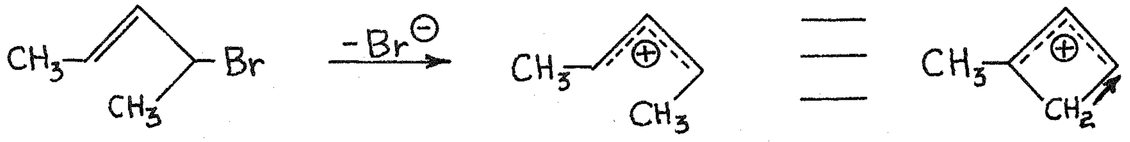


As mentioned earlier in this section, secondary-tertiary allylic compounds generally solvolyze at comparable rates regardless of which end constitutes the reacting center. On this basis, the best models for XVIII would be α,α,γ-trimethylallyl or α,γ,γ-trimethylallyl bromide, which are the simplest aliphatic secondary-tertiary allylic bromides.

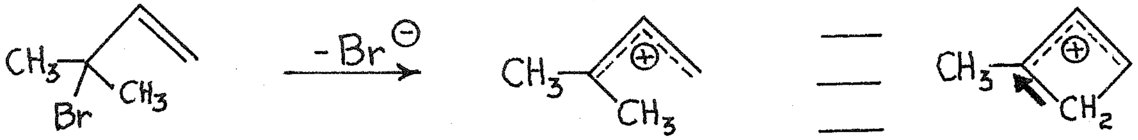


XX

It will immediately be seen, however, that cation XX has <u>three</u> alkyl groups on the allylic system, whereas XIX has only two; the 4-methylene group is attached at both ends of the system. Since the total number of alkyl groups is of primary importance, rather than the number of alkyl groups attached at each end, it would seem reasonable that a five-carbon secondary-secondary (or primary-tertiary) allylic bromide would constitute a better model for XVIII.

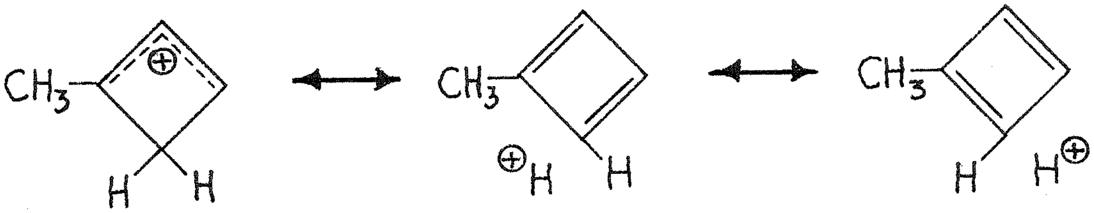


XXI



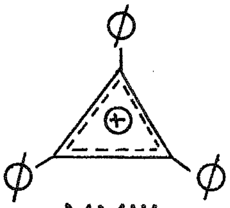
XXII

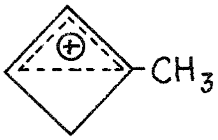
In terms of the inductive effects of alkyl substituents, either XXI or XXII can be considered roughly equivalent to XIX. However, if one concedes that a significant part of the rate-enhancing effect of alkyl substituents is due to hydrogen hyperconjugation in the electron-deficient transition state, then it can be argued that XIX has only <u>one</u> effective alkyl group, and even XXI and XXII will not suffice as models. This postulate depends on the observation that the "no-bond" resonance forms resulting from hyperconjugation involving the 4-methylene group of XIX contain the electronically unstable methylcyclobutadiene.



Such a phenomenon might be termed "electronic prohibition" of hyperconjugation, by analogy with the steric inhibition of hyperconjugation proposed to explain the low solvolysis rates of certain bicyclic systems (12).

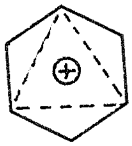
It is acknowledged that whether or not hydrogen hyperconjugation is prohibited in XIX, the inductive effect of the ring methylene group must contribute some stabilizing influence, so that the most appropriate model for XVIII would be a hypothetical compound (henceforth designated "H.C.") intermediate between α,α-dimethylallyl and α-methylallyl bromide. For the purposes of discussion it will be assumed, not entirely without justification (75-79), that the 4-methylene group in XVIII is 2/3 as effective as an ordinary methyl group in stabilizing the solvolysis transition state; this will require that our hypothetical model "H.C." undergo solvolysis at a relative rate 2/3 as great as the difference between α,α-dimethylallyl and α-methylallyl bromide (on a logarithmic scale). Although the solvolysis rates of these two compounds have not been reported, they can be estimated satisfactorily from the rates of the other allylic bromides studied in this work and the extensive rate data for allylic chlorides provided by DeWolfe and Young (37). Log k for α,α-dimethylallyl bromide at 0° in 80% ethanol is -3.2; for α-methylallyl bromide, log k = -7.0. "H.C." would thus show log k = -4.48, k = 3.3×10^{-5} sec^{-1}. The measured rate constant for XVIII under the same conditions is 1.6×10^{-4} sec^{-1}, which is <u>greater</u> than that of "H.C." by a factor of 5. Recall (page 36) that the solvolysis of XVIII was predicted to be <u>slower</u> than that of "H.C." by a factor of 10^5 at 0°, so the allylic system thus shows a rate enhancement of 5×10^5, when the homoallylic 3-methylenecyclobutyl system is used as a basis for comparison. If this rate enhancement were ascribed entirely to 1,3-interaction, the added stabilization of the allylic transition state would amount to 7.2 kcal./mole, which is well within the range (4.1 to 10.9 kcal.) predicted by molecular orbital theory (see page 4) (4). It is instructive to consider carbonium ion XXIV as a "homocyclopropenyl" cation, by analogy with the cyclopropenyl (XXIII), <u>bis</u>-homocyclopropenyl (XXV), and <u>tris</u>-homocyclopropenyl (XXVI) cations studied by Breslow (85,86), Roberts (12), and Winstein (87), respectively.


XXIII



XXIV


XXV

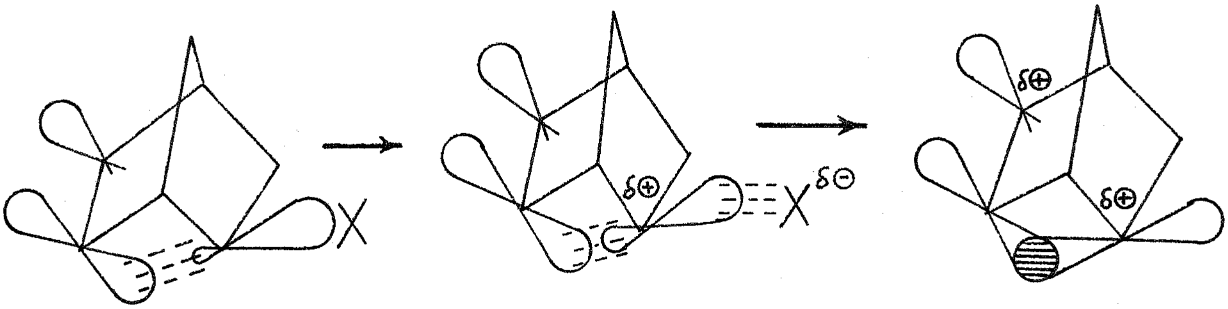

XXVI

It must be mentioned that the assignment of a numerical value for 1,3-interaction in XIX by comparison of a tertiary allylic system with a secondary homoallylic system leaves considerable room for doubt. In particular, a significant degree of S_N2 displacement by solvent in allylmethylcarbinyl bromide may be contributing to the apparent rate enhancement of XVIII relative to "H.C." If one can assume that 1-methylcyclobutyl chloride does not exhibit any rate enhancement due to anchimeric assistance, then the systems 1-methylcyclobutyl and t-butyl can be compared with XVIII and "H.C." with little fear of complications arising from bimolecular displacement.

Again assuming all factors except non-bonded repulsions, angle strain, and 1,3-interaction to be equivalent in the two systems, one can calculate what the rates of 1-methylcyclobutyl chloride and 1-methyl-1-bromocyclobut-2-ene (XVIII) should be, relative to their respective aliphatic analogs, t-butyl chloride and "H.C." 1-Methylcyclobutyl chloride, with two H-Cl repulsions and two H-CH_3 repulsions, gains 1.8 kcal. more on ionization than XVIII, with one H-Br and one H-CH_3 repulsion. The difference in angle strain increase on ionization is approximately 0.5 kcal.

in favor of the saturated chloride, so the net increase in stability of 1-methylcyclobutyl is about 2.3 kcal./mole. In its simplest form, this can be taken to mean that the activation energy for the solvolysis of 1-methylcyclobutyl chloride relative to *t*-butyl chloride should be 2.3 kcal. less than that of XVIII relative to "H.C.", before 1,3-interactions are considered. The solvolysis of 1-methylcyclobutyl chloride is slower than that of *t*-butyl chloride by a factor of 17 at 0° (69). When this rate factor is multiplied by the factor of 67 which results from the 2.3 kcal. difference in relative activation energies, a value of 1140 is obtained, which represents the expected difference in rate between XVIII and "H.C." at 0°, in the absence of 1,3-interaction. It has already been shown that XVIII solvolyzes faster than "H.C." by a factor of 5, so the maximum rate enhancement due to 1,3-interaction is 5 x 1140 = 5700 when 1-methylcyclobutyl chloride is used for comparison instead of 3-methylenecyclobutyl bromide. In terms of stabilization energy, the rate differential of 5700 amounts to 4.7 kcal./mole at 0°, which is still within the predicted range, though not as large as the value derived from the treatment involving the homoallylic systems.

The most reasonable explanation for the failure of 3-methylenecyclobutyl bromide and, to a lesser extent, XVIII, to exhibit the striking rate enhancements observed in the polycyclic systems (pages 7-13) involves the relative orientation of the *p*-orbitals at the 1- and 3-positions of the homoallylic carbonium ion. In every case for which large rate enhancements were observed, the geometry of the system was such that the π-electron cloud at the 3-position could assist in the ionization of the C-X bond by σ-type overlap with the "tail" of the developing p-orbital, as illustrated for exo-dehydronorbornyl below.



In the 3-methylenecyclobutyl and 1-methylcyclobutenyl cations, the axes of the p-orbitals on C1 and C3 are roughly parallel, and σ-type overlap cannot occur. Although π-type orbital overlap is still possible, it cannot contribute the same degree of assistance to the actual ionization process; furthermore, Simonetta and Winstein (81) have pointed out that $2p\pi$-type orbital overlap decreases rapidly with increasing inter-nuclear distance (88), being only about 1/3 as effective as $2p\sigma$-overlap at 2.1 Å, the distance between C1 and C3 in XVII. The same phenomenon was observed in the solvolysis of 3-cyclopentenyl tosylate (89), which is slower than cyclopentyl tosylate by a factor of about 10. Although open-chain homoallylic carbonium ions can assume a favorable geometry for σ-type orbital overlap (81), no examples of significant rate-enhancement in purely aliphatic systems have been observed, possibly because the stabilization energy provided by electron delocalization is outweighed by the increase in entropy associated with the loss of rotational freedom in the transition state.

As mentioned in the Introduction, the solvolysis of anti-7-camphenyl tosylate (see page 11) is rather anomalous in that the geometry and internuclear distances are reasonably favorable for 1,3-orbital overlap of the σ-type, yet no significant rate enhancement is observed. Since the stereochemistry of solvolysis strongly suggests that some 1,3-interaction does occur in this system, an explanation for the low rate might be found in the ground-state free energy picture discussed by Winstein and Kosower (9).

Ground-state free energy differences may also be responsible for the rate enhancement of the methylcyclobutenyl system in comparison with the 3-methylenecyclobutyl system. A more appealing explanation for the relative behavior of these two systems, however, can be based on the molecular orbital calculations which inspired this work: a much greater degree of stabilization is provided by a small amount of 1,3-interaction in the allylic system than in the homoallylic system (4.1 kcal./mole vs. 0.8 kcal./mole, respectively, when $\beta_{13} = 0.2\beta$).

III. EXPERIMENTAL

All melting points and boiling points are uncorrected. Elemental analyses were performed by Dr. Adalbert Elek, Elek Microanalytical Laboratories, Los Angeles, California. All commercial chemicals used were reagent grade, except as noted. Infrared spectra were obtained with a Perkin-Elmer recording double-beam infrared spectrophotometer, Model 21, or a Beckman infrared spectrophotometer, Model IR-7. Nuclear magnetic resonance (n.m.r.) spectra were recorded at 60 Mc. using the Varian Associates high resolution nuclear magnetic resonance spectrometer, Model V-4300B, equipped with a 12-inch electromagnet and super-stabilizer. The vapor-phase chromatography (v.p.c.) data were obtained with a Perkin-Elmer Vapor Fractometer, Model 154-C. A description of distillation columns #1-6 is included in the Appendix.

Allene (90,91) was usually prepared immediately before use. A typical large-scale preparation follows: In a 1-liter, three-necked, round-bottomed flask, fitted with a pressure-equalizing dropping funnel, ball-joint sealed paddle stirrer, and Friedrichs condenser, were placed 180 g. of zinc dust and 235 ml. of 80% ethanol. The condenser was connected to a train which consisted of a large ice-cooled trap, a U-tube filled with indicating Drierite and calcium chloride, two traps cooled to -25° and -78° in Dry Ice-acetone, and a drying tube filled with calcium chloride. The reaction mixture was heated to reflux with a heating mantle and stirred vigorously as 2,3-dichloropropene (Eastman; 135 g., 1.22 moles) was added from the dropping funnel at a rate sufficient to maintain reflux after removal of the heating mantle.

After the addition was complete, the mixture was again heated to reflux for 40 minutes. To collect the last of the allene, the traps at 0° and -25° were allowed to warm slowly to room temperature. The yield of crude allene was 45-48 g. (92-96%). Usually, this material was used without further purification, which could be accomplished best by low-temperature fractional distillation.

Vinyl Benzoate.--In a 1-liter, round-bottomed flask, fitted with a condenser and drying tube, were placed 533 g. (6.20 moles) of vinyl acetate (Matheson, 99.5% grade, redistilled, b.p. 72.2°), 129 g. (1.05 mole) of benzoic acid (m.p. 121.2-121.8°), 2.58 g. of mercuric acetate, and 0.65 g. of 20% fuming sulfuric acid (47). The sulfuric acid was added dropwise, with vigorous swirling. The mixture was heated to 50° to dissolve the benzoic acid and kept at 40-50° for 8 hours, then allowed to stand 14 hours at room temperature. Anhydrous sodium acetate (2.5 g.) was then added to quench the reaction, and the vinyl acetate and acetic acid were removed under aspirator pressure. Pentane (250 ml.) was added, and the solution was extracted once with ice water and dried over sodium sulfate. When the solution was cooled to 0°, unreacted benzoic acid (3.8 g.) separated and was removed by filtration, m.p. 121.6-122.4°. The pentane was removed from the filtrate with the aspirator, and the oily, colorless residue distilled through Column #1 under reduced pressure to yield 118 g.

of vinyl benzoate, b.p. 47° (1.5 mm.), $\underline{n}^{21.5}D$ 1.5263 (reported 1.5259) (47). The yield, based on benzoic acid, was 76%.

3-Methylenecyclobutyl Benzoate (X).--The reaction of vinyl benzoate and allene was carried out eight times on a preparative scale, under conditions ranging from 4 hours at 230° to 10 hours at 300°. Polymerization of vinyl benzoate became serious at temperatures above 260°. Although the maximum total yield of X was obtained at 265°, the best yield based on reacted vinyl benzoate (11%) was realized in a run at 240-250° for 4 hours. Even at best, the reaction was quite impractical as a preparative method because of the minute overall yields, on the order of 1-2% , and the difficulty of purifying the product.

In a typical preparation, a 500-ml. stainless-steel Parr bomb was cooled to -40° and charged with 78 g. (0.527 mole) of vinyl benzoate, 12.6 g. (0.315 mole) of allene, 100 ml. of benzene, and 0.5 g. of phenothiazine as a polymerization inhibitor. The bomb was sealed and heated slowly, with rocking, to 240°, then maintained at 240-260° for 4 hours and allowed to cool overnight; it was cooled further to -40° in Dry Ice, opened and allowed to warm to about 10° as unreacted allene (6 g., 48% recovery) was distilled into a Dry Ice-cooled receiver. The remaining contents were transferred to a round-bottomed flask and distilled through Column #3.

Frac.	B. P., °C	Wt., g.	Composition, by v.p.c.
1	10-70	4.0	Allene, benzene, acetaldehyde, "H"
2	70-73.5	18.2	Benzene
3	78.5	40.5	Benzene
4	42 (150 mm.)	15.8	Benzene
5	97 (22 mm.) - 41 (1 mm.)	54.3	Vinyl benzoate
6	41-42 (1 mm.)	14.8	Vinyl benzoate
7	70-95 (1 mm.)	2.6	Vinyl benzoate, $C_6H_5CO_2H$, X, others

Acetaldehyde was identified by its infrared spectrum and 2,4-dinitrophenylhydrazone derivative. "H" was a low-boiling, rather unstable compound which was not identified. The recovery of vinyl benzoate was 69.6 g. (90%).

Frac. 7, when dissolved in boiling pentane and cooled to 0°, deposited 0.85 g. of benzoic acid, m.p. 121.5-122.0°. The residue after evaporation of pentane consisted of about 10% vinyl benzoate, 20% miscellaneous side-products, and 70% X, as determined by vapor-phase chromatography.

The combined, crude product from two runs (2.61 g.) was dissolved in 125 ml. of pentane and chromatographed on 80 g. of alumina. The results are summarized in Table IV (see next page).

Fractions 8-11 probably consisted of low-molecular-weight allene polymers. Vinyl benzoate apparently was not eluted at all. The recovery of pure X (fractions 13-14) was only 56%, assuming that X comprised 70% of the original material.

TABLE IV.

PURIFICATION OF 3-METHYLENECYCLOBUTYL BENZOATE (X) BY ELUTION CHROMATOGRAPHY

Frac.	Eluent	Volume, ml.	Residue, g.	Composition of Residue
8	Pentane	250	0.19	Hydrocarbons
9	Pentane	150	0.11	Hydrocarbons
10	Pentane	200	0.07	--
11	Pentane	200	0.05	--
12	9:1 Pentane-ether	150	0.17	X, Hydrocarbons
13	9:1 Pentane-ether	150	0.76	X
14	9:1 Pentane-ether	200	0.26	X
15	3:1 Pentane-ether	200	0.04	--
16	Ether	250	--	--

Several attempts were made to crystallize X, without success. The identification was based on n.m.r. and infrared spectra and reduction to benzyl alcohol and 3-methylenecyclobutanol; the latter was synthesized by an independent route. The n.m.r. spectrum of X is included in the Appendix, page 85. The infrared spectrum exhibited the characteristic benzoate ester absorption (intense bands at 1730, 1275, 1112 and 710 cm.$^{-1}$) and also showed bands at 1686 and 885 cm.$^{-1}$, characteristic of the methylenecyclobutyl structure. The reduction products were identified by comparison of their infrared and n.m.r. spectra with those of authentic samples.

3-Methylenecyclobutanecarbonitrile (XI) was prepared from allene and acrylonitrile by the method of Caserio, et. al., (2) using hydroquinone as an inhibitor and toluene as a moderator. The yields for five 1-mole runs were 47-55%.

3-Methylenecyclobutanecarboxylic acid (XII) was prepared by the method of Caserio, et. al. (2). From 105 g. (1.13 moles) of XI and 200 g. of potassium hydroxide in 1 l. of 50% ethanol there was obtained 123 g. (97%) of XII, b.p. 70° (2 mm.). The n.m.r. spectrum was consistent with the structure and showed no detectable impurities.

3-Methylenecyclobutanecarbonyl chloride (XIII) was prepared according to the procedure of Applequist and Roberts (1). From 130 g. (1.16 moles) of XII and 155 g. of (1.30 moles) thionyl chloride was obtained 133 g. (88%) of XIII, b.p. 64-68° (30 mm.).

Ethyl N-(3-methylenecyclobutyl)-carbamate (XIV) was prepared according to the method of Applequist and Roberts by rearrangement of the acid azide in ethanol (1). From 130 g. of XIII and 80 g. of sodium azide, in four batches, there was obtained 133 g. of crude, solid XIV (86% yield).

3-Methylenecyclobutylamine (XV) was prepared by basic hydrolysis of the urethan as described by Applequist and Roberts (1). The work-up, however, was changed as follows: Instead of extraction with methylene chloride, the basic reaction mixture, after dilution with water, was acidified strongly with concentrated hydrochloric acid and extracted continuously with ether for four days to remove alcohols, ester, acid, unreacted urethan, and neutral and acidic tars. The aqueous solution was then made basic with 40% sodium hydroxide and extracted with fresh ether for 2 days. The extract was dried over sodium sulfate, then over barium oxide, and distilled. The yield was 44 g. (62%) of XV, b.p. 105-108°. Part of the amine was obtained as an azeotrope with water, b.p. 93°, which contained 62-65% of amine by weight, as determined by comparison of v.p.c. spectra with artificial mixtures.

When the isolation procedure of Applequist and Roberts was used, the yield of amine was 44%. Considerable time was saved in a third run by extracting the reaction mixture directly with ether, acidifying the ether extracts with aqueous perchloric acid and concentrating the acidic solution of amine salt under reduced pressure to remove ether and alcohols. The aqueous solution was then used directly in the preparation of 3-methylenecyclobutanol. The yield of amine, as determined by acid titer, was 55%, but the yield of alcohol from the subsequent reaction was poor.

3-Methylenecyclobutanol (XVI). A. From 3-Methylenecyclobutylamine.--Most of alcohol XVI was prepared by nitrous acid deamination of XV. In a 1500-ml. round-bottomed flask, fitted with a magnetic stirrer and condenser were placed 120 g. of 60% perchloric acid (0.72 mole), 800 ml. of water, and 47 g. (0.57 mole) of XV. The solution was cooled in ice as a solution of 90 g. (1.2 moles) of sodium nitrite in 300 ml. of water was added dropwise over 1.5 hours. When the addition was complete, the cooling bath was removed, and stirring was continued for 6 hours. The cloudy, brown solution was then saturated with sodium chloride and extracted continuously with ether for 24 hours. The ether extract was flash-distilled under vacuum, and the distillate was dried over magnesium sulfate and redistilled through Column #1. The yield of XVI, b.p. 57-58° (20 mm.), was 37.5 g. (78%).

Anal. calcd. for C_5H_8O: C, 71.39; H, 9.58. Found: C, 71.26; H, 9.52.

XVI prepared by this method exhibited a band in the infrared spectrum at 1550 cm.$^{-1}$ which was not present in the spectrum of XVI prepared by reduction of the benzoate (X). Otherwise, the spectra were identical. The major bands in the spectrum could also be superimposed with those present in the spectrum of an impure sample prepared by Silver (28) by the pyrolysis of 3-hydroxycyclobutylcarbinyltrimethylammonium hydroxide.

The n.m.r. spectra of the material obtained from X and XV were also identical.

B. From Reduction of 3-Methylenecyclobutyl Benzoate (X).-- When 200 mg. of XVI was stirred with a two-fold excess of 1N sodium hydroxide for two hours at 100°, it was quantitatively converted to a dark, base-insoluble tar, presumably by way of ring-opening to aldehyde, followed by condensation. This result seemed to rule out the possibility of obtaining XVI from the benzoate by simple saponification. Accordingly, 4.50 g. (0.0238 mole) of X in 20 ml. of dry ether was added during 30 minutes to a stirred suspension of 1.00 g. of lithium aluminum hydride in 40 ml. of ether, with ice cooling. The mixture was stirred for an additional 30 minutes at room temperature and the product isolated in the usual manner. Careful distillation through Column #5 yielded 1.68 g. (84%) of 3-methylenecyclobutanol.

Attempted Isomerization of 3-Methylenecyclobutanol (XVI).-- In several attempts to convert XVI to its allylic isomer, 1-methylcyclobutenol-3, XVI was treated with acid under a variety of conditions, including solution of the alcohol in excess perchloric and fluoboric acids and treatment of the alcohol with a trace of fluoboric acid, neat or in pentane solution. Treatment of XVI with hydrogen bromide or hydrogen iodide in water, methanol, or pentane resulted in addition of the acid to give 1-methyl-1-bromocyclobutanol-3. Dehydrobromination of this adduct with triethylamine or pyridine seemed to be the most promising method. In all the above cases, however, the only volatile products isolated were the starting alcohol and varying amounts of β-methylcrotonaldehyde. The latter was identified as the 2,4-dinitrophenylhydrazone (dark red needles from alcohol, m.p. 178-179.3°; λ_{max} 380 mμ, (ϵ 30,000); reported (92) m.p. 179°; λ_{max} 380 mμ (ϵ 28,000)).

An indication that the β,γ-unsaturated aldehyde is probably first formed and subsequently isomerized is given by the initial appearance of a pale orange 2,4-dinitrophenylhydrazone from the product of the reaction of 1-methyl-3-hydroxycyclobutyl iodide and triethylamine. On standing in strong acid solution, the derivative rapidly turned dark red.

Attempted Oxidation of 3-Methylenecyclobutanol.--The failure of direct isomerization of XVI led to the hope that oxidation to

3-methylenecyclobutanone, which would isomerize immediately to the conjugated ketone (3), could be accomplished. The product could then be reduced to 1-methylcyclobutenol-3.

Oxidation of 1.75 g. of XVI in acetone solution by dropwise addition of a solution of chromic anhydride in dilute sulfuric acid at 0° resulted in the isolation of 0.38 g. of volatile material which consisted mainly of XVI and showed a profusion of bands in the carbonyl region of the infrared spectrum. 1-Methylcyclobutenone-3 could not be identified in the mixture, and if it was present, the yield could not have exceeded 10%.

When 4.0 g. of XVI was treated with 50 ml. of chromic anhydride-pyridine complex (93) at room temperature for 18 hours, the only volatile material isolated was 2.3 g. (57% recovery) of XVI. It appears as though the ketone is more sensitive to oxidation than the alcohol.

3-Methylenecyclobutyl Bromide (XVII).--After an unsuccessful attempt to convert XVI to the bromide with phosphorus tribromide in ether (phosphite ester was the only product), the following procedure (94) was followed: 17.4 g. (0.207 mole) of XVI, 39.2 g. (0.206 mole) of p-toluenesulfonyl chloride, and 52 g. (0.43 mole) of 2,4,6-collidine were mixed in a 250-ml. flask protected by a drying tube, and allowed to stand overnight at room temperature. The thick, pinkish mixture was then treated with 75 ml. of methylene chloride and acidified with 40% sulfuric acid (ice-cooling). The layers were separated, and the aqueous layer was washed with two more portions of methylene chloride. The combined organic extracts were washed once with dilute sulfuric acid and dried over Drierite. After removal of the solvent under reduced pressure, at a final pressure of 1 mm., the crude tosylate weighed 46.6 g. (94%).

No attempt was made to crystallize or distill the tosylate, but instead it was added directly to a solution of 73 g. (4.3-fold excess) of freshly fused lithium bromide in 450 ml. of dry acetone. The resulting solution was heated under reflux, with magnetic stirring, for 50 hours. The amber-colored solution, containing a small amount of precipitated lithium tosylate, was then poured into 1500 ml. of water, and the small lower layer separated. The aqueous solution was extracted with three 100-ml. portions of pentane, which were combined with the neat bromide and dried over Drierite. After the pentane was removed through Column #4, the residue was distilled through Column #3 at reduced pressure, yielding 22.7 g. (79%) of 3-methylenecyclobutyl bromide (XVII), b.p. 57-60° (80 mm.), $\underline{n}^{25}D$ 1.4843, density 1.29. Although v.p.c. (Column A) seemed to indicate that the product was pure, the n.m.r. and infrared spectra showed extraneous absorptions. Analysis by v.p.c. (Column K) indicated the presence of two impurities, comprising a total of about 10% of the mixture. Since the ratio of components was approximately the same for each fraction, it was assumed that XVII could not be purified easily by distillation, so 0.40 g. was purified by v.p.c. (Column K, 95°; ten separate injections required). The n.m.r. and infrared spectra of the purified material were entirely consistent with the assigned structure. The impurities, whose density indicated the absence of bromine, were not identified.

Anal. calcd. for C_5H_7Br: C, 40.85; H, 4.80; Br, 54.35. Found: C, 40.77; H, 4.85; Br, 54.40.

Attempted Isomerization of 3-Methylenecyclobutyl Bromide (XVII).--XVII (150 mg., purified by v.p.c.) was placed in a thick-walled n.m.r. tube; a few crystals of freshly-fused zinc bromide were added; the tube was sealed, and the n.m.r. spectrum recorded immediately. The spectrum was recorded again after the tube had been immersed in an oil bath at 95° for 1 minute, 10 minutes, and 45 minutes, and finally at 120° for 2 hours. After this treatment, the material in the tube was black and opaque, but essentially no change in the spectrum could be observed other than some line broadening. After standing in an oil bath at 120° for 48 hours, the material in the tube was a black, amorphous solid, and the n.m.r. spectrum was so poorly resolved that no definite information could be obtained from it.

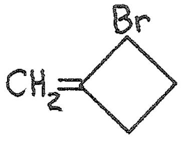
Methylenecyclobutene.--In a 200-ml. three-necked, round-bottomed flask, fitted with a dropping funnel, magnetic stirrer, and a short, upright condenser leading through a Dry Ice-cooled trap to the vacuum line, were placed 100 ml. of diethylene glycol and 4.0 g. (0.074 mole) of sodium methoxide. The mixture was stirred and heated to 170° in a silicone-oil bath, and the pressure was reduced to about 300 ml. as 5.3 g. (0.036 mole) of 3-methylenecyclobutyl bromide (containing about 10% impurities) was added from the dropping funnel during 1.5 hours. Heating was continued for an additional 45 minutes after all the bromide had been added. The material in the Dry Ice trap was warmed to about 0° and washed twice with 10 ml. of ice water. The crude diene was then transferred to a small pear-shaped flask and distilled into a Dry Ice-cooled receiver at 100 mm. pressure. The yield of pure methylenecyclobutene was 1.92 g. (81%). The infrared spectrum of this material was identical to that prepared by Applequist and Roberts (1).

In earlier runs, a lower bath temperature (130-140°) and lower pressure were employed for the dehydrobromination, and about 10% of the XVII was actually recovered after distillation of the diene.

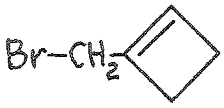
<u>3-Bromo-3-methylcyclobutene (XVIII)</u>.--In a 25-ml. pear-shaped flask were placed 15 ml. of pentane and 1.92 g. (0.0291 mole) of methylenecyclobutene. The flask was weighed and then cooled in Dry Ice as anhydrous hydrogen bromide was passed in from a cylinder. The flask was stoppered and weighed periodically to determine the amount of gas which had been added. After 2.25 g. (0.0278 mole) had been absorbed, the flask was tightly stoppered and allowed to warm slowly to 0° in the refrigerator. Pentane and excess diene were then distilled from an ice bath at 100 mm. pressure into a Dry Ice-cooled receiver. When the distillation appeared to be over, the pressure was reduced to 20 mm. for 30 minutes to remove the last traces of pentane. The residue was then distilled rapidly at 20 mm. through Column #3. The yield of 3-bromo-3-methylcyclobutene (XVIII), b.p. 40° (20 mm.), was 3.31 g. (82%).

The compound gave a positive Beilstein test for halogen, an instantaneous, heavy precipitate with alcoholic silver nitrate, and a light precipitate after a few minutes with sodium iodide in acetone.

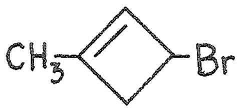
Identification of XVIII must of necessity be based partly on negative and indirect evidence. If one assumes the compound to be an allylic bromide (a valid assumption from synthesis and chemical tests) with a cyclobutane ring as witnessed by conversion to 1- and 3-methylcyclobutanol, then there are only four reasonable possibilities:



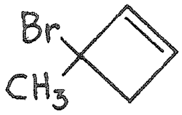
(A)



(B)



(C)



(D)

The presence of a methyl group in the infrared and n.m.r. spectra eliminates A and B. Compound A can also be eliminated by the absence of double-bond absorption at 1640-1700 cm^{-1} in the infrared. Compound B seems ruled out further by its failure to react rapidly with sodium iodide in acetone. It is possible (in fact, it would seem logical) that the material is a mixture of C and D, but the n.m.r. spectrum seems to preclude this possibility. If C and D were equilibrating slowly or not at all, one would expect a more complicated spectrum with more than four different kinds of hydrogen. On the other hand, if C and D were in rapid equilibrium, one would expect the two secondary ring protons at the 4-position to be equivalent and unsplit (100).

The case for structure D rests entirely on the lack of normal AB-type splitting (100) in either of the low-field protons in the n.m.r. spectrum. (The spectrum is included in the Appendix, page 85.) This phenomenon is rather striking in any case, but if one of the protons were tertiary, as in C, instead of vinylic, the spectrum would indeed be anomalous. If both of these protons are vinylic, as in D, one might rationalize the lack of significant (>5 cps) splitting on the basis of angular dependence of spin-spin coupling. Furthermore, in the spectrum of the material from a subsequent run (see Appendix, page 85), there are some small extraneous peaks which might be assigned to C.

Attempted Isomerization of XVIII.--In an attempt to convert XVIII to an equilibrium mixture of allylic isomers C and D, a sealed n.m.r. sample was kept at 80° for 10 hours. No change in the spectrum was observed. The tube was then opened, and a crystal of anhydrous zinc bromide was added. The liquid immediately darkened, but no change in the spectrum could be detected (except line broadening), until the tube was heated for 40 minutes at 100°. At this point, most of the material appeared to have decomposed, but there seemed to be a significant increase in the relative area of the small, high-field singlet assigned to the methyl group in C. Whether or not this represents an actual increase in the amount of C, rather than just a decrease in the intensity of the rest of the spectrum, could not be determined.

One is forced to conclude that if the compound in question is really 1-methyl-1-bromocyclobutene, then either the conversion to the secondary allylic isomer is extremely sluggish, or (more likely but still unprecedented) the equilibrium lies almost entirely on the side of the tertiary isomer.

Hydrolysis of XVIII.--In a 50-ml. round-bottomed flask were placed 20 ml. of water and 996 mg. of XVIII. The heterogeneous mixture was stirred magnetically until hydrolysis was complete; then the solution was neutralized with sodium hydroxide and extracted five times with ether, and the combined ether solutions dried and distilled under reduced pressure. The material recovered amounted to 385 mg. (68%), and was analyzed by n.m.r. The most noticeable features of the resulting spectrum were the presence of a sharp doublet in the aldehyde proton region, and a recurrence of the same pattern which characterized the bromide, assigned to 1-methylcyclobutenol-1. The absorptions due to β-methylcrotonaldehyde could be easily picked out. The remainder of the spectrum was assigned to 1-methylcyclobutenol-3.

On a second run, the aqueous solution was kept roughly neutral by adding bromthymol blue indicator and titrating continuously with 5% sodium hydroxide solution as the hydrolysis progressed. The n.m.r. spectrum of the product was very similar to that of the material obtained under acidic conditions. If anything, there appeared to be a slightly higher proportion of β-methylcrotonaldehyde, an observation which seems at variance with the proposed mechanism of formation of this compound. The only other difference with respect to Run #1 was that the total yield of high-boiling products was only 39%, which may indicate that some elimination occurred under neutral, and sometimes slightly basic, conditions.

<u>Hydrogenation of Hydrolysis Products from XVIII</u>.--In a 50-ml. hydrogenation flask (an Erlenmeyer flask with a dropping funnel sealed onto a side-arm) were placed 10 ml. of dry ether and 0.1481 g. of 10% palladium-on-charcoal. The flask was attached to a 500-ml. semimicro hydrogenation apparatus and the system flushed four times with hydrogen while the solvent-catalyst mixture was cooled in Dry Ice. The mixture was then allowed to warm to room temperature, with magnetic stirring. Finally, 0.3386 g. of the mixture of products from the hydrolysis of XVIII was added through the side-arm dropping funnel, with the aid of 10 ml. of dry ether. The mixture absorbed 80 ml. of hydrogen (87% of theory, assuming the reaction for all compounds present was $C_5H_8O \rightarrow C_5H_{10}O$) in 35 minutes, then appeared to stop abruptly. More catalyst was added, and the mixture was allowed to stir overnight, during which time it absorbed an additional 30 ml. of hydrogen, but it is not known how much of this increase was due to leakage in the system. The catalyst was then removed by filtration, and the solvent distilled below room temperature, under reduced pressure. The residue, after vacuum-distillation at room temperature, amounted to 0.170 g. (49%).*

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*In all the small-scale experiments described on the last few pages, the primary consideration in product isolation was the avoidance of any decomposition or isomerization of products, rather than realization of maximum yield. The rapid, low-temperature distillations employed to this end undoubtedly resulted in appreciable loss of product during solvent removal.

The hydrogenation product was found to consist of isovaleraldehyde, 1-methylcyclobutanol, cis- and trans-3-methylcyclobutanol, and a small amount of what may be 2-methylcyclobutanone.* The identification of the last-named compound is based solely on the appearance of a band at 1783 cm.$^{-1}$ in the infrared spectrum of the mixture. A spectrum of authentic 2-methylcyclobutanone prepared by Silver (28) showed a band at 1784 cm.$^{-1}$. The formation of this compound might also help to explain the failure of the mixture to absorb the theoretical quantity of hydrogen.

Allylmethylcarbinol was prepared by the method of Whitmore (49) on one-fifth the scale described. From 45 g. (1.85 g.-atom) of magnesium turnings, 169.4 g. (1.40 moles) of allyl bromide, and 61.4 g. (1.40 moles) of acetaldehyde there was obtained, after distillation through Column #1, 45 g. (38%) of allylmethylcarbinol,

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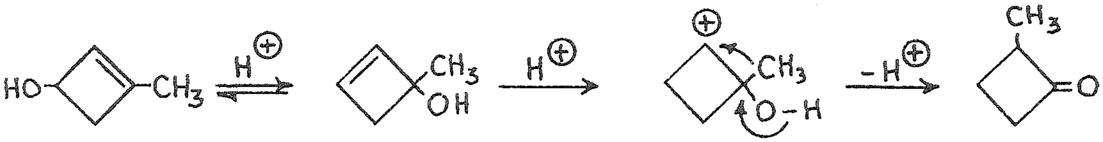
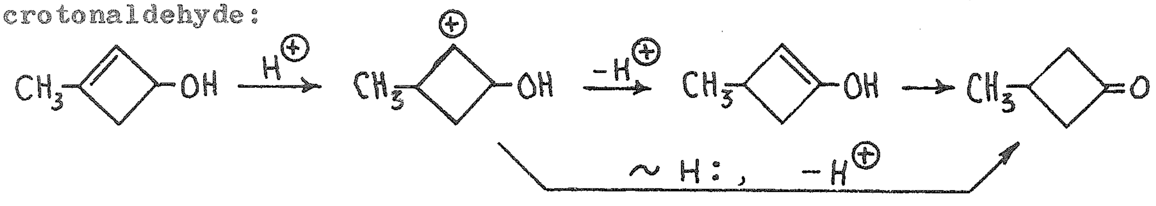
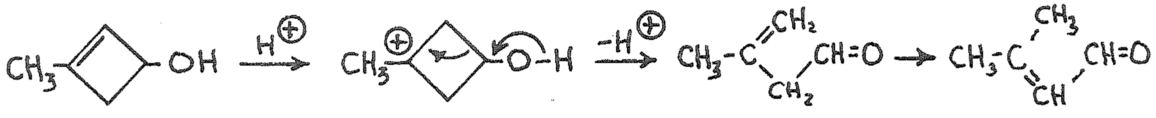
*A reasonable mechanism for the formation of 2-methylcyclobutanone might be the following:



3-Methylcyclobutanone could also be a possible product, but this seems less likely, since protonation of 1-methylcyclobutenol-3 is believed to occur at the 1-position, giving rise to β-methylcrotonaldehyde:





b.p. 69-72° (150 mm.). Reported (49) b.p. 114° (740 mm.).

Allylmethylcarbinyl bromide was prepared by the method of Wood and Horning (95). A solution of 5.0 g. (0.058 mole) of allylmethylcarbinol and 0.5 ml. of dry pyridine in 10 ml. of anhydrous ether was added dropwise to 5.5 g. (0.020 mole) of phosphorus tribromide in 20 ml. of ether, at such a rate that the mixture became warm, but did not boil. After addition was complete, the mixture was heated under reflux for one hour, cooled, and poured over ice. The layers were separated; the aqueous phase was washed once with ether, and the combined ether solutions were washed twice with cold, dilute sodium bicarbonate solution and dried over sodium sulfate. Distillation through Column #3 yielded 3.25 g. (37%) of allylmethylcarbinyl bromide, b.p. 55-57° (100 mm.). Reported (100) b.p. 114-116°.

Displacement of the tosylate with lithium bromide in acetone gave a slightly higher yield, but the procedure was much more tedious.

2-Penten-4-ol was prepared by the procedure of Coburn (50) on one-fourth scale, except that methyl iodide was used in place of methyl chloride. From 15.0 g. (0.62 g.-atom) of magnesium turnings, 90 g. (0.63 mole) of methyl iodide, and 36 g. (0.515 mole) of crotonaldehyde, there was obtained 41.4 g. (93%) of 2-penten-4-ol, b.p. 69-70° (90 mm.), $\underline{n}^{25}D$ 1.4260. Reported (101) b.p. 120° (740 mm.).

2-Methyl-2-penten-4-ol.--A suspension of 19.0 g. (0.50 mole) of freshly ground lithium aluminum hydride in 300 ml. of anhydrous ether was stirred for one hour, then cooled in ice as 92 g. (0.90 mole) of mesityl oxide in 200 ml. of ether was added dropwise during 2 hours. The mixture was stirred for an additional 45 minutes, then hydrolyzed by dropwise addition of water (20 ml.), 15% sodium hydroxide (20 ml.), and water (60 ml.). Some of the material was lost when hydrogen evolution became too vigorous during early hydrolysis and the mixture foamed over. The flocculent white solid was filtered off and the ether solution dried and distilled, yielding 71.8 g. (75%) of 2-methyl-2-penten-4-ol, b.p. 66-68° (42 mm.), $\underline{n}^{25}D$ 1.4357. Reported (51) b.p. 139°, $\underline{n}^{25}D$ 1.4310.

4-Bromo-2-pentene.--Phosphorus tribromide (22.5 g., 0.083 mole) was dissolved in 75 ml. of anhydrous ether, cooled to -35°, and stirred magnetically as 20 g. (0.23 mole) of 3-penten-2-ol in 25 ml. of ether was added over 45 minutes. The colorless solution was then allowed to warm slowly to room temperature, stirred for one hour, and poured over ice. The aqueous phase was washed once with ether, and the combined ether solutions washed with ice-cold 5% sodium bicarbonate, dried, and distilled. The yield of 4-bromo-2-pentene, b.p. 55-56° (80 mm.), $\underline{n}^{25}D$ 1.4712, was 28.7 g. (83%). Reported (96) b.p. 70.2-72.2° (145 mm.).

4-Bromo-2-methyl-2-pentene.--The procedure described above was used, except that instead of the reaction mixture being poured over ice, it was distilled directly at reduced pressure. Washing, even with ice water, caused extensive hydrolysis to occur. The yield from 20 g. of alcohol and 18.5 g. of phosphorus tribromide was about 60%. The bromide was tested for free acid by dissolving 1 g. in 5 ml. of pentane and adding triethylamine at Dry Ice temperature. No precipitate was observed, even on warming, until the temperature reached about 0°.

<u>3-Bromocyclopentene</u>.--Cyclopentadiene (23.0 g., 0.35 mole, obtained by cracking dicyclopentadiene) was dissolved in 30 ml. of pentane, cooled to -30°, and 25.7 g. (0.32 mole) of anhydrous hydrogen bromide was passed in from a cylinder during one hour. The solution was allowed to stand at Dry Ice temperature overnight; then the pentane and excess diene were distilled at aspirator pressure. The clear, colorless residue was distilled at reduced pressure, yielding 34 g. (70%) of 3-bromocyclopentene, b.p. 37-38° (18 mm.). Reported (56) b.p. 34-36° (17 mm.). A sizeable forerun and residue were discarded. Since the forerun rapidly darkened at 0°, the pure bromide was immediately sealed under nitrogen in an ampoule and stored in Dry Ice.

<u>3-Bromocyclohexene</u>.--By the procedure of Ziegler (53), 16.5 g. (86%) of 3-bromocyclohexene, b.p. 39-40° (6 mm.), was prepared from 45 g. of cyclohexene and 22.5 g. of N-bromosuccinimide. Reported (97) b.p. 74° (28 mm.).

<u>Kinetics of Solvolysis of Allylic Bromides</u>.--The solvent chosen for the measurement of solvolysis rates of the allylic bromides (2-bromo-1-methylcyclobut-2-ene, 3-bromocyclopentene, 3-bromocyclohexene, 4-bromo-2-pentene, 4-bromo-2-methyl-2-pentene) was "80% ethanol," prepared by pipetting 250 ml. of freshly boiled distilled water into 1 l. of absolute ethanol which had

been distilled over sodium through Column #6. The solvent was chosen on the basis of minimum solvolysis rate and complications such as internal return, combined with maximum rate of solution of the allylic bromides at low temperatures. The standard base solution was 0.0997 N sodium hydroxide in 80% ethanol, prepared by pipetting 125 ml. of approximately 0.5 N aqueous sodium hydroxide into 500 ml. purified ethanol, and standardizing against potassium biphthalate.

The solvolysis rates were measured by dissolving approximately 100 mg. of the organic bromide in 100 ml. of 80% ethanol, which had previously been temperature-equilibrated in a 500-ml., three-necked, round-bottomed flask fitted with a low-temperature thermometer, a ball-joint-sealed Hershberg stirrer, an Ascarite tube, and a 10-ml. burette. Temperature control in the range -30 to -64° was maintained with a cooling bath of liquid nitrogen and methanol in a ½-gallon Dewar Flask. At temperatures of -20 to +20°, the cooling bath was an ice-salt slurry. Zero time was taken uniformly to be 2 seconds after addition of the bromide to the flask from a micro pipette. After the reaction had begun, standard base was added from the burette until the bromthymol blue indicator turned blue; then the time was noted on a stopwatch as the color changed back to yellow. The burette was read, and after an appropriate time interval, this procedure was repeated. At least 20 points were recorded on each run, except one which had a half-life of over 2 hours. The error due to absorption of atmospheric carbon dioxide did not exceed 1%, as determined by blank runs. The maximum sources of error are believed to be uncertainties in the time readings in the first few points on runs having a half-life of less than 10 minutes, and temperature control on runs below -30°.

The two bromides which had been prepared from the alcohols (4-bromo-2-pentene and 4-bromo-2-methyl-2-pentene) titrated to less than 90% of theory, so after the infinity titer had been measured, the solutions were heated to 60° for several hours to determine whether a less reactive bromide might be present, but none was found. The impurities were probably the corresponding alcohols and/or dienes, and their effect on the rate of solvolysis was assumed to be negligible.

The experimental data for the kinetic measurements are included in the Appendix, page 77. The first-order rate constants were derived by averaging the calculated rate constants for each experimental point, omitting a maximum of 2 points in each run if they deviated widely from the mean. The constants derived in this way were in good agreement with those obtained by the method of least-squares analysis, for the cases in which the comparison was made.

A summary of the experimental results is included in the Discussion section, page 25.

Kinetics of Solvolysis of Homoallylic Bromides.--The solvent for the solvolysis of 3-methylenecyclobutyl bromide and allylmethylcarbinyl bromide was "50% ethanol," prepared by pipetting 500 ml. of freshly boiled distilled water into 500 ml. purified ethanol (distilled from sodium through Column #6). The standard base solution was carbonate-free 0.01963 N aqueous sodium hydroxide. The kinetic measurements were made by weighing approximately 300-mg. samples of the bromide into a 100-ml. volumetric flask and filling to the mark with 50% ethanol at 20°. The flask was shaken thoroughly to dissolve the bromide, and approximately 6-ml. portions were pipetted into clean, 15 x 125-mm. pyrex test tubes, constricted at the neck. Fifteen samples, including a solvent blank, were prepared for each run. The tubes were sealed and immersed in a constant-temperature, mineral-oil bath. Zero time was taken as three minutes after the bath had returned to equilibrium. The tubes were removed from the bath at appropriate time intervals, quenched in ice water, and placed in the refrigerator, so that all the samples from a given run could be titrated together. For titration, a tube was opened and a 5.00-ml. aliquot was pipetted into a 10-ml. wide-mouthed test tube containing a small magnetic stirring bar and fitted with an Ascarite tube and a 1-ml. micro burette with a capillary tip which extended below the surface of the liquid. One drop of a mixed indicator composed of 0.1% bromcresol purple and 0.1% bromthymol blue in 50% ethanol was added, and the sample was titrated, with slow stirring, to the almost colorless endpoint at pH 7.0-7.2.

The experimental data for the kinetic measurements are included in the Appendix, page 77. The first-order rate constants were determined by the method used for the allylic bromides. A summary of the experimental results is included in the Discussion section, page 25.

Methyl 1-Methyl-2,2-dichloro-3,3-difluorocyclobutanecarboxylate (III).--In a 1-l. Parr bomb were placed 288 g. (2.16 moles) of unsym-difluorodichloroethylene (Genetron 1112A), 306 g. (3.06 moles) of methyl methacrylate, and 1.6 g. of phenothiazine. The bomb was sealed and heated, with rocking, to 150-170° for 10 hours. Distillation of the reaction mixture through Column #3 yielded 474 g. (94%) of IV , b.p. 91° (26 mm.), $n^{25.5}D$ 1.4346. Reported (46) b.p. 102° (51 mm.), $n^{25.9}D$ 1.4344.

1-Methyl-2,2-dichloro-3,3-difluorocyclobutanecarboxylic Acid (IV).--Sodium hydroxide (100 g., 2.5 moles), water (1500 ml.), and III (300 g., 1.28 moles) were heated under reflux for 1.5 hours in a 3-l., round-bottomed flask. The cooled reaction mixture was then acidified with sulfuric acid and extracted four times with ether. The ether extracts were combined, the ether distilled, and the residue taken up in 1500 ml. of petroleum ether (30-60°). After being dried over magnesium sulfate and filtered through charcoal, the petroleum ether solution was concentrated to about 600 ml. on a steam bath and cooled to 0°, to deposit 245 g. of IV, m.p. 127.3-130.5°. A second crop of 22 g. was collected, bringing the total yield of slightly impure IV to 268 g. (95%). After two recrystallizations, a sample melted at 130.6-131.0°. Reported (46) m.p. 129.8-130.4°.

Sodium 1-methyl-2,2-dichloro-3,3-difluorocyclobutanecarboxylate (V) was obtained by dissolving 268 g. of IV in 1.5 l. of hot water containing a slight excess of sodium hydroxide, and evaporating the solution on a steam bath in a stream of air until crystals first began to form, then redissolving the salt and cooling the solution to 0°. The deposited V was collected by filtration and air-dried. Two more crops of V were collected in the same manner. The salt was quite hygroscopic and required 24 hours in a vacuum oven at 115° to remove the last traces of water.

1-Methyl-2-chloro-3,3-difluorocyclobutene (VI).--In a 300-ml. round-bottomed flask, connected through a Dry Ice-cooled trap to the vacuum line, was placed 61.0 g. of V which had been vacuum-dried at 115° for 3 days. The flask was heated in a Woods' metal bath at 100 mm. pressure until, at about 250°, a colorless liquid began to distill. The bath temperature was raised gradually to 290°, at which point the pyrolysis seemed to be complete. The pressure was reduced to 30 mm. to distill any remaining product, and the liquid in the trap was filtered to remove some salt which had blown over with the distillate. The product, which consisted of pure VI, weighed 33.6 g. (96%), and had b.p. 105°, $n^{25}D$ 1.4020 , density 1.21. Redistillation was judged to be unnecessary, as v.p.c., n.m.r., and infrared spectra showed no detectable impurities. The spectra were entirely consistent with the assigned structure.

Anal. calcd. for $C_5H_5ClF_2$: C, 43.34; H, 3.64. Found: C, 43.39; H, 3.76.

If the pyrolysis was carried out with a flame, the product contained traces of side-products, detectable by v.p.c. With less efficient drying, water distilled just before pyrolysis began, and the yields of VI were in the range 70-80%.

Compound VI was also prepared in 75% yield by zinc dechlorination of 1-methyl-1-acetoxy-2,2-dichloro-3,3-difluorocyclobutane, which was obtained in 20% yield from the cycloaddition reaction of difluorodichloroethylene and isopropenyl acetate (see page 74).

<u>1-Methyl-2-chlorocyclobutenone-3 (VII)</u>.--In a 200-ml., three-necked, round-bottomed flask, fitted with a condenser, a ball-joint-sealed glass stirrer, and a pressure-equalizing dropping funnel, was placed 125 ml. of 96% sulfuric acid. The acid was heated on the steam bath and stirred vigorously as 27.3 g. (0.197 mole) of VI was added from the dropping funnel during 5 minutes. Heating was continued for an additional 5 minutes; then the hot solution was poured over 1 l. of ice. The resulting emulsion was extracted five times with ether, and the combined ether solutions dried over magnesium sulfate in two stages. The ether was removed through Column #1, and the yellow residue distilled through Column #3 at reduced pressure. The yield of VII, b.p. 59-60° (14 mm.), was 18.5 g. (81%).

The structure of VII was determined by infrared (bands at 1620 and 1780 cm.$^{-1}$), ultraviolet (λ_{max} 234 mμ in ethanol) and n.m.r. spectra (2 multiplets of splitting 1-2 c.p.s., area ratio 2:3). Although the compound formed a 2,4-dinitrophenylhydrazone and a semicarbazone, attempts to prepare a derivative which showed a reproducible melting point on recrystallization were unsuccessful.

VII was also obtained as the major constituent of a mixture of products formed in the treatment of VI with excess 2 <u>N</u> methanolic potassium hydroxide.

When 2-chloro-3,3-difluorocyclobutene, obtained in 67% yield by zinc dechlorination of the adduct of difluorodichloroethylene and vinyl chloride (see page 74), was treated with 96% sulfuric acid as described above, hydrogen fluoride was evolved, and a product was obtained which decomposed vigorously on attempted distillation at 70°. No further experiments were done with this system.

Reduction of VII was attempted with lithium aluminum hydride in ether and with sodium borohydride in methanol (4). The product in both cases appeared to be a mixture of compounds, apparently formed during hydrolysis of the first-formed cyclobutenol (see page 17). When 10.5 g. of VII was treated with one equivalent of sodium borohydride in methanol at -15°, and the solution rapidly neutralized to pH 8, a product was obtained which appeared from the infrared to be mainly the expected alcohol, 1-methyl-2-chlorocyclobutenol-3. No further work was done on this product.

Attempted Dechlorination of VI.--When VI (12.3 g.) was treated with a two-fold excess of lithium and *t*-butanol in tetrahydrofuran as described by Winstein (98), an exothermic reaction occurred which caused spontaneous reflux for about 20 minutes. After decomposition of the excess lithium with ice water, the product was taken up in pentane and washed four times with water, to remove tetrahydrofuran. When the pentane solution was distilled carefully through Column #1, however, no separate fraction boiling between pentane and tetrahydrofuran could be collected. Analysis of the 5 fractions by v.p.c. showed the presence of two compounds with retention times intermediate between pentane and tetrahydrofuran, but it was estimated from relative peak areas that the total weight of both products could not have exceeded about 1.7 g. The theoretical yield of 1-methyl-3,3-difluorocyclobutene was 9.2 g. A small amount of a tan-colored solid which floated at the interface of pentane and water was discarded.

Wohl-Ziegler Bromination of Methylenecyclopentane.--In a 250-ml. round-bottomed flask, fitted with a magnetic stirrer and condenser, were placed 80 ml. of dry carbon tetrachloride, 17.8 g. (0.10 mole) of N-bromosuccinimide (vacuum-dried over phosphorus pentoxide), 20 mg. of benzoyl peroxide, and 10.1 g. (0.123 mole) of methylenecyclopentane. The last-named compound was obtained in three steps from cyclopentanone in 77% overall yield by the method of Arnold, Amidon, and Dodson (54).

The mixture was stirred and heated gently for 15 minutes, until a vigorous, exothermic reaction occurred which caused heavy reflux for a few minutes after the heating mantle was removed. After reflux subsided, external heating was resumed for 20 minutes; then the mixture was cooled, filtered free of succinimide, and distilled through Column #1. Although the solvent and excess olefin were removed at reduced pressure, with the pot temperature never exceeding 60°, the material in the pot became very dark during the distillation. The residue was flash-distilled into a Dry Ice-cooled receiver, and the resulting distillate redistilled through Column #3. A total of 6.2 g. of material was collected in three fractions, b.p. 43-52° (17 mm.), representing a yield of 38% monobrominated products. The product could not be obtained colorless, and darkened rapidly even when stored at 0°. All three fractions appeared from their infrared spectra to be mixtures of several components, with cyclopentenylcarbinyl bromide and 2-methylenecyclopentyl bromide predominating. Since the equilibrium between allylic isomers seemed to be very mobile, no attempt was made to obtain pure 2-methylenecyclobutyl bromide. As expected, solvolysis of the mixture in 80% ethanol at -10° was immeasurably fast.

<u>1,1-Dichloro-2,2-difluoro-3-methylenecyclobutane</u>.--The reaction of allene and difluorodichloroethylene was carried out five times on a preparative scale; the yields of adduct were consistently in the range 15-22%. Approximately equimolar quantities of the reagents were heated to 140-160° for 10-40 hours in a 500-ml. Parr bomb with 1.0 g. phenothiazine inhibitor. Distillation of the reaction mixture yielded an azeotropic mixture, b.p. 121-122°, consisting of the adduct and 1,1,2,2-tetrachloro-3,3,4,4-tetrafluorocyclobutane in approximately a 1:1 ratio, as determined by v.p.c. Separation of the mixture by preparative v.p.c. at 120° yielded pure 1,1-dichloro-2,2-difluoro-3-methylenecyclobutane, b.p. 125°, $\underline{n}^{25}D$ 1.4310. The structure was verified by n.m.r. and infrared spectra, and by the liberation of chloride ion on treatment with alcoholic potassium hydroxide.

<u>Anal</u>. calcd. for $C_5H_4Cl_2F_2$: C, 34.71; H, 2.33; Cl, 40.99. Found: C, 34.49; H, 2.45; Cl, 40.99.

<u>1,1-Difluoro-2,2-dichloro-3-acetoxycyclobutane</u> was prepared in 27% yield by the reaction of difluorodichloroethylene (116 g.,

0.87 mole) with vinyl acetate (106 g., 1.23 moles) at 150° for 60 hours in a 500-ml. Parr bomb, using 1.0 g. of phenothiazine as an inhibitor. The structure was assigned on the basis of elemental analysis, n.m.r. and infrared spectra, and acid hydrolysis to the corresponding alcohol. The ester had b.p. 80° (17 mm.) and $\underline{n}^{25}$D 1.4282.

Anal. calcd. for $C_6H_6Cl_2F_2O_2$: C, 32.90; H, 2.74. Found: C, 33.00; H, 2.85.

1,1-Difluoro-2,2-dichloro-3-methyl-3-acetoxycyclobutane was prepared in 20% yield by the reaction of difluorodichloroethylene (23.5 g., 0.177 mole) and isopropenyl acetate (23.3 g., 0.27 mole) at 140° for 60 hours in a 19 x 25-mm. pyrex combustion tube, using 0.3 g. of phenothiazine as an inhibitor. The structure was assigned on the basis of n.m.r. and infrared spectra and by conversion to 1-methyl-2-chloro-3,3-difluorocyclobutene (VI) with zinc dust and ethanol. The ester had b.p. 69-70° (8 mm.) and $\underline{n}^{25}$D 1.4320.

1,1-Difluoro-2,2,3-trichlorocyclobutane was prepared in 18% yield by the reaction of difluorodichloroethylene (1.9 moles) and vinyl chloride (2.0 moles) at 180° for 6 hours in a 1000-ml. Parr bomb. Phenothiazine (1.0 g.) was used as an inhibitor and benzene (100 ml.) as a moderator. Vacuum distillation through Column #1 failed to effect a separation of the adduct from difluorodichloroethylene dimer. Careful distillation through Column #4 at atmospheric pressure yielded 90 g. of an azeotropic mixture, b.p. 129°, consisting of about 90% tetrafluorotetrachlorocyclobutane and 10% 1,1-difluoro-2,2,3-trichlorocyclobutane; and 57 g. of pure 1,1-difluoro-2,2,3-trichlorocyclobutane, b.p. 135.5-136.2° (744 mm.). The structure of the adduct was assigned on the basis of its n.m.r. and infrared spectra, and by zinc dechlorination to 1,1-difluoro-2-chlorocyclobut-2-ene, which was also obtained in small yield by treatment of 1,1-difluoro-2,2-dichloro-3-acetoxycyclobutane with zinc dust. 1,1-Difluoro-2-chlorocyclobut-2-ene proved to be rather unstable, forming a flocculent, white polymer with the liberation of hydrogen fluoride. Sulfuric acid hydrolysis of this compound liberated hydrogen fluoride and resulted in a lachrymatory compound, probably 2-chlorocyclobutenone-3, which formed a 2,4-dinitrophenylhydrazone derivative and decomposed vigorously on attempted distillation.

TABLE V.

SUMMARY OF RESULTS OF CYCLOADDITION REACTIONS

Reactants	Reaction Vessel	No. of Runs	Time (hrs.)	Temp. (°C)	Yield of Adduct(%)
Allene + Ketene diethyl acetal[a]	n.m.r. tube 9 x 13-mm. tube	9 2	2-6 4	180-220 200	0 0
Allene + Ketene dimethyl acetal[b]	n.m.r. tube	8	10-18	240-290	0
Allene + Vinyl acetate	9 x 13-mm. tube	3	4-36	200-220	0
Allene + Vinyl benzoate[c]	500-ml. bomb	8	4-10	230-300	0.5-3
Allene + α-Acetoxyacrylonitrile[d]	500-ml. bomb	3	4-6	180-210	6-9
Allene + Acrylonitrile[e]	500-ml. bomb	5	8-10	240-270	47-55
$CF_2=CCl_2$ + Allene[f]	500-ml. bomb	5	4-40	135-200	15-22
$CF_2=CCl_2$ + Methyl methacrylate[g]	500-ml. bomb	1	10	170	94
$CF_2=CCl_2$ + Vinyl acetate[h]	500-ml. bomb	1	60	150	27
$CF_2=CCl_2$ + Isopropenyl acetate[i]	19 x 25-mm. tube	1	60	140	20
$CF_2=CCl_2$ + Vinyl chloride[j]	1000-ml. bomb	1	6	180	18

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[a] Ketene diethyl acetal kindly supplied by Professor S. M. McElvain.

[b] Ketene dimethyl acetal was synthesized by the procedure of McElvain (40).

[c] See pages 46-48.

[d] α-Acetoxyacrylonitrile was prepared from ketene and hydrogen cyanide by the method of Johnson and Newton (45). Reaction with allene has been reported by Cripps, Williams, and Sharkey (26).

[e] See page 49.

[f] See page 73.

[g] See page 68.

[h] See pages 73-74.

[i] See page 74.

[j] See pages 74-75.

IV. APPENDIX

Description of Distillation Columns

Column #1.--A 2.0 x 25-cm. column packed with glass helices and equipped with electrically heated asbestos jacket and a variable reflux head.

Column #2.--The same as Column #1, except that the dimensions were 1.0 x 22 cm.

Column #3.--A 0.8 x 15-cm. Vigreux column with an electrically heated asbestos jacket and total take-off head.

Column #4.--A 1.3 x 80-cm. column packed with glass helices and equipped with an electrically heated air jacket and a total reflux head.

Column #5.--A 0.8 x 25-cm. column packed with a tantalum wire coil and equipped with an electrically heated, evacuated jacket and a partial reflux head.

Column #6.--A 1.3 x 80-cm. column packed with stainless steel Helipaks and equipped with a total reflux, solenoid-operated head and an electrically heated air jacket.

Kinetic Measurements

A total of 25 kinetic runs were made; four each for allylmethylcarbinyl bromide, 3-bromocyclohexene, 3-bromocyclopentene, 1-bromo-1-methylcyclobut-2-ene (XVIII), and 4-bromo-2-methyl-2-pentene; three runs for 4-bromo-2-pentene, and two for 3-methylenecyclobutyl bromide (XVII). Representative runs for each compound are included in Tables VI-XII. The experimental procedures are described on pages 64-67.

TABLE VI.

SOLVOLYSIS OF 0.01860 M ALLYLMETHYLCARBINYL BROMIDE IN "50% ETHANOL"

Temperature = 99.0° Base: 0.01995 N NaOH Aliquots: 5.00 ml.

Time (sec.)	Ml. of Base	% Unreacted	$k_1(10^4 \text{ sec.}^{-1})$
0	0.530	--	--
240	0.721	94.2	2.45
480	0.898	89.0	2.44
720	1.061	83.9	2.43
960	1.232	78.9	2.46
1200	1.375	74.6	2.44
1440	1.504	70.4	2.43
1680	1.664	66.0	2.47
1920	1.786	62.3	2.46
2160	1.896	58.9	2.44
2400	2.004	55.7	2.44
2700	2.129	51.9	2.43
3300	2.391	44.0	2.47

$k_1 = 2.45 \pm 0.01 \times 10^{-4} \text{ sec.}^{-1}$

TABLE VII.

SOLVOLYSIS OF 0.02562 M 3-METHYLENECYCLOBUTYL BROMIDE IN "50% ETHANOL"

Temperature: 99.0° Base: 0.01995 N NaOH Aliquots: 5.00 ml.

Time (10^{-4} sec.)	Ml. of Base	% Unreacted	k_1(10^6 sec.$^{-1}$)
0	0.068	--	--
1.890	0.308	96.0	2.20
3.980	0.493	92.9	1.88
7.170	0.730	88.8	1.66
9.770	0.921	85.7	1.59
13.65	1.198	80.9	1.55
15.51	1.335	78.6	1.56
17.90	1.522	75.5	1.57
19.70	1.635	73.6	1.56
21.86	1.793	70.9	1.57
23.55	1.915	68.9	1.59
25.35	2.048	66.7	1.61
31.20	2.338	61.7	1.56
40.78	2.873	52.7	1.57

$k_1 = 1.58 \pm 0.02 \times 10^{-6}$ sec.$^{-1}$

TABLE VIII.

SOLVOLYSIS OF 0.00529 M 4-BROMO-2-METHYL-2-PENTENE IN "80% ETHANOL"

Temperature: -46.2 ± 0.05° Base: 0.0997 N NaOH in 80% ethanol

Time (sec.)	Ml. of Base	% Unreacted	$k_1(10^3 \text{ sec.}^{-1})$
0	0.07	--	--
19	0.51	91.7	4.57
47	1.11	80.4	4.64
87	1.83	66.8	4.63
120	2.35	57.0	4.68
149	2.68	50.7	4.55
189	3.07	43.4	4.42
232	3.44	36.5	4.35
292	3.88	28.0	4.35
355	4.25	21.0	4.37
420	4.51	16.0	4.33
480	4.70	12.5	4.30
542	4.85	9.5	4.28
590	4.95	8.0	4.29

$k_1 = 4.45 \pm 0.10 \times 10^{-3} \text{ sec.}^{-1}$

TABLE IX.

SOLVOLYSIS OF 0.00635 M 3-BROMOCYCLOPENTENE IN "80% ETHANOL"

Temperature: -46.1 ± 0.5° Base: 0.0997 N NaOH in 80% ethanol

Time (sec.)	Ml. of Base	% Unreacted	$k_1 (10^4 \text{ sec.}^{-1})$
0	0.00	--	--
38	0.12	98.1	4.96
80	0.24	96.2	4.78
235	0.67	89.5	4.72
340	0.97	84.7	4.85
440	1.21	81.0	4.79
542	1.46	77.0	4.80
725	1.88	70.5	4.82
861	2.18	66	4.86
1017	2.49	61	4.87
1290	2.99	53	4.90
1510	3.34	47.5	4.91
1805	3.74	41	4.90
2112	4.11	35.5	4.91
2412	4.44	30.5	4.94
2730	4.74	25.5	4.99
3010	4.94	22.5	4.96

$k_1 = 4.88 \pm 0.05 \times 10^{-4} \text{ sec.}^{-1}$

TABLE X.

SOLVOLYSIS OF 0.00806 M 4-BROMO-2-PENTENE IN "80% ETHANOL"

Temperature: 0.1 ± 0.2° Base: 0.0997 N NaOH in 80% ethanol

Time (sec.)	Ml. of Base	% Unreacted	$k_1(10^3 \text{ sec.}^{-1})$
0	0.06	--	--
43	0.85	90.0	2.39
63	1.16	86.4	2.32
82	1.50	82.0	2.39
99	1.76	79	2.38
127	2.15	74	2.36
165	2.69	67	2.38
197	3.08	62.5	2.37
237	3.52	57	2.36
267	3.83	53	2.36
294	4.08	50	2.34
348	4.55	44.5	2.32
397	4.93	39.5	2.32
452	5.28	35.5	2.30
516	5.65	31	2.28
585	5.98	26.5	2.25
635	6.17	24	2.22
685	6.32	22.5	2.21

$k_1 = 2.32 \pm 0.05 \times 10^{-3}$ sec.$^{-1}$

TABLE XI.

SOLVOLYSIS OF 0.00801 M 3-BROMOCYCLOHEXENE IN "80% ETHANOL"

Temperature: 10.0 ± 0.2°   Base: 0.0997 N NaOH in 80% ethanol

Time (sec.)	Ml. of Base	% Unreacted	$k_1(10^3\ \mathrm{sec.}^{-1})$
0	0.12	--	--
18	0.35	97.1	1.74
34	0.57	94.4	1.69
65	0.95	89.7	1.68
94	1.30	85.4	1.69
132	1.72	80.1	1.68
175	2.19	74.4	1.70
253	2.94	65.0	1.71
332	3.62	56.5	1.72
404	4.16	49.7	1.73
498	4.77	42.1	1.73
579	5.22	36.5	1.74
669	5.64	31.3	1.74
790	6.13	25.2	1.74
900	6.50	20.6	1.75
1000	6.77	17.2	1.76
1132	7.08	13.3	1.78
1233	7.25	11.2	1.77
1402	7.47	8.5	1.76

$k_1 = 1.72 \pm 0.02 \times 10^{-3}\ \mathrm{sec.}^{-1}$

TABLE XII.

SOLVOLYSIS OF 0.00703 M 1-BROMO-1-METHYLCYCLOBUT-2-ENE (XVIII) IN "80% ETHANOL"

Temperature: 16.1 ± 0.2° Base: 0.0991 N NaOH in 80% ethanol

Time (sec.)	Ml. of Base	% Unreacted	$k_1(10^3 \text{ sec.}^{-1})$
0	0.00	--	--
50	0.52	92.7	1.54
67	0.67	90.5	1.49
101	0.97	86.2	1.47
128	1.19	83.0	1.45
156	1.42	79.9	1.45
192	1.70	75.9	1.45
229	1.96	72.2	1.43
287	2.36	65.5	1.43
364	2.84	59.7	1.42
425	3.18	54.8	1.42
490	3.51	50.2	1.41
550	3.80	45.9	1.42
615	4.08	42.0	1.41
693	4.39	37.5	1.42
780	4.68	33.5	1.41
903	5.05	28.2	1.41
1035	5.39	23.4	1.41
1165	5.66	19.5	1.41
1308	5.91	16.0	1.41
1496	6.17	12.2	1.41
1752	6.42	8.7	1.40

$k_1 = 1.42 \pm 0.01 \times 10^{-3}$ sec.$^{-1}$

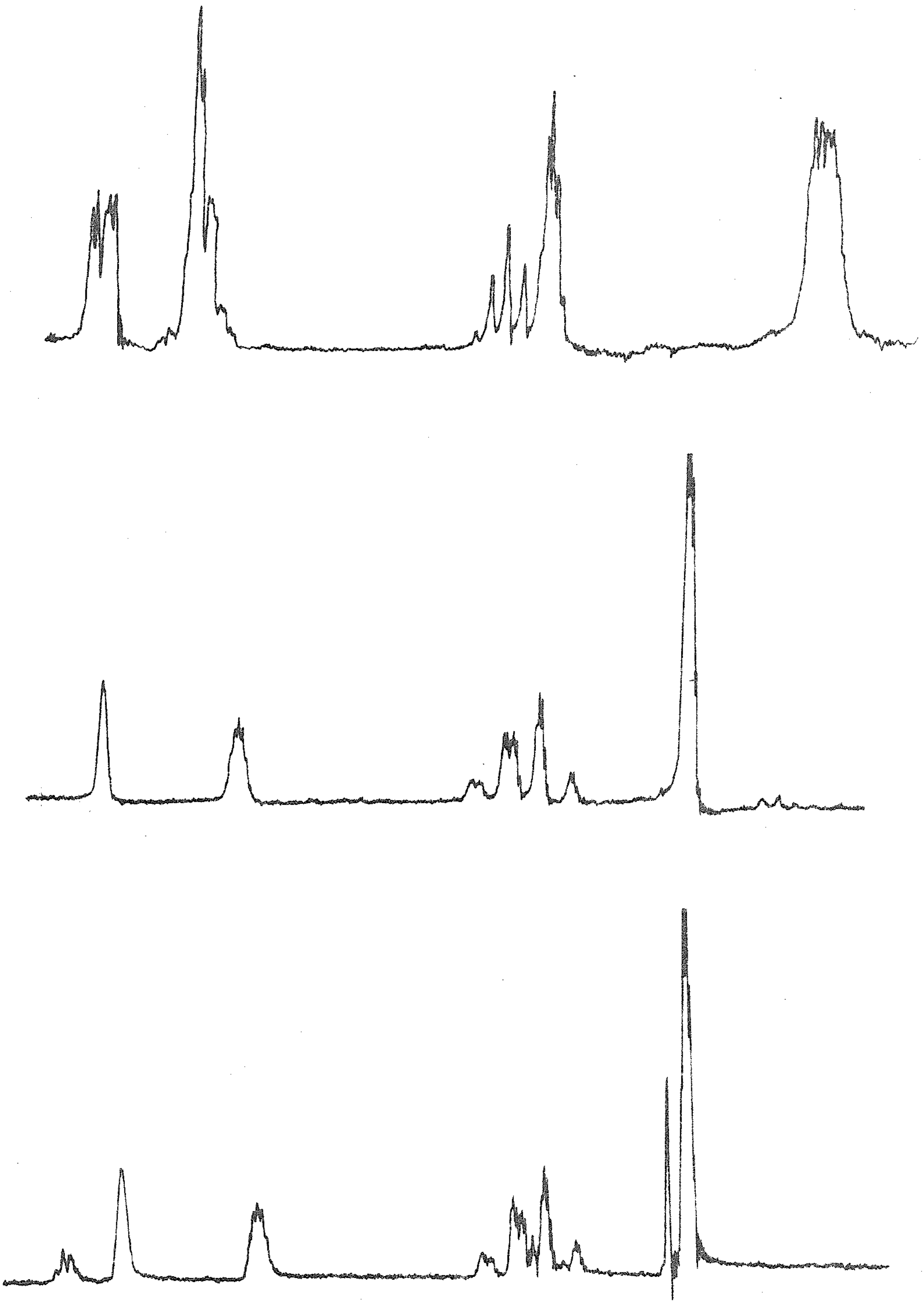

Figure 3.

Nuclear Magnetic Resonance Spectra.

TOP: 3-Methylenecyclobutyl Benzoate.
MIDDLE: 1-Bromo-1-methylcyclobut-2-ene, Run #1.
BOTTOM: 1-Bromo-1-methylcyclobut-2-ene, Run #2.

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VI. PROPOSITIONS

1. A reaction of considerable synthetic utility which has been in use in these laboratories for several years (1) is the conversion of a gem-difluoro compound to a carbonyl compound by treatment with hot, concentrated sulfuric acid. The reaction is generally characterized by vigorous evolution of hydrogen fluoride and a dark red color. Good yields of ketones are usually obtained in the cyclobutane series when the fluorine atoms are conjugated with one or more double bonds, but examples have been observed for which this condition is neither necessary (2,3) nor sufficient (4-6) to promote hydrolysis.

Isolation of a ketone from this reaction is accomplished by pouring the hot acid solution over ice. The fact that the resulting ketone is not the species present in sulfuric acid solution has been demonstrated in at least one case (5). It is proposed that a study of the mechanism of this reaction be carried out in order to determine the nature of the intermediate which is present in the sulfuric acid solution. Following the techniques employed by Hart in his study of the sulfuric acid hydrolysis of pentamethylbenzotrichloride (7), this could be accomplished by collection and measurement of the evolved hydrogen fluoride, analysis of the ultraviolet spectrum of the solution, and determination of the van't Hoff i-factor in 100% sulfuric acid. The n.m.r. spectrum of the solution might also be instructive. It would also be of interest to investigate the action of other Lewis acids, such as boron trifluoride, on allylic gem-difluoro compounds.

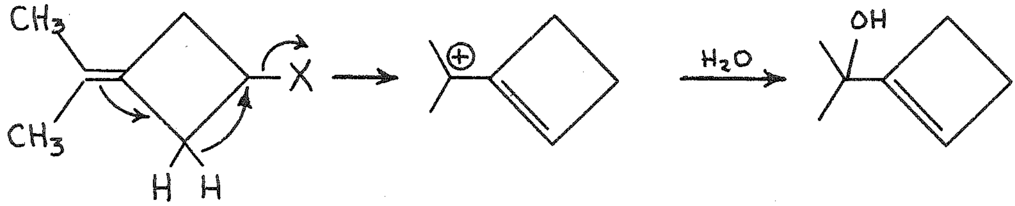
2. Walling and Peisach (8) have determined the molar volume of the transition state for the dimerization of isoprene at various pressures from the relationship:

$$\frac{d\ln k}{dP} = -\Delta V^{\ddagger}/RT$$

where $\Delta V^{\ddagger}$ represents the "activation volume." They suggested on the basis of their results that the transition state for this reaction involves an open-chain diradical. It is proposed that a similar study be made on the dimerization of fluorinated olefins to cyclobutanes, with the hope of shedding some light on the mechanism of the cycloaddition reaction (9).

3. One of the difficulties encountered in the present work (10) was in the estimation of the importance of 1,3-π-interaction in the 3-methylenecyclobutonium ion; the difficulty arose from a lack of information regarding various other factors which could contribute to solvolysis rate differences between cyclobutyl and aliphatic derivatives. It is therefore proposed that the relative solvolysis rates of arylsulfonate esters of 3-methylenecyclobutanol and 3-isopropylidinecyclobutanol be determined. If homoallylic resonance is possible in these systems, it should be more pronounced in the latter, due to the added electron-releasing capabilities of the two methyl groups on the exocyclic double bond, and such additional stabilization of the carbonium ion should be reflected in the

solvolysis rate. The great advantage in these systems lies in the elimination of rate variations due to factors other than 1,3-interaction, such as angle-strain and conformational effects. The rather striking ability of even one δ-methyl group to stabilize a non-classical homoallylic cation has been demonstrated by Sneen (11) in his study of 6-methylcholesteryl derivatives. If rate enhancement were observed in the solvolysis of 3-isopropylidinecyclobutyl derivatives, a product study would be necessary to determine whether β-hydrogen migration had occurred, however, since this type of rearrangement would lead to a stable tertiary carbonium ion:



A synthesis of 3-isopropylidinecyclobutyl p-toluenesulfonate from 1,1-dimethylallene (12) and vinyl benzoate is proposed.

4. Winstein and co-workers have had notable success (13) in reducing chlorinated "bird-cage" structures to the corresponding hydrocarbons with lithium and t-butanol in tetrahydrofuran; the method presumably involves the formation of an alkyllithium which reacts immediately with the proton donor to produce hydrocarbon and lithium t-butoxide. Alicyclic, vinylic, and bridgehead carbon atoms are apparently reduced indiscriminately. In the present work (14), a single attempt to reduce 1-methyl-

2-chloro-3,3-difluorocyclobutene by the Winstein method gave rise to chloride ion and a small amount of a pale, high-melting solid, but none of the expected product, 1-methyl-3,3-difluorocyclobutene, was isolated. No starting material was recovered. A more careful study of this reaction is proposed, particularly with regard to the nature of the non-volatile product(s).

5. H. C. Brown's hydroboration-oxidation method (15) for the hydration of olefins has been utilized by Winstein and co-workers (16) for the synthesis of homoallyl and homobenzyl alcohols and their derivatives. It is proposed that hydroboration of methylenecyclobutene (17), which should give rise to the unknown Δ^2-cyclobutenylcarbinol, be carried out. Derivatives of this homoallylic alcohol are expected to be very reactive in solvolysis, because of extensive possibilities for electron delocalization and rearrangement in the carbonium ion.

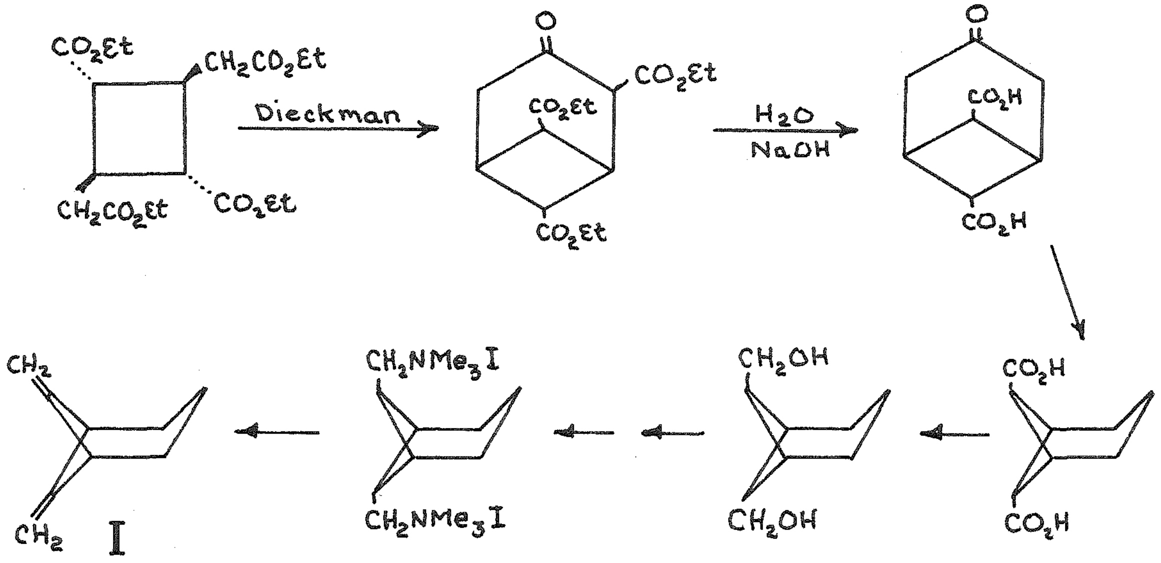
6. Several workers (18-20) have described in some detail the characteristic colors produced by aromatic compounds when dissolved in nitromethane containing a small amount of aluminum chloride or other strong Lewis acid. The colors were found (18) to be due to mono- or dipositive ions resulting from the transfer of one or two electrons from the aromatic compound to the Lewis acid-nitromethane system. Since the colors produced by this system seem to be more sensitive to minor structural variations than those in, for example, the rather undependable aluminum chloride-chloroform test (21), it is

proposed that reaction with aluminum chloride-nitromethane be investigated for use as a method of characterizing aromatic compounds in qualitative organic analysis.

7. Until quite recently, the synthesis of bicyclo (2,2,1) heptane derivatives substituted at the 7-position has often been quite difficult. A possible synthetic route to derivatives of this system is proposed, involving the condensation of malononitrile, perhaps in one step, with the di-_p_-toluenesulfonate of _cis_-1,4-dihydroxycyclohexane, in the presence of a non-nucleophilic base such as sodium triphenylmethide. Displacement of one of the tosyl groups by the anion of malononitrile would result in an intermediate with the proper stereochemistry for a second, transannular displacement, giving rise to 7,7-dicyanobicyclo(2,2,1)heptane. High dilution techniques might be required to prevent intermolecular condensation of the intermediate.

8. Caserio, Parker, Piccolini and Roberts (22) were unable to detect evidence for cross-ring interaction of the π-electrons in 1,3-dimethylenecyclobutane from spectral data. Electron-diffraction studies (23) subsequently showed that the molecule was essentially planar, thus prohibiting σ-type overlap of the _p_-orbitals. It is proposed that if this molecule were forced to assume a bent configuration by a hydrocarbon bridge connecting the 2- and 4-positions, more efficient orbital overlap at the 1- and 3-positions would result, which might be detectable by spectroscopy. A synthesis of 2,7-dimethylene-

bicyclo(3,1,1)-heptane (I) is proposed, as outline below.

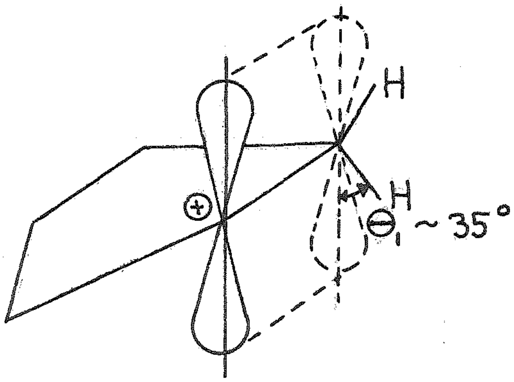


The starting material is available from the Michael reaction of diethyl glutaconate (24) or triethyl γ-carboxyglutaconate (25).

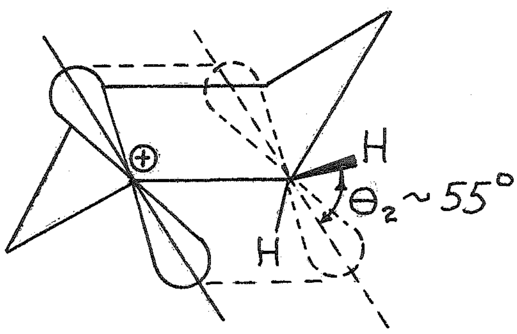
9. The β-deuterium isotope effect in carbonium-ion reactions has almost universally been attributed to hydrogen hyperconjugative stabilization of the transition state (26). Recently, Bartell (27) has postulated that isotope effects in solvolysis reactions, as well as differences in bond lengths and energies, can be accounted for by changes in non-bonded repulsions between substituents. His argument is based on the principle that the vibrational amplitudes of hydrogen atoms are larger than those of deuterium by a readily calculable amount, thus attributing a larger effective steric volume to hydrogen. His predicted isotope effects are claimed (the details have not yet been

published) (28) to be in good agreement with experimental values, in cases for which structural parameters are well known.

Non-bonded repulsions are known to be important in the quasi-planar (29) cyclopentane ring; relief of these repulsions is thought to contribute to the enhanced solvolysis rates of cyclopentyl derivatives. Relief of non-bonded repulsions is of little or no importance in the ionization of derivatives of cyclohexane. It is proposed that the acetolysis rates of cyclohexyl-2,2,6,6-$\underline{d}_4$ tosylate and cyclohexyl tosylate be studied and the β-isotope effect compared with the value of Streitwieser, *et.* *al.* (30) for the corresponding cyclopentyl derivatives. If the β-deuterium isotope effect is due to relief of non-bonded repulsions, the effect should be negligible in the cyclohexyl case, compared to the value of k_H/k_D = 2.06 obtained by Streitwieser. If the isotope effect is due to hyperconjugation, it should be roughly half as large in the cyclohexyl system because of the larger angle between the developing *p*-orbital and the α-C-H bonds.



(Cyclopentyl)$^{\oplus}$



(Cyclohexyl)$^{\oplus}$

Dotted Line = Projection of axis of *p*-orbital onto α-carbon.

This experiment would also provide a simple test of the angular dependence of hyperconjugation, in the absence of possible complications arising from anchimeric assistance (31).

10. Muller and Pritchard (32) and Shoolery (33) have recently shown that C^{13}-H splittings in nuclear magnetic resonance spectra of hydrocarbons are directly proportional to the degree of s-character in the C^{13}-H bond. Their data give remarkably consistent results for certain alkanes, alkenes, alkynes, aromatics, and alkyl halides and for acetaldehyde. It has also been shown (32) that the C^{13}-H coupling constants are quite insensitive to changes in the bond polarity. It is proposed that the n.m.r. spectrum of 7-norbornadienol (34), as a concentrated solution in boron trichloride or 100% sulfuric acid, be observed at high gain, and the C^{13}-H coupling constant measured, if possible, in order to gain information as to the hybridization at C-7 of the proposed norbornadienyl non-classical ion (34,35).

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