THE UNIVERSITY OF ALBERTA

THE PREPARATION AND HYDRIDE REDUCTION OF SOME C-2 SUBSTITUTED-1,3-DIOXOLANES.

by

HARRY ALLAN DAVIS

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The undersigned certify that they have read, and recommend to the Faculty of Graduate Studies for acceptance, a thesis entitled

THE PREPARATION AND HYDRIDE REDUCTION OF SOME C-2 SUBSTITUTED-1,3-DIOXOLANES.

submitted by HARRY ALLAN DAVIS, in partial fulfilment of the requirements for the degree of Doctor of Philosophy.

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ABSTRACT

PART I

In the mixed hydride hydrogenolysis of some 1,3-dioxolanes, it was found that only one hydride ion of the reagent $AlClH_2$ was reactive in the hydrogenolysis of these compounds.

The rate of the mixed hydride hydrogenolysis of some C-2 substituted-1,3-dioxolanes with a heteroatom (O, S, N, Br) β to the anomeric carbon was found to be retarded compared to the rate for 2-methyl-1,3-dioxolane. This rate retardation was attributed to: (a) the electronegativity of the heteroatom causing destabilization of the intermediate carbonium ion and (b) the association of the reducing species with the p electrons of the substituent heteroatom.

The hydrogenolysis of some 2-vinyl- and 2-phenyl-1,3-dioxolanes with $AlClH_2$ was found to be a faster reaction than that for 2-methyl-1,3-dioxolane. These findings were attributed to the greater ease of formation of the carbonium ion intermediate in the above mentioned molecules due to the additional allylic or benzylic stabilization. Also, the 2-vinyl-1,3-dioxolanes were found to undergo hydrogenolysis with $LiAlH_4$ alone in the solvents 1,2-dimethoxyethane and di-n-propyl ether at elevated temperatures. Evidence for Li cation participation in opening of the dioxolane ring was found.

The hydrogenolysis of two norbornenyl-1,3-dioxolanes with $AlClH_2$ was found to be slower than that of the saturated analog. This retardation was attributed to the peculiar geometry of these

molecules permitting the reducing species to form a strong association with the π lobes of the double bond and the p electrons of the oxygen atom thus decreasing the effective concentration of the Lewis acid reducing species.

PART II

In the potassium t-butoxide catalyzed dehydrobromination of some α-bromo dialkyl- and ethyleneacetals in t-butyl alcohol, it was found that the anomeric hydrogen was removed by base if this hydrogen atom is sterically available. In the dialkyl acetals, proton removal occurred preferentially at the β carbon atom due to the steric hindrance to approach to the anomeric centre as a result of the freely rotating alkoxyl moieties of the acetal. Proton removal at the anomeric carbon was found to occur preferentially in the ethyleneacetals due to the steric availability of the anomeric hydrogen as a result of the fixed structure of the 1,3-dioxolane ring.

The site of proton removal in the ethyleneacetals was found to be changed in the solvent dimethylsulfoxide. In this solvent, more proton removal occurred at the β carbon atom. This observation was attributed to a change in the mechanism of the elimination in this solvent due to the more basic nature of the alkoxide ions in dimethylsulfoxide. The increase in base strength increased the amount of C-H stretching in the transition state thus lending El_{CB} character to the elimination reaction.

No isomerization of the ketene acetals to the α,β-unsaturated acetals was observed in this work.

ACKNOWLEDGEMENTS

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PART II

PART I

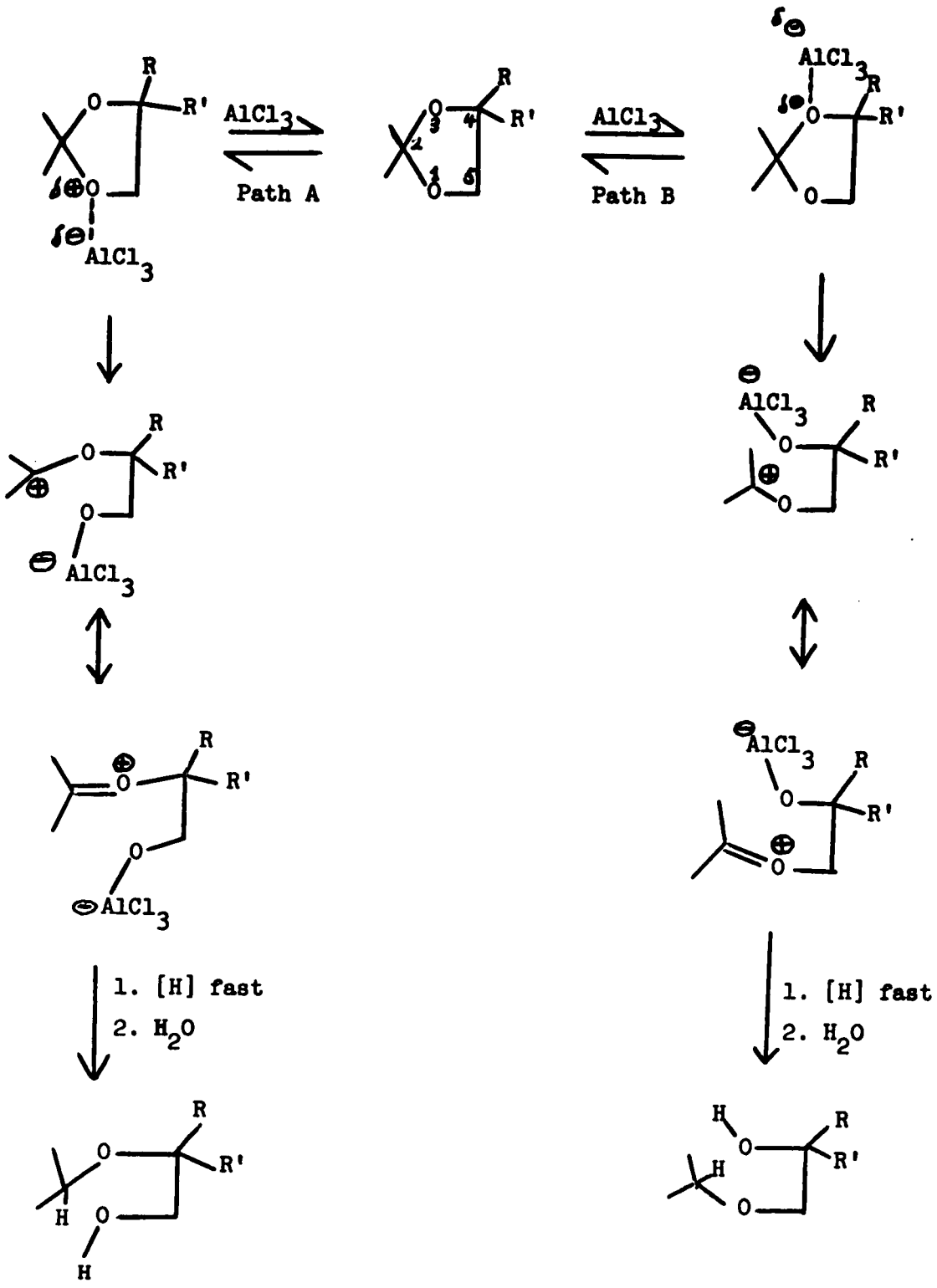
HYDROGENOLYSIS OF SOME C-2 SUBSTITUTED-1,3-DIOXOLANES

INTRODUCTION

A. The Problem

A considerable amount of work has been reported on the hydrogenolysis of 1,3-dioxolanes (1) and 1,3-dioxanes (2) with the mixed hydride reagents (a mixture of $LiAlH_4$ and $AlCl_3$). Leggetter and Brown (1) proposed that the polar effect of substituents on C-4 and C-5 of the dioxolane ring could stabilize or destabilize the intermediate carbonium ion, believed to be formed as one step of the reaction, and thus affect the direction of C-O bond cleavage. The mechanistic sequence proposed by Leggetter and Brown (1) for the two possible directions of cleavage of the dioxolane ring are shown in Scheme 1. Cleavage by Path A is favored if R and R' are electron donating groups, due to the greater stabilization of the intermediate oxocarbonium ion, while Path B is favored when R and R' are electron withdrawing groups because the oxocarbonium ion formed in Path A would be destabilized compared to that in Path B.

Leggetter and Brown (1) also reported that substituents on C-2 of the dioxolane ring had a greater effect on the rate of reductive cleavage than did the same substituents situated on any



Scheme 1

other ring carbon atom. They found electron donating substituents (methyl and phenyl) attached to C-2 accelerated the cleavage whereas electron withdrawing groups (chloromethyl and dichloromethyl) on C-2 retarded the reductive cleavage.

The purpose of the present investigation was to synthesize a number of 1,3-dioxolanes with C-2 substituents which could participate in the formation and stabilization of the oxocarbonium ion. As well it was hoped to determine if groups suitably chosen and situated in the substituent attached to C-2 would provide any anchimeric assistance in stabilizing the formation of the oxocarbonium ion and hence accelerate the reductive cleavage. Such substitution was necessarily limited by the condition that the functional groups chosen must also be stable to the reducing agent.

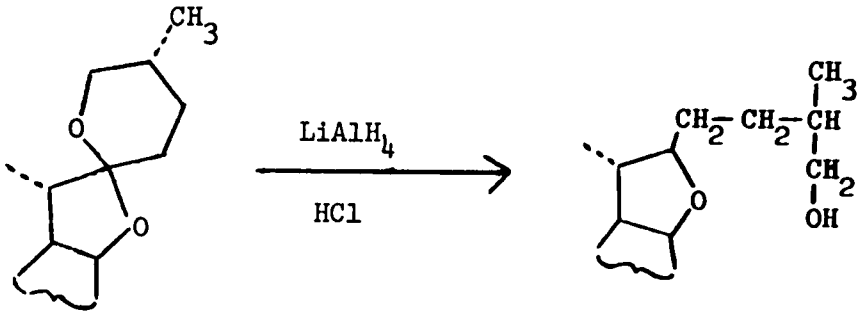
B. Literature Survey

1. Brief History of the Development of the Hydrogenolysis of Acetals and Ketals.

The introduction of $LiAlH_4$ as a reducing agent (3) led to a facile method for the reduction of many functional groups in organic molecules, especially the carbonyl group. Ethers were generally used as solvents for the reduction reactions as they were found to be inert to this reagent. This stability of ethers to $LiAlH_4$ led to the practice of protecting the carbonyl group of aldehydes and ketones against reduction by converting them to acetal or ketal derivatives (which are simply geminal diethers) so that the reduction

of other functional groups in the molecule could be carried out leaving the carbonyl group unaffected. Gaylord (4) has made an extensive review of the use of hydrides in these and in many other reactions.

The addition of acid, however, was found to drastically change this reducing system. In 1953, Doukas and Fontaine (5) found that spirostanols could be reduced to furostanols by $LiAlH_4$ in an ether solution saturated with HCl or HBr (Scheme 2). The change in



Scheme 2

properties of this reducing system with the addition of acid was attributed to the <u>in situ</u> formation of $AlCl_3$ which then formed a $LiAlH_4$-$AlCl_3$ complex thought to be the reactive reducing species (6). A mixture of $LiAlH_4$-$AlCl_3$ (the mixed hydride) has been used since that time to reduce a variety of acetals, ketals, hemithioacetals and hemithioketals (7,8). A review of these reactions has been published by Eliel (9).

2. <u>Nature of the Reducing Species</u>

The presence of AlH_3 was reported by Finholt and coworkers (10) in 1947 who found that the reaction of a 3 to 1 molar ratio of $LiAlH_4$ and $AlCl_3$ gave solutions of the unstable AlH_3. More recently, Ashby and Prather (11) have shown that AlH_3, $AlClH_2$ or $AlCl_2H$ are

formed respectively from 1 to 3, 1 to 1, and 3 to 1 molar ratio mixtures of $AlCl_3$ and $LiAlH_4$. Equations illustrating the formation of these hydride species are shown below. These hydride species were

$$3\ LiAlH_4 + AlX_3 \longrightarrow 4\ AlH_3 + 3\ LiX$$

$$LiAlH_4 + AlX_3 \longrightarrow 2\ AlXH_2 + LiX$$

$$LiAlH_4 + 3\ AlX_3 \longrightarrow 4\ AlX_2H + LiX$$

where X = I, Br, Cl

characterized by elemental analysis of the respective triethylamine adducts isolated from a benzene solution. It was also reported by Ashby and Prather (11) that each of the triethylamine adducts of these three hydride species in benzene solution exhibited a characteristic infrared absorption band due to the Al-H stretching frequency. These were positioned at 5.6 μ, 5.4 μ and 5.27 μ for AlH_3, $AlClH_2$ and $AlCl_2H$ respectively. A recent report from these laboratories (12) showed that ether solutions of these three hydride species exhibited similar absorption bands (5.59 μ, 5.39 μ and 5.23 μ respectively) where the hydride species would be present as a diethyl ether adduct. It was also shown (12) that the interconversion of the hydride species was a fast and reversible reaction as shown below. This interconversion could be accomplished by the addition

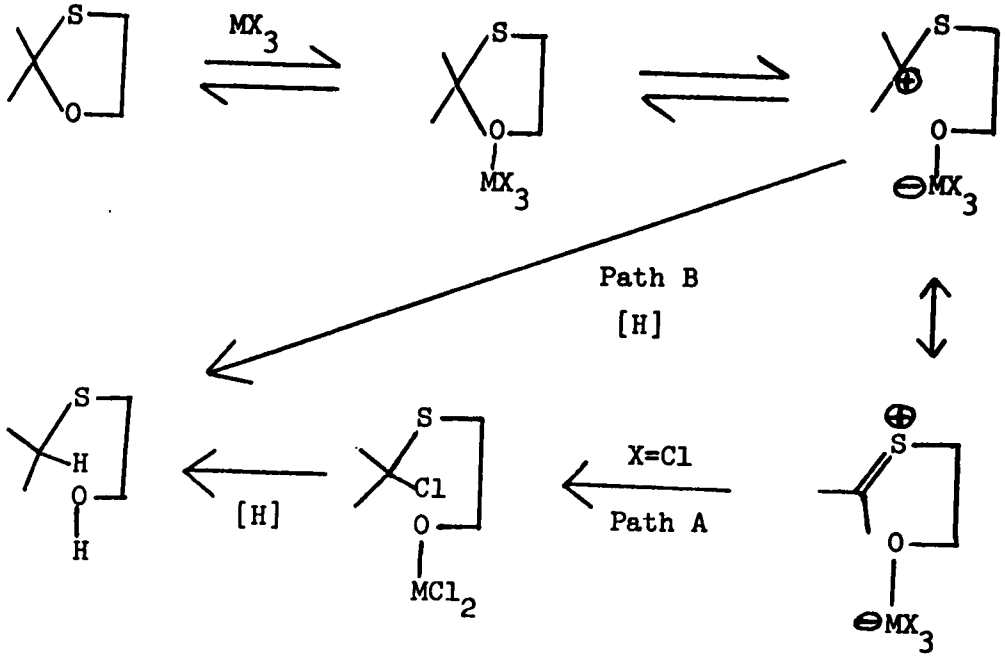
$$AlH_3 \rightleftharpoons AlClH_2 \rightleftharpoons AlCl_2H$$

of appropriate amounts of $LiAlH_4$ or $AlCl_3$ to solutions of any one of the above mentioned hydride species and could be followed by the appearance and disappearance of the corresponding absorption band in the infrared spectrum.

3. Hydrogenolysis of Acetals and Ketals

The hydrogenolysis of acetals and ketals has been proposed to proceed via an oxocarbonium ion (13), a possibility that Eliel (6) had also considered previously. Initially it had been proposed (8) that in the reduction of the ethylene hemithioketal of 4-t-butylcyclohexanone, an α-chlorothioether intermediate was formed which was then easily reduced by $LiAlH_4$ to the observed product (Scheme 3, Path A). Eliel (8) had proposed the formation of the α-chlorothioether in the reaction with $AlCl_3$ and $LiAlH_4$ because when a similar reaction was done using BF_3 in the place of $AlCl_3$ no reduction occurred. He attributed the lack of reaction in the latter case to the fact that the fluorine atom of BF_3 is not as nucleophilic as is the chlorine atom of $AlCl_3$ (14) and thus the α-fluorothioether intermediate was not formed.

Leggetter and Brown (13) showed, however, that a prior mixing of BF_3 and the oxathiolane followed by addition of $LiAlH_4$ did result in reductive cleavage. The sequence of addition of reagents used by Eliel et. al. (8) involved the initial formation of a mixture of $LiAlH_4$ and BF_3 to which was then added the oxathiolane. This procedure first produced BH_3 which, because of its insolubility in the solvent, was lost before reduction of the hemithioketal could occur and hence accounts for the lack of reduction observed by Eliel (8). Since reduction was obtained with the BF_3-$LiAlH_4$ system (13), the main argument supporting the initial formation of an α-haloether was no longer valid. Leggetter and Brown (13) thus proposed, simply, a direct reduction of the intermediate oxocarbonium ion (Path B, Scheme 3).



Scheme 3

An extensive investigation into the reductive cleavage of acetals and ketals was also carried out by Leggetter and Brown (1) in a search for the factors influencing the direction and ease of ring cleavage. The observed results were found to be best explained by polar and inductive effects of the various substituents in their ability to stabilize the transition state leading to the oxocarbonium ion. The mechanistic scheme proposed to explain the results is shown in Scheme 1 and is quite similar to Scheme 3 (Path B) which was also proposed by Leggetter and Brown (13) for the hydrogenolysis of oxathiolanes.

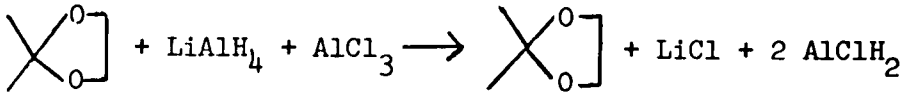
As previously mentioned, electron donating groups R and R' on C-4 or C-5 of the dioxolane ring favor cleavage by Path A (Scheme 1) as they assist the adjacent oxygen atom in stabilization of the

transition state leading to the intermediate oxocarbonium ion whereas electron withdrawing groups, R and R', favor cleavage by Path B (Scheme 1). The latter result is due to the destabilizing effect these electron withdrawing groups would have on the transition state leading to the intermediate oxocarbonium ion produced in Path A (Scheme 1). Since it is the relative ease of formation of these two intermediate oxocarbonium ions which determines the product ratios, their rate of formation was considered to be the rate determining step in the reductive cleavage of acetals and ketals. This assumption was further verified (15) when no isomerization was observed in the recovered cis or trans-2,4-dimethyl-1,3-dioxolane obtained from partial hydrogenolysis. This demonstrates that the formation of the oxocarbonium ion is the slow step and that the oxocarbonium ion is immediately reduced before it can revert to the other isomer.

The rate controlling formation of the oxocarbonium ion has also been demonstrated by Zajac and Byrne (16) in a study of the relative rates of hydrogenolysis of some cycloalkanone dimethyl ketals to the corresponding cycloalkyl methyl ethers using $AlCl_2H$ as the reducing agent. The order of reactivity was consistent with the concept of I (internal) strain and it was concluded that the formation of the oxocarbonium ion is the rate controlling step in the hydrogenolysis reaction.

RESULTS AND DISCUSSION

The procedure used for the hydrogenolysis of the acetals and ketals in this work was a modification of the method used by Leggetter and Brown (1) in the initial studies on reactions of this type. The original work by these authors involved the prior mixing of one mole of the acetal to be reduced and one mole of $LiAlH_4$ in an ether solution followed by the dropwise addition of one mole of $AlCl_3$ in an ether solution. This procedure resulted in the acetal first coming into contact with AlH_3 and then, as more $AlCl_3$ solution was added, with $AlClH_2$ as was reported by Diner, Davis and Brown (12). With a slow-reacting acetal, little if any reaction occurs in the presence of the AlH_3 before this hydride species is converted into $AlClH_2$. However, with more reactive acetals, substantial reduction can occur with the initially formed AlH_3. Also, by using these proportions, an excess of $AlClH_2$ was formed as is shown in Scheme 4.



Scheme 4

To simplify the reaction conditions in this work, the desired mixed hydride was first formed in ether solution by mixing ether solutions of the appropriate molar proportions of $LiAlH_4$ and $AlCl_3$. The acetal to be reduced was then added in the amount required to give a one to one molar ratio of acetal to mixed hydride. This

procedure had two distinct advantages over that used by Leggetter and Brown (1). First, reduction takes place by one known species in an equimolar amount with respect to the acetal, and second, the two vigorous reactions of mixed hydride formation and acetal reduction were not occurring at the same time. As a result, the acetal could be added to the reducing species at a rate much faster than the addition of a solution of $AlCl_3$ to the $LiAlH_4$-acetal solution.

The work-up procedure was also modified from that reported by Leggetter and Brown (1). Instead of the addition of an excess of water followed by continuous extraction of the resulting aqueous solution, a 15 per cent aqueous solution of potassium hydroxide was added until no further reaction was observed and a white, granular precipitate of lithium aluminate ($LiAlO_2$) resulted. This method of decomposing $LiAlH_4$ reduction complexes had previously been found to be the preferred procedure (17). The white precipitate was then simply removed by suction filtration and the ether removed by distillation giving recovered yields of 80 to 95 per cent. Only in the cases where the recovery was poor and for the competitive hydrogenolysis reactions, where maximum recovery was desired, was the continuous extraction procedure of Leggetter and Brown (1) employed.

The hydrogenolysis reactions were usually done on small amounts of material and the recovered product mixtures were analyzed by gas liquid chromatography (g.l.c.), comparing the retention times of the products with those of authentic materials. If there was any doubt as to the identity of a reaction product, the material was

isolated by preparative g.l.c. and identified by its n.m.r. and i.r. spectra and its elemental analysis. The identification of the unknown products from the hydrogenolysis of the various 2-substituted-1,3-dioxolanes was facilitated by the knowledge that the products would be 2-substituted ethanol molecules if the reduction went in the normal manner.

The relative peak areas of the hydrogenolysis products found on g.l.c. were used to determine the product ratios with no corrections applied. The difference in peak size for equimolar amounts of hydrogenolysis products was checked in a number of cases using equimolar amounts of authentic hydrogenolysis products and in the cases checked there was found to be at most a 10 per cent variation in peak size but normally the variation was within 5 per cent. Since the proportions of hydrogenolysis products were usually well outside of this range, no correction was applied to give an exact indication of the molar ratio of the products.

The mechanistic scheme proposed by Leggetter and Brown (1) to explain the direction of hydrogenolysis of 1,3-dioxolanes (Scheme 1) was used here to explain the change in relative rates of hydrogenolysis of dioxolanes differing in the substituent at C-2 of the dioxolane ring. As previously mentioned, the formation of the oxocarbonium ion intermediate as shown in Scheme 1 is facilitated by electron donating groups R and R' on C-4 or C-5. Leggetter and Brown (1) also reported that the rate of hydrogenolysis was affected to a greater extent by the nature of the substituent on C-2 of the dioxolane ring as

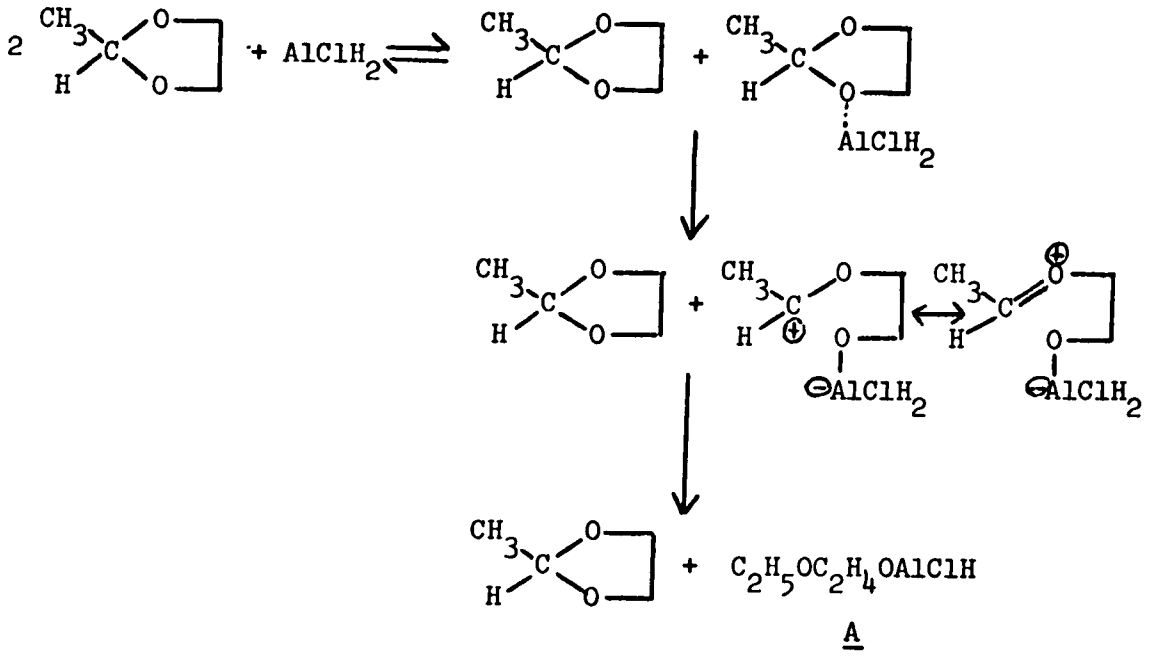
compared to the effect of C-4 substitution on the rate. In order to determine the extent of participation of substituents on C-2 of the dioxolane ring with respect to the reactivity of the acetal towards hydrogenolysis, a number of C-2 substituted 1,3-dioxolanes were synthesized and subjected to hydrogenolysis with the mixed hydride species AlH_3 and $AlClH_2$. Competitive hydrogenolyses were also carried out to determine the relative reactivity of the acetals to hydrogenolysis. A mixture of equimolar amounts of two acetals was reduced with an equimolar amount of mixed hydride and the reaction mixture was analyzed by g.l.c. for the extent of reaction of the two starting acetals. In this way, relative rates were determined for a number of the compounds studied. Each acetal was competitively reduced at least twice, either both times against a second acetal or against two different acetals which had themselves been subjected to competitive reduction with each other.

1. Determination of the Number of Hydride Ions Available for Reduction by the Mixed Hydride $AlClH_2$

In the hydrogenolysis experiments carried out in this work equimolar amounts of the mixed hydride and acetal were used. When $AlClH_2$ was used as the reducing species in an equimolar proportion to the dioxolane, two hydride ions could be available for the reduction of the acetal. In an attempt to determine if both or only one of the hydride ions of $AlClH_2$ are available for reduction, the following investigation was performed.

The reduction of 2-methyl-1,3-dioxolane was carried out

using a 2 to 1 molar ratio of acetal to $AlClH_2$. Only 50 per cent reduction was observed under these conditions even after an extended reaction time of 48 hours. (This acetal is normally completely reduced in less than 30 minutes by an equimolar amount of this reducing species). On the basis of the mechanism proposed by Leggetter and Brown (1), the reduction of 2-methyl-1,3-dioxolane would result in the formation of an intermediate alkoxyhydridoaluminum chloride as shown in Scheme 5. After reduction of one-half of the 2-methyl-1,3-dioxolane, a one to one mixture of the intermediate alkoxyhydridoaluminum chloride A (Scheme 5) and starting acetal would result.



Scheme 5

Alkoxyaluminum hydrides have been postulated as intermediates in the reduction of epoxides involving mixed hydride reagents (11, 18). Recently Cooke, Ashby and Lott (19) have prepared authentic

alkoxyaluminum hydrides in tetrahydrofuran solution by the reaction of AlH_3 and the desired alcohol in the proper stoichiometric ratio, and have used these species for the reduction of some epoxides. The slower reaction of the epoxides with the alkoxyaluminum hydrides and the decrease in the amount of rearrangement products by using these species as compared to the results obtained using the hydridoaluminum chlorides was attributed to the difference in the Lewis acidity of these two types of mixed hydrides. The hydridoaluminum chlorides, due to their greater Lewis acidity, cause faster epoxide opening and give a greater amount of rearrangement products than is found with the alkoxyaluminum hydrides (19). The decrease in Lewis acidity of the alkoxyaluminum hydrides was attributed to the association of these species through bridging of the alkoxy groups (19) as shown in Figure 1.

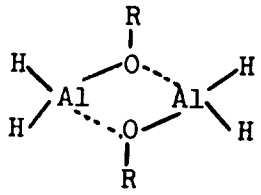


Figure 1

On the basis of the work of Cooke, Ashby and Lott (19), the proposed intermediate alkoxyhydridoaluminum chloride expected from the reduction of 2-methyl-1,3-dioxolane with $AlClH_2$ (A, Scheme 5) was actually formed in a separate experiment by the addition of one molar equivalent of 2-ethoxyethanol to an ether solution of $AlClH_2$. The acetal, 2-methyl-1,3-dioxolane, was then added and the mixture stirred at room temperature for 48 hours. At the end of this time

no reduction was observed. Reduction of benzaldehyde with this reducing species (A of Scheme 5), however, was found to be a fast reaction giving total conversion to benzyl alcohol in less than one hour. The hydride ion of the intermediate species A (Scheme 5) therefore appears to be reactive in the reduction of compounds where no Lewis acid character is necessary.

The ease of reduction of some acetals was then investigated using the alkoxyhydridoaluminum chloride formed by the addition of one molar equivalent of ethyl alcohol to an ether solution of $AlClH_2$ (Scheme 6). The results for these reductions along with the results

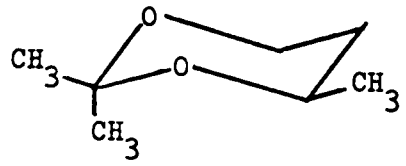
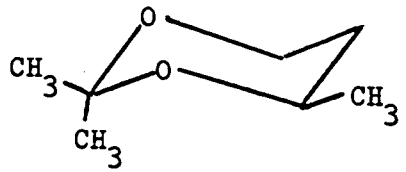
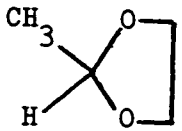
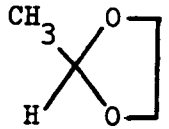
$$AlClH_2 + C_2H_5OH \longrightarrow AlClH(OC_2H_5) + H_2$$

Scheme 6

for the $AlClH_2$ reductions of the same molecules are shown in Table 1. As can be seen from the results of Table 1, the ease of reduction of these acetals by either $AlClH_2$ or $AlClH(OC_2H_5)$ are practically the same. This observed similarity in reducing ability of these two reducing species as compared to the difference in properties of AlH_3 and $AlH_2(OC_2H_5)$ as reported by Cooke, Ashby and Lott (19) may be due to the greater Lewis acidity of the chlorine substituted species giving more facile ring opening and hence faster reduction. The greater reactivity of the chlorine substituted species ($AlClHOC_2H_5$) was demonstrated by the observation that the reduction of 2,2,4-trimethyl-1,3-dioxane with $AlH_2(OC_2H_5)$, prepared by the method of Cooke, Ashby and Lott (19), was only 60 per cent complete in 16 hours.

Table 1

Reductions of some acetals with $AlClH_2$ and with $AlClH(OC_2H_5)$.

Experiment Number	Compound	Time, Hours	Reducing Species	Amount of Reduction %	Total Recovery %	Products	Relative Amounts %
1		0.25	$AlClH_2$	98	90	ROH R'OH	80 20
2		0.25	$AlClH(OC_2H_5)$	90	90	ROH R'OH	80 20
3		0.5	$AlClH_2$	100	85	$C_2H_5OC_2H_4OH$	
4		0.5	$AlClH(OC_2H_5)$	100	87	$C_2H_5OC_2H_4OH$	

R = $(CH_3)_2CHOCH(CH_3)CH_2CH_2$

R'= $(CH_3)_2CHOCH_2CH_2CH(CH_3)$

The observed reactivity of $AlClH(OC_2H_5)$ in its rapid hydrogenolysis of acetals as compared to the stability of 2-methyl-1,3-dioxolane when treated with $AlClH(OC_2H_4OC_2H_5)$ implied the possibility of an intramolecular Lewis acid-base complex (Figure 2) which would prevent the necessary complexation of the aluminum species with the oxygen atoms of the dioxolane ring. Evidence for this

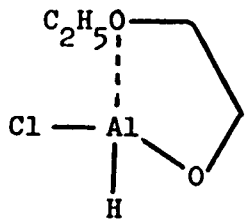


Figure 2

intramolecular complex formation was obtained by synthesizing the corresponding reducing species with a thioether linkage (Scheme 7).

$$AlClH_2 + CH_3SC_2H_4OH \longrightarrow AlClH(OC_2H_4SCH_3) + H_2$$

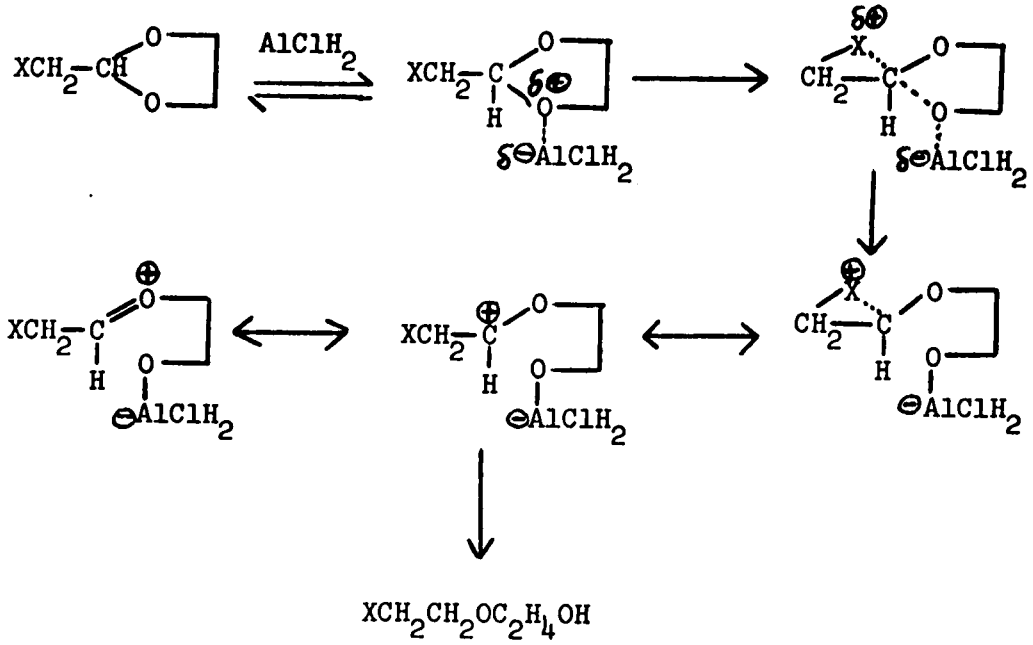
Scheme 7

Leggetter and Brown (13) and Eliel and coworkers (8) had previously shown that in the mixed hydride hydrogenolysis of some 1,3-oxathiolanes, ring cleavage always occurred at the C-O bond. This observation was attributed to the greater tendency of the hydridoaluminum chloride reducing species to complex with the oxygen atom than with the sulfur atom. With the alkoxyhydridoaluminum chloride formed in Scheme 7, the internal Lewis acid-base complex analogous to that shown in Figure 2 was thus expected less likely to occur. Using this species for the hydrogenolysis of 2-methyl-1,3-dioxolane, 50 per cent reduction was observed in one hour. These results thus show that in the

hydrogenolysis of 1,3-dioxolanes, only one hydride ion of the mixed hydride $AlClH_2$ is available for the reduction of these compounds. This is believed to be due to the formation of a strong intramolecular oxygen-aluminum association in the intermediate aluminum species which decreases the Lewis acid character of the intermediate and hence inhibits further reaction.

2. Hydrogenolysis of Some C-2 Substituted-1,3-dioxolanes Containing a Heteroatom β to the Anomeric Carbon.

The enhancement of reaction rate due to participation of neighboring groups has been recognized for some time (20, 21). For such rate enhancement to occur, participation of the neighboring group must take place during the rate determining step of the reaction. The rate determining step in the hydrogenolysis of 1,3-dioxolanes, has been shown to be the formation of the oxocarbonium ion intermediate. In order to investigate the possible participation in formation of the aforementioned intermediate oxocarbonium ion by various cyclic "onium" ions, a number of C-2 substituted-1,3-dioxolanes were synthesized which contained a heteroatom β to the anomeric carbon. The heteroatoms tried were oxygen, sulfur, nitrogen and bromine. The participation of these atoms in assisting in the formation of carbonium ion intermediates is well known and is shown in Scheme 8 for the possible participation in formation of the intermediate carbonium ion, considered to be the rate controlling step in the hydrogenolysis of 1,3-dioxolanes. If such stabilization in the formation of the intermediate carbonium ion occurred during the rate controlling step



X = O,S,N or Br.

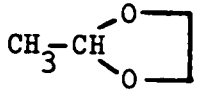
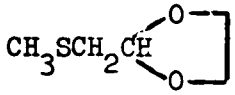
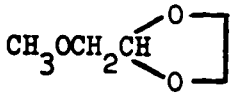
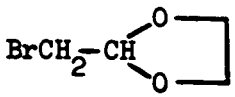
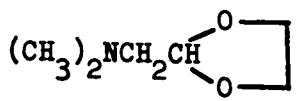
Scheme 8

of this hydrogenolysis, an increase in the overall rate of hydrogenolysis would be expected. The results of the hydrogenolysis of some of these compounds are shown in Table 2.

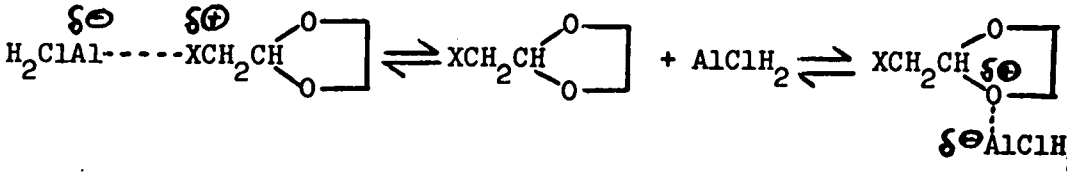
From the results in Table 2 it can be seen that the presence of a heteroatom β to the anomeric centre causes a rate retardation compared to the rate of hydrogenolysis of a simple C-2 alkyl-substituted compound such as 2-methyl-1,3-dioxolane. Such a rate retardation can be explained either by the electronegative effect of these substituents causing destabilization of the intermediate carbonium ion or by the reversible complexation of the $AlClH_2$ with the p electrons of the heteroatom of the C-2 substituent as well as with the dioxolane ring oxygen atoms as shown in Scheme 9.

Table 2

Hydrogenolysis by $AlClH_2$ of some C-2 substituted-1,3-dioxolanes containing a heteroatom β to the anomeric carbon.

Experiment Number	Compound	Time, Hours	Amount of Reduction %	Total Recovery %	Products
1		0.5	100	90	$C_2H_5OC_2H_4OH$
2		0.5	45	90	$CH_3SC_2H_4OC_2H_4OH$
3		24	70	90	$CH_3OC_2H_4OC_2H_4OH$
4		24	17	90	$BrC_2H_4OC_2H_4OH$
5		24	0	30*	

* This recovery could not be improved.



Scheme 9

This would also slow the rate of ring cleavage and hence hydrogenolysis. Such a complex formation with the nitrogen atom of the compound 2-(N,N-dimethylaminomethyl)-1,3-dioxolane would be very strong and probably irreversible and thus explains the lack of hydrogenolysis observed in this case.

The effect of the sulfur and oxygen substituents on the rate of hydrogenolysis of these compounds is similar to that observed by Speck, Rynbrandt and Kochevar (22) reported in their study of the rate of hydrolysis of some diethyl acetals. The results of their work are shown in Table 3. These authors suggested that the rate

Table 3

Rate of hydrolysis of some diethyl acetals.

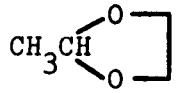
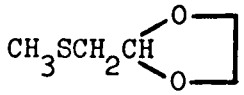
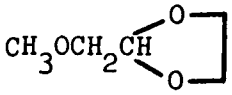
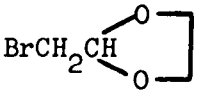
Compound	k 1. mole^{-1}sec.$^{-1}$
$CH_3CH(OC_2H_5)_2$	0.254
$CH_3OCH_2CH(OC_2H_5)_2$	2×10^{-4}
$C_2H_5OCH_2CH(OC_2H_5)_2$	2×10^{-4}
$CH_3SCH_2CH(OC_2H_5)_2$	2.33×10^{-2}

retardation observed for the substituted acetaldehyde diethylacetals was due to the electronegativity of the substituents resulting in destabilization of the formation of the intermediate carbonium ion.

The larger rate retardation observed for the alkoxy substituted compounds as compared to that found for the sulfur analog was attributed to the more likely protonation of the oxygen atom than the sulfur atom. In order to compare the relative effect of these substituents on the rate of hydrogenolysis of the 1,3-dioxolanes, some competitive hydrogenolyses were carried out. The results of these experiments are shown in Table 4.

Table 4

Relative rates of hydrogenolysis by $AlClH_2$ of some C-2 substituted-1,3-dioxolanes containing a heteroatom β to the anomeric carbon.

Compound	Relative rate
	1
	0.15
	0.02
	<0.02

The difference in observed relative rates between the alkoxy substituted compound and the sulfur analog is similar to the results obtained by Speck et. al. (22). The rate retardation observed for 2-(methylthiomethyl)-1,3-dioxolane is probably due simply to the electronegativity of this substituent since complexation of the reducing species ($AlClH_2$) with the sulfur atom has previously been

shown (8, 13) not to occur to any significant extent when the reaction solvent is ether. The further decrease in rate observed for the hydrogenolysis of 2-methoxymethyl-1,3-dioxolane may be partly due to the complexation of the reducing species with the substituent oxygen atom as shown in Scheme 9. The great rate retardation observed for the hydrogenolysis of 2-bromomethyl-1,3-dioxolane is at first unexpected on the basis of the electronegativity of the heteroatomic substituents (O,3.50; Br, 2.95; S, 2.60) (23). The effect due to a bromine substituent on the rate of hydrogenolysis would be expected to be intermediate between the effect observed for the oxygen and sulfur substituted compounds if electronegativity was the only retarding effect. The much greater effect observed for the bromine substituent may thus be due to formation of a complex as shown in Figure 3. Complexes of this type between an alkyl halide and a

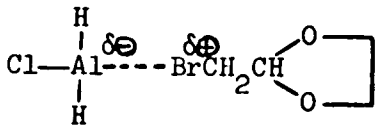


Figure 3

Lewis acid are well known in the Friedel-Crafts alkylation.

Thus the effect of heteroatoms situated on the carbon atom attached to the anomeric carbon is one of retardation of the rate of hydrogenolysis of the relevant 1,3-dioxolanes. This appears to be due to the electronegativity of the substituent and the ability of the heteroatom to complex with the reducing species. There seems to be no tendency of the atoms to form cyclic onium ions to stabilize the formation of the intermediate carbonium ion.

3. Hydrogenolysis of 2-Substituted -1,3-dioxolanes in which the Anomeric Carbon is α to a Vinyl or Phenyl Group.

Leggetter and Brown (1) reported that the hydrogenolysis of 2-phenyl-1,3-dioxolane with a 1:1 molar ratio of $LiAlH_4$ and $AlCl_3$ was much faster than the hydrogenolysis of 2-methyl-1,3-dioxolane under the same conditions. In the current work, a further investigation was carried out to determine the effect which a number of substituted vinyl and phenyl systems attached to C-2 of the dioxolane ring might have on the rate of hydrogenolysis of the dioxolane ring. These molecules were subjected to reduction first with $LiAlH_4$ alone to see if the Lewis acid, $AlCl_3$, was necessary to effect reduction in these systems. The results of these reductions are shown in Table 5.

Although reduction of carbon-carbon double bonds does not normally occur with $LiAlH_4$, reduction of olefinic bonds in α,β-unsaturated carbonyl systems with this reagent has been known for some time. Also, while reduction with $LiAlH_4$ normally gives 1,2 addition of this reagent, the reduction of α,β-unsaturated ketones such as the dibenzoylethylenes proceeds with 1,4-addition to the conjugated unsaturated system (24,25). The attack of the hydride occurs by a Michael addition and this is most likely a result of the strong polarization of the double bond due to the conjugated carbonyl group as shown in Figure 4 facilitating hydride donation at the β carbon atom.

Table 5

Hydrogenolysis of some C-2 vinyl or phenyl substituted-1,3-dioxolanes with $LiAlH_4$ in ether[a].

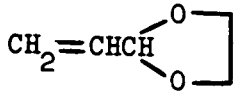
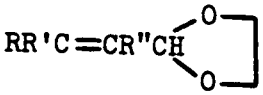
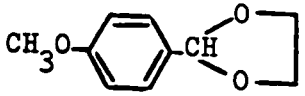
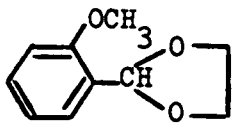
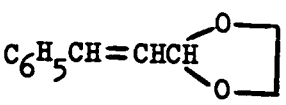
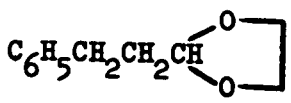
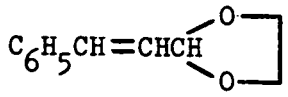
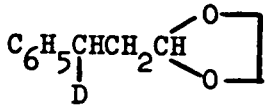
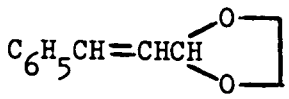
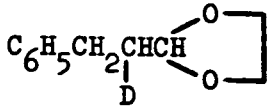
Experiment Number	Compound	Time, Hours	Amount of Reduction %	Total Recovery %	Products
1		24	32	80	$CH_3CH{=}CHOC_2H_4OH$
		48	76	80	
2(a-d)[b]		96	0	85	
3		72	0	90	
4		144	0	90	
5		24	100	90	

Table 5-Continued

Experiment Number	Compound	Time, Hours	Amount of Reduction %	Total Recovery %	Products
6[c]		24	100	90	
7[d]		24	100	90	

a. Reaction was done at room temperature in all cases.

b. 2a R = CH_3, R' = R" = H

2b R = R' = H, R" = CH_3

2c R = C_2H_5, R' = R" = H

2d R = R' = CH_3, R" = H

c. D_2O was used in the work-up of this reaction.

d. $LiAlD_4$ was used for the reduction followed by H_2O work-up.

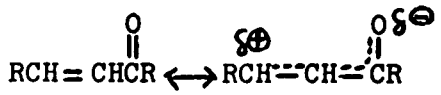


Figure 4

Such polarization may also be present to a small extent in α,β-unsaturated-1,3-dioxolanes due to the electronegativity of the oxygen atoms of the dioxolane ring as shown in Figure 5. This type

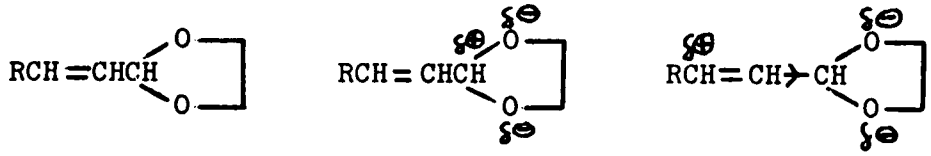


Figure 5

of polarization would be much less in these molecules as compared to the polarization present in the carbonyl precursors since in the carbonyl compounds the oxygen atom is in direct conjugation with the carbon-carbon double bond. The polarization of the α,β-unsaturated-1,3-dioxolanes may, however, be sufficient to allow the hydride ion to react by a Michael addition as is actually observed in the case of 2-vinyl-1,3-dioxolane (Experiment 1, Table 5). The hydride donation to the β carbon atom would occur at the same time as double bond migration and opening of the dioxolane ring. The absence of hydride addition at the anomeric carbon, a reaction which might be expected considering the possible polarization of the molecule as shown in Figure 5, is probably due to the polar repulsion experienced by the AlH_4^- ion in its approach to the anomeric carbon due to the two adjacent partially negatively charged oxygen atoms.

The observed reactivity of 2-vinyl-1,3-dioxolane under these reaction conditions ($LiAlH_4$ in ether at room temperature) was difficult

to explain in view of the stability observed for the alkyl substituted 2-vinyl-1,3-dioxolanes of Experiment 2 (a-d), Table 5 under the same reaction conditions. Substitution of alkyl groups on the vinylic linkage would, by their known electron donating ability, decrease the partial positive character at the β carbon atom as is shown in Figure 6.

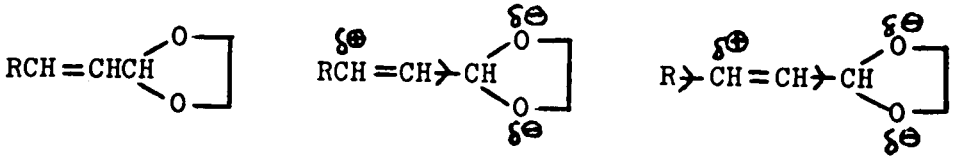


Figure 6

The resulting subtle decrease in the partial positive character at the β carbon atom plus an increase in steric hindrance at that centre to approach by the AlH_4^- ion due to the alkyl substituents may be sufficient to cause the total lack of reactivity observed for the alkyl substituted vinyl acetals which is in sharp contrast to the reaction noted with 2-vinyl-1,3-dioxolane itself. The observation that methacraldehyde ethyleneacetal (where the methyl substituent is on the α carbon atom of the vinyl substituent) is also stable to these conditions (Experiment 2b, Table 5) implies that the electronic rather than steric factor is more important as a cause of the stability of these molecules (Experiment 2(a-d), Table 5) to $LiAlH_4$ in ether.

Reduction of cinnamaldehyde ethyleneacetal under the same reaction conditions (Experiment 5, Table 5) was attempted in order to determine the effect of a substituent on the β carbon atom of the vinyl linkage capable of stabilizing carbonium ion character at the β carbon atom. Reduction of this molecule with $LiAlH_4$ in ether

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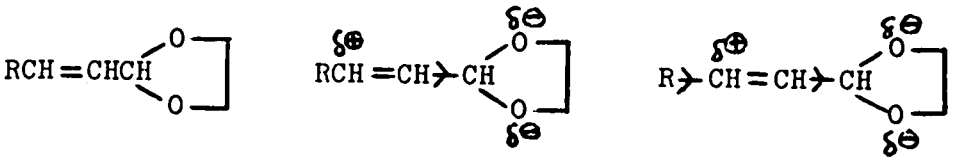

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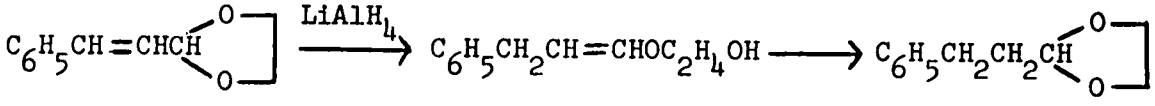
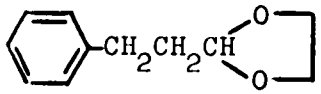
provided β-phenylpropionaldehyde ethyleneacetal as the only product. In order to determine if this product arose from direct reduction of the double bond or from reduction with double bond migration and ring opening (as apparently observed for the reduction of 2-vinyl-1,3-dioxolane) followed by cyclization of the resulting 2-hydroxyethyl 3-phenyl-1-propenyl ether to the saturated product as shown in Scheme 10, the reduction was also carried out using $LiAlD_4$. The site of donation



Scheme 10

of the hydride (and deuteride) was shown to be the carbon atom α to the anomeric carbon by using this reducing agent and hence it was concluded this product arose from direct reduction of the double bond.

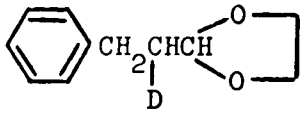
The 60 MHz n.m.r. spectrum of β-phenylpropionaldehyde ethyleneacetal 1 (Figure 7) obtained from the $LiAlH_4$ reduction of



1

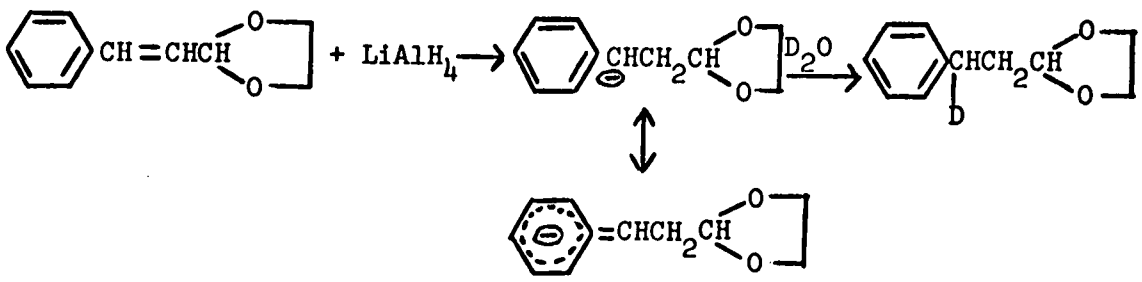
cinnamaldehyde ethyleneacetal showed a singlet (5H) at τ 2.87 assigned to the five phenyl protons, a triplet (1H) centred at τ 5.24 (J_{obs}, 4.5 Hz) assigned to the anomeric proton, a multiplet (4H) between τ 6.04 and τ 6.34 assigned to the four protons of the ethylene linkage of the dioxolane ring and two (2H) multiplets, one between τ 7.14 and τ 7.46 and the other between τ 7.92 and τ 8.33 can be assigned to the four methylene protons. The 60 MHz n.m.r. spectrum

(Figure 8) of the product isolated from the $LiAlD_4$ reduction of cinnamaldehyde ethyleneacetal exhibited similar absorptions for the five phenyl protons and the four protons of the ethylene linkage of the dioxolane ring. In place of the triplet observed previously for the anomeric proton signal there was now a doublet (1H) at τ 5.23. The two proton multiplet signal between τ 7.92 and τ 8.33 observed for β-phenylpropionaldehyde ethyleneacetal was now evident as a one proton multiplet in the same position. Also, the multiplet (2H) previously observed between τ 7.14 and τ 7.46 had collapsed to a doublet (2H) centred at τ 7.33. This information showed that the deuteride ion had reacted at the carbon atom α to the anomeric carbon to give the deuterated β-phenylpropionaldehyde ethyleneacetal 2.



2

The ease of reduction observed for cinnamaldehyde ethyleneacetal and the site of donation of the hydride ion indicate that the formation of the benzylic carbanion intermediate (Scheme 11) must be an energetically more favorable process than donation of the hydride to the carbon atom β to the anomeric centre in conjunction with double bond migration and C-O bond cleavage. The existence of this carbanion was shown by the product isolated upon quenching the reduction with D_2O. The 60 MHz n.m.r. spectrum of the product isolated by D_2O quenching exhibited absorptions similar to those described for the protons of β-phenylpropionaldehyde ethyleneacetal 1



Scheme 11

with the following changes. The two proton multiplet between τ 7.14 and τ 7.46 previously attributed to the benzylic protons was now present as a one proton multiplet showing the deuterium atom was incorporated at this centre by deuterolysis of the intermediate benzylic carbanion. The observation that substitution of a β hydrogen of 2-vinyl-1,3-dioxolane by a phenyl group promotes reaction with $LiAlH_4$ while substitution of an α and/or a β hydrogen by an alkyl group completely eliminates reaction with $LiAlH_4$ shows that the reaction of $LiAlH_4$ with 2-vinyl-1,3-dioxolanes is facilitated by substituents on the double bond which are capable of electron withdrawal. The ease of reduction and the direction of reduction of cinnamaldehyde ethyleneacetal also shows that the polarization of the double bond by the 1,3-dioxolane ring is relatively quite weak since the direction of hydride donation can easily be changed by the presence of a group on the β carbon atom capable of electron withdrawal.

The hydrogenolysis of the dioxolanes of Experiment 2 (Table 5) with $LiAlH_4$ was found to occur if the reaction was carried out in refluxing 1,2-dimethoxyethane (DME). The results of these

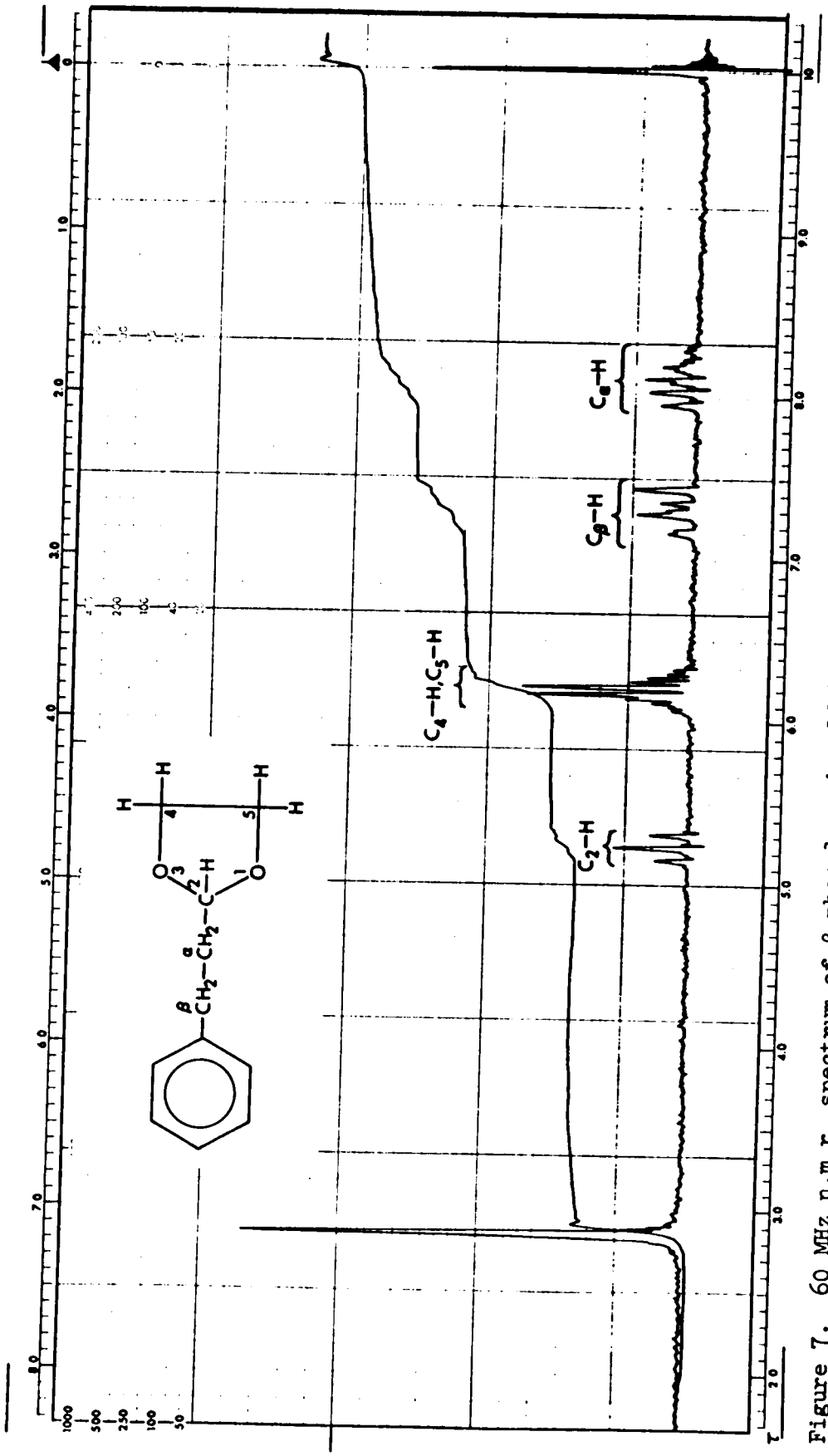


Figure 7. 60 MHz n.m.r. spectrum of β-phenylpropionaldehyde ethyleneacetal in CCl_4 referred to tetramethylsilane.

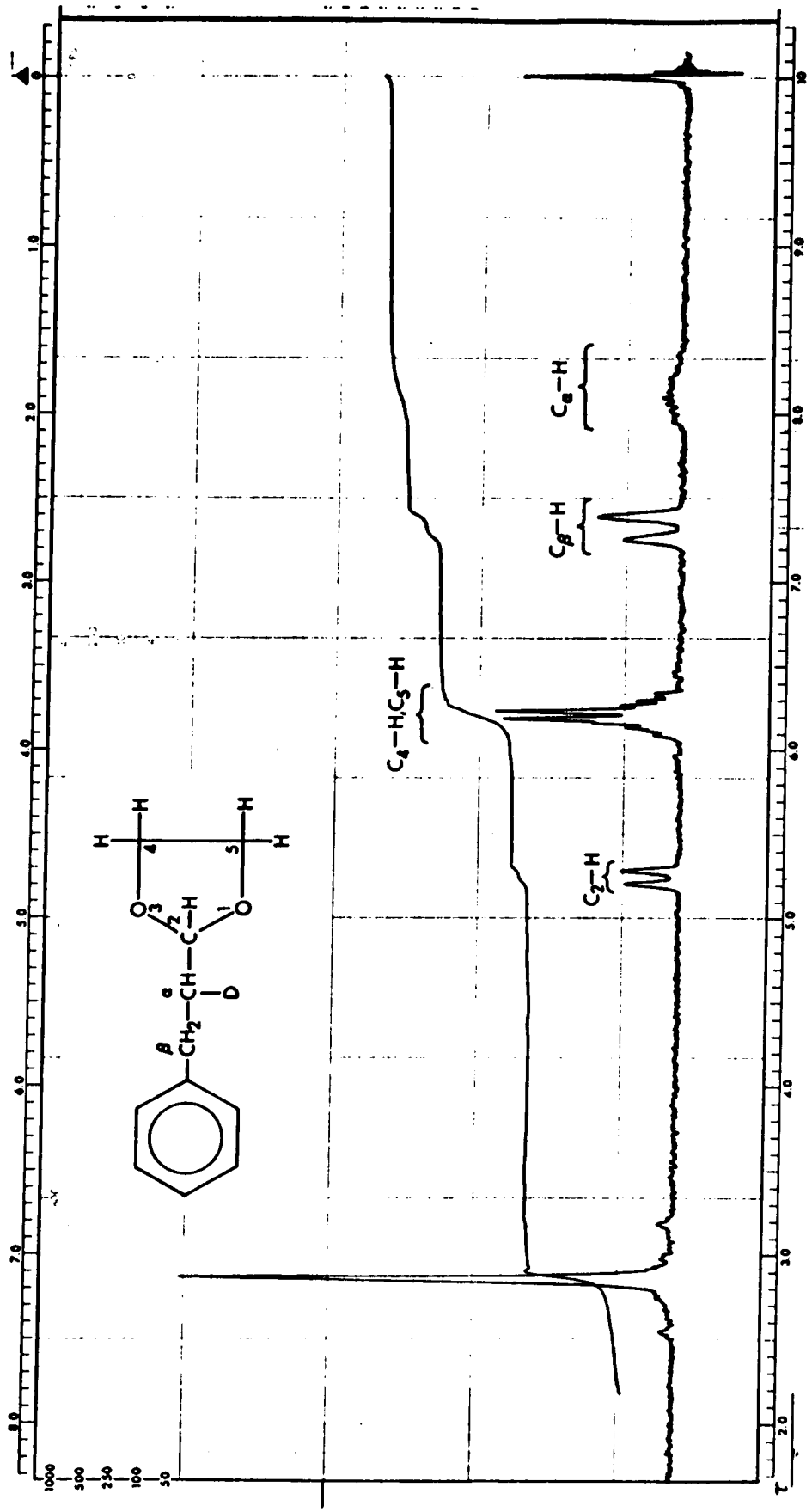


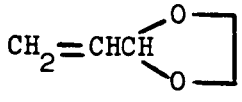
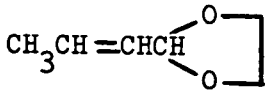
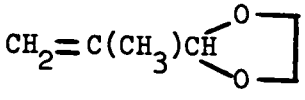
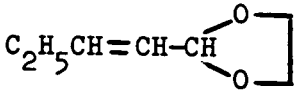
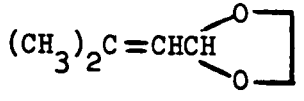
Figure 8. 60 MHz n.m.r. spectrum of α-deutero-β-phenylpropionaldehyde ethyleneacetal in CCl_4 referred to tetramethylsilane.

hydrogenolyses are shown in Table 6. The observation that these compounds are now reduced to the extent of 45 per cent or better upon raising the temperature of the reaction and that there is still a predominance of the α,β-unsaturated ether reduction product in most cases, is indicative that some polarization of the type shown in Figure 6 might be present even in the alkyl substituted 2-vinyl-1,3-dioxolanes. As a result, hydride donation occurs predominately at the β carbon atom of the vinyl group except where, due to increased steric effect of the alkyl substituents at this position, as in 2-isopentenal ethyleneacetal (Experiment 5, Table 6), attack of the bulky AlH_4^- ion is hindered at the β carbon atom. In this latter case, the increased steric hindrance to attack at the β position results in a greater amount of hydride donation occurring at the anomeric carbon. The increase in steric hindrance to reaction with the AlH_4^- ion at the β carbon due to alkyl substitution also results in a general retardation in the reaction rate. An explanation for the slow reaction of the methacraldehyde ethyleneacetal under these conditions could not be found.

The opening of the dioxolane ring in these reduction reactions using $LiAlH_4$ may also be assisted by the presence of the Li cation which may complex in a Lewis acid manner with the unshared electrons of the ring oxygen atoms and thus increase the leaving ability of this moiety. Coordination of the Li cation in this manner would be more likely to occur in the solvent diethyl ether than in the solvent 1,2-dimethoxyethane in which the Li cation

Table 6

Hydrogenolysis of some C-2 vinyl substituted-1,3-dioxolanes with $LiAlH_4$ in DME* at 80°C.

Experiment Number	Compound	Time, Hours	Amount of Reduction %	Total Recovery %	Products	Relative Amounts %
1		24	100	80	$CH_2=CHCH_2OC_2H_4OH$	0
					$CH_3CH=CHOC_2H_4OH$	100
2		70	70	80	$CH_3CH=CHCH_2OC_2H_4OH$	5
					$C_2H_5CH=CHOC_2H_4OH$	95
3		70	45	80	$CH_2=C(CH_3)CH_2OC_2H_4OH$	0
					$(CH_3)_2C=CHOC_2H_4OH$	100
4		70	65	80	$C_2H_5CH=CHCH_2OC_2H_4OH$	6
					$C_3H_7CH=CHOC_2H_4OH$	94
5		70	60	80	$(CH_3)_2C=CHCH_2OC_2H_4OH$	65
					$(CH_3)_2CHCH=CHOC_2H_4OH$	35

* DME = 1,2-dimethoxyethane

would tend to be strongly solvated as shown in Figure 9. When the

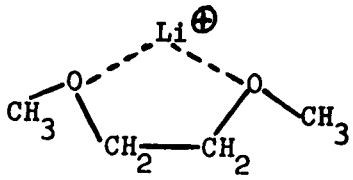


Figure 9

reduction of 2-vinyl-1,3-dioxolane with $LiAlH_4$ was carried out in DME at room temperature, only a trace of reduction was observed in 24 hours as compared to 32 per cent reduction observed in the same time using diethyl ether as the solvent, also at room temperature. These observations seem to agree with the idea mentioned above that the Li cation might participate in the dioxolane ring opening. However, these results are not in agreement with the observations of Jorgenson and Thacher (26). They found that, in the $LiAlH_4$ reduction of the double bond in cinnamyl alcohol, the rate of reduction was increased when the solvent was changed from diethyl ether to 1,2-dimethoxyethane. The rate enhancement observed in their work was attributed to the specific solvation of the Li cation in 1,2-dimethoxyethane and hence the freeing of the AlH_4^- ion to act as a stronger reducing agent. The rate retardation of the room temperature reaction in DME compared to the faster reaction in diethyl ether, also at room temperature, evident in our work may be interpreted to mean that the Li cation, if it is not strongly held by the solvent, can assist in this reaction by coordination with the dioxolane oxygen atoms. Consequently it provides assistance in the concerted action of double bond migration and ring opening

during hydrogenolysis.

Further evidence for the view that participation of the Li cation might assist in promoting cleavage of the dioxolane ring was obtained by carrying out the hydrogenolysis of the compounds shown in Table 6 in the solvent di-n-propyl ether at elevated temperatures. This solvent was chosen for its similarity in structure to diethyl ether and its similarity in boiling point (92°C) to that of 1,2-dimethoxyethane. The results of these hydrogenolyses are shown in Table 7.

It is clear from the results in Table 7 that more extensive reduction of the α,β-unsaturated-1,3-dioxolanes occurs in di-n-propyl ether at elevated temperatures than is found when 1,2-dimethoxyethane is used as the solvent. This again suggests that, in the reduction of these α,β-unsaturated acetals, the Li cation can possibly assist in the opening of the dioxolane ring. In the solvent 1,2-dimethoxyethane, as previously mentioned, the Li cation is strongly solvated whereas, in the solvent di-n-propyl ether, which is less likely to hold the Li cation so strongly, this cation can more readily associate itself with the oxygen atoms of the dioxolane ring. The equilibrating association of the Li cation with the solvent and with the dioxolane oxygen atoms is shown in Scheme 12.

The predominance of the β,γ-unsaturated ethers as the main products observed in these reductions is also evident of a strong C-O bond polarization giving reduction at the anomeric carbon.

Table 7

Hydrogenolysis of some 2-vinyl-1,3-dioxolanes with $LiAlH_4$ in di-n-propyl ether.

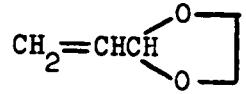
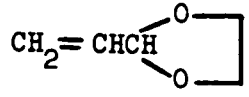
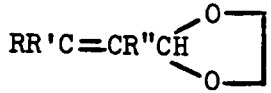
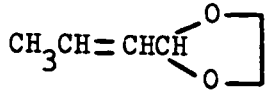
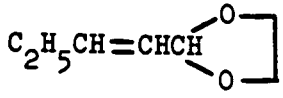
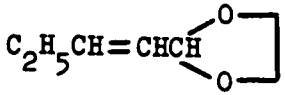
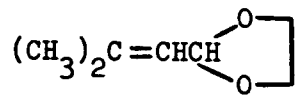
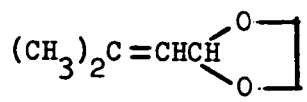
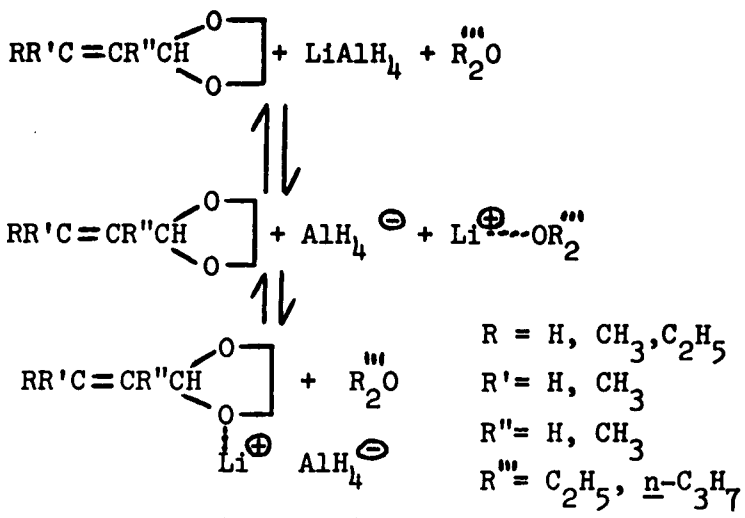
Experiment Number	Compound	Temperature °C	Time, Hours	Amount of Reduction %	Total Recovery %	Products
1		25	24	70	90	$CH_3CH{=}CHOC_2H_4OH$
2		90	2	100	90	$CH_3CH{=}CHOC_2H_4OH$
3(a-c)*		25	24	0	85	
4		90	2	100	90	$CH_3CH{=}CHCH_2OC_2H_4OH$
5		90	2	50	90	$C_2H_5CH{=}CHCH_2OC_2H_4OH$
6		90	12	100	90	$C_2H_5CH{=}CHCH_2OC_2H_4OH$

Table 7-Continued

Experiment Number	Compound	Temperature °C	Time, Hours	Amount of Reduction %	Total Recovery %	Products
7		90	2	80	90	$(CH_3)_2C{=}CHCH_2OC_2H_4OH$
8		90	12	100	90	$(CH_3)_2C{=}CHCH_2OC_2H_4OH$

* 3a $R = CH_3$, $R' = R'' = H$
3b $R = C_2H_5$, $R' = R'' = H$
3c $R = R' = CH_3$, $R'' = H$



Scheme 12

As will be shown, this is also the case when hydrogenolysis is carried out in the presence of a strong Lewis acid such as $AlClH_2$. It is significant that the α,β-unsaturated ether is formed exclusively from the reduction of 2-vinyl-1,3-dioxolane whereas the compounds possessing one or more alkyl groups on the vinyl group (Experiments 4-8, Table 7) give only the corresponding β,γ-unsaturated ethers. This shows that here also in di-n-propyl ether there seems to be a polar effect preventing approach of the AlH_4^- ion to the region of the anomeric carbon as well as a steric effect hindering approach of the AlH_4^- ion to the region of the alkyl substituted β carbon atom. However, the actual magnitude of the polar effect may not be as great in di-n-propyl ether as it is in DME because in the former due to the greater possibility of Li cation association with the dioxolane ring oxygen atoms, the following dual effect may result. (a) There may be some partial positive character developed at the anomeric carbon facilitating hydride donation at that position and

(b) in the solvent di-n-propyl ether, an intimate ion pair of $Li^{+}AlH_4^{-}$ may occur and thus the Li cation would hold the AlH_4^{-} ion in close proximity to the anomeric carbon, producing a 5-centre transition state as shown in Figure 10. The greater reactivity of

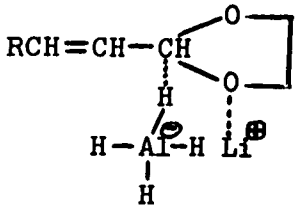


Figure 10

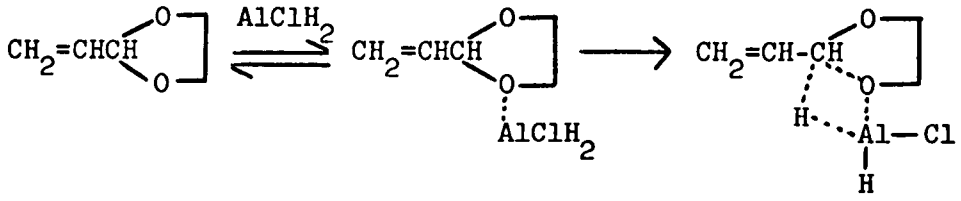
2-vinyl-1,3-dioxolane in the solvent di-n-propyl ether at room temperature compared to the lesser extent of reduction of this dioxolane in diethyl ether at room temperature could not be explained.

The work above thus indicates that in the solvents which permit the Li cation to coordinate with the dioxolane oxygen atoms, there does seem to be some Lewis acid character exhibited by the Li cation which causes both enhancement of the rate of hydrogenolysis and an increase in the extent of attack of the hydride species at the anomeric carbon. However, elevated temperatures are still found necessary to cause reduction of the alkyl substituted 2-vinyl-1,3-dioxolanes even in the simple ether solvents and this indicates that the action of the Li cation must also be assisted by heat to increase the C-O bond stretching enough to cause polarization in these molecules and hence reduction by the AlH_4^{-} ion.

The effect of added $AlCl_3$ (i.e. formation of the mixed

hydride reagent) on the $LiAlH_4$ hydrogenolysis of 2-vinyl-, 2-substituted vinyl- and 2-phenyl-1,3-dioxolanes was also studied. The results of the hydrogenolyses of these compounds with $AlClH_2$ are shown in Table 8.

In all cases of the hydrogenolysis of the 2-vinyl-1,3-dioxolanes the only product isolated from these reactions was the corresponding β,γ-unsaturated ether. The observed exclusive donation of the hydride ion to the anomeric carbon is indicative that either the hydride donation to the anomeric centre is faster than is any rearrangement of the double bond (possibly <u>via</u> a four centre transition state as shown in Scheme 13), and/or that the carbonium ion generated at the anomeric carbon (as shown in Scheme 14) is the most stable of the two canonical forms. By analogy with the



Scheme 13

hydrogenolysis of other 1,3-dioxolanes where it has been shown that the formation of the carbonium ion intermediate is the rate controlling step, such carbonium ion formation in the hydrogenolysis of these dioxolanes of Table 8 should also take place. In the reduction of the 2-vinyl-1,3-dioxolanes, the carbonium ion at the anomeric centre must be the most stable of the positively charged species indicated in Scheme 14, since it is stabilized by both the two adjacent oxygen atoms and the allylic system. Even in the case of

Table 8

Hydrogenolysis of some 2-vinyl- and 2-phenyl-1,3-dioxolanes with $AlClH_2$ in ether at 25°C.*

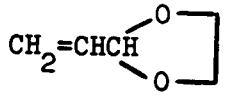
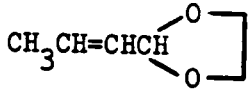
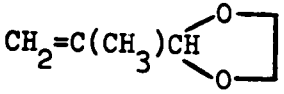
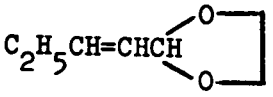
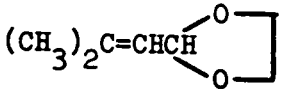
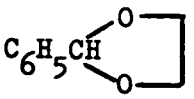
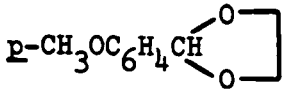
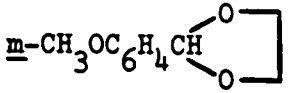
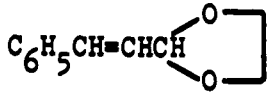
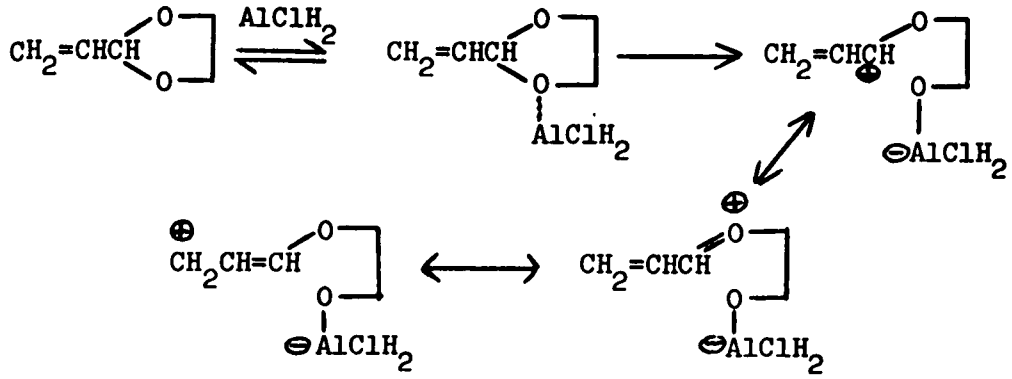
Experiment Number	Compound	Amount of Reduction %	Total Recovery%	Products
1		100	80	$CH_2=CHCH_2OC_2H_4OH$
2		100	85	$CH_3CH=CHCH_2OC_2H_4OH$
3		100	85	$CH_2=C(CH_3)CH_2OC_2H_4OH$
4		100	90	$C_2H_5CH=CHCH_2OC_2H_4OH$
5		100	90	$(CH_3)_2C=CHCH_2OC_2H_4OH$
6		100	90	$C_6H_5CH_2OC_2H_4OH$

Table 8-Continued

Experiment Number	Compound	Amount of Reduction%	Total Recovery%	Products
7		100	90	p-$CH_3OC_6H_4CH_2OC_2H_4OH$
8		100	90	m-$CH_3OC_6H_4CH_2OC_2H_4OH$
9		100	90	$C_6H_5CH=CHCH_2OC_2H_4OH$

* Reaction time in all cases was 30 minutes.



Scheme 14

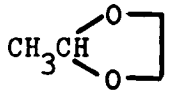
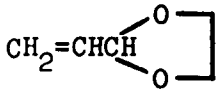
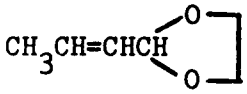
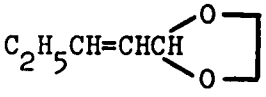
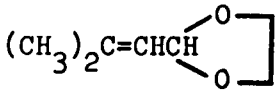
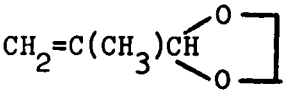
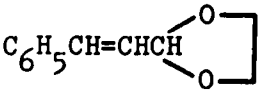
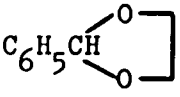
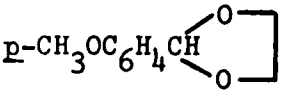
2-isopentenal ethyleneacetal, where carbonium ion formation at the β carbon would be stabilized because it is both tertiary and allylic, hydride donation occurs only at the anomeric carbon.

The hydrogenolysis of the compounds of Table 8 and of 2-methyl-1,3-dioxolane with $AlClH_2$ were all fast reactions, being complete in less than 30 minutes. Thus it is difficult to estimate the effects of the various C-2 substituents on the rate of hydrogenolysis. In order to determine the relative effect of these substituents on the rate of hydrogenolysis, competitive hydrogenolyses were carried out using AlH_3 as the reducing agent. This hydride species was chosen since previous work (12) showed that hydrogenolysis with this species was found to be slower in most cases than is hydrogenolysis with $AlClH_2$. Accordingly it was thought that by using this reducing reagent, more selectivity might be observed in the rate at which the various 2-substituted-1,3-dioxolanes would be hydrogenolyzed. These competitive hydrogenolyses were carried out by reducing an equimolar mixture of two dioxolanes with a limited amount of reducing species and

comparing the amount of product formed from each. This method had been used previously by Leggetter and Brown (1) and by Zajac and Byrne (16) to determine the relative reactivity of various acetals and ketals. The relative rates of hydrogenolysis of some 2-substituted-1,3-dioxolanes are shown in Table 9. The products obtained in these competitive hydrogenolysis reactions were the same as those reported in Table 8.

Table 9

Relative rates of hydrogenolysis of some 2-substituted-1,3-dioxolanes with AlH_3 in ether at 25°C.

Compound	Relative Rate
	0.025
	1
	4
	7
	15
	1.6
	very great
	1.7
	20

These results show that there is an additional assistance in the formation of the carbonium ion intermediate provided by a vinyl or phenyl group attached to the anomeric carbon. This causes an enhancement in the rate of hydrogenolysis of the 2-vinyl- and 2-phenyl-1,3-dioxolanes compared to the rate of hydrogenolysis of 2-alkyl substituted-1,3-dioxolanes such as 2-methyl-1,3-dioxolane. Furthermore, the stabilization of the carbonium ion intermediate by the vinyl or phenyl substituent appears to be sensitive to further electron donation by substituents attached to the vinyl or phenyl substituent themselves. The increase in rate observed for alkyl substitution ($H < CH_3 < C_2H_5 < 2CH_3$) at the β carbon of the vinyl moiety agrees with the known order of electron donating ability of these alkyl groups and their ability to stabilize a carbonium ion. The rate enhancement observed for methyl substitution at the α carbon of the vinyl moiety (i.e. methacraldehyde ethlene-acetal) is smaller than that observed for methyl substitution at the β carbon of the vinyl moiety (i.e. crotonaldehyde ethyleneacetal). This could be due to the fact that in the resonance forms of the carbonium ion intermediate as shown in Scheme 14, the α carbon atom does not become positively charged in any of the canonical forms and therefore methyl substitution at this position would not have as great a stabilizing effect as would methyl substitution on the β carbon. In the case of 2-(p-methoxyphenyl)-1,3-dioxolane, the increase in relative rate is still greater. This could be due to resonance electron donation by the methoxy group through the

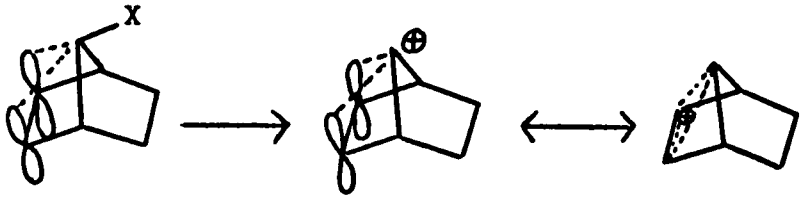
aryl ring to stabilize the oxocarbonium ion. An explanation for the extremely fast reaction of cinnamaldehyde ethyleneacetal could not be found.

Rate enhancement of the mixed hydride hydrogenolysis of 1,3-dioxolanes has thus been shown to occur to a large extent if the anomeric carbon is made part of either an allylic or benzylic system. Furthermore, substitution on the phenyl or vinyl moiety of groups capable of stabilizing carbonium ion intermediates provides further rate enhancement in these reactions. This has been shown using AlH_3 as the reducing species but would be the same for either $AlClH_2$ or $AlCl_2H$ as the reaction scheme is the same for these species as well. The only difference with the two hydridoaluminum chlorides might be that the observed differences in reactivity of the substituted vinyl or phenyl dioxolanes would be smaller since the greater Lewis acidity of these two species would cause faster ring opening and would require less assistance from the C-2 substituent of the 1.3-dioxolane ring.

4. Hydrogenolysis of the Ethylene Ketals of some Norbornenones.

It has been known for some time that the π electrons of a carbon-carbon double bond provide anchimeric assistance in the reactions of anti-7-norbornenyl derivatives (27, 28). For example, the anti-7-tosylate is solvolyzed over a billion times faster than is the saturated analog and also 10^5 times faster than the syn form. As shown in Scheme 15, the π electron lobes of the double bond in the anti-7-norbornenyl derivatives lie near C-7 on the side opposite the leaving group. These electrons may not only

help "push off" the leaving group but, after its departure, they may help accommodate the positive charge by drifting towards C-7 and allowing this charge to be distributed over three carbon atoms rather than being confined to just one. Scheme 15 illustrates this.



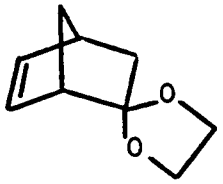
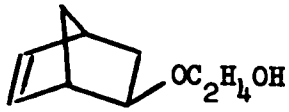
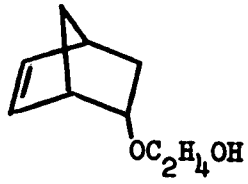
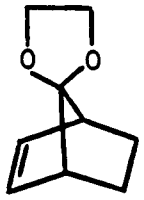
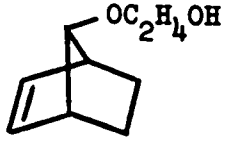
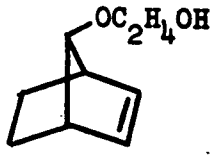
Scheme 15

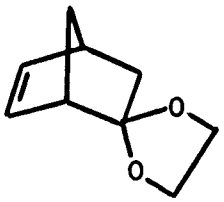
The π electron lobes associated with the double bond between C-2 and C-3 of the norbornenyl system are spatially disposed so that they are closer to C-7 than to C-5 and C-6. As a result of this, much less assistance is experienced in the ionization of substituents at C-5 and C-6 than in ionization of substituents at C-7. Exo-2-chloro-5-norbornene undergoes solvolysis in 80 per cent ethanol about 150 times faster than the endo isomer, a difference in reactivity not much greater than that observed for the corresponding saturated chlorides (29).

In this work, the hydrogenolysis of 5-norbornen-2-one ethylene ketal 3 and 2-norbornen-7-one ethylene ketal 4 were carried out using the mixed hydride $AlClH_2$ in order to see if any anchimeric assistance to the formation of the carbonium ion intermediate was present in these reactions. The results of the hydrogenolysis of these compounds are shown in Table 10. The

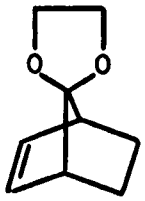
Table 10

Hydrogenolysis by $AlClH_2$ of some norbornenyl-1,3-dioxolanes in ether at room temperature.

Experiment Number	Compound	Time, Hours	Amount of Reduction%	Total Recovery%	Products	Relative Amounts %
1		72	100	95		0
						100
2		72	65	95		36
						64



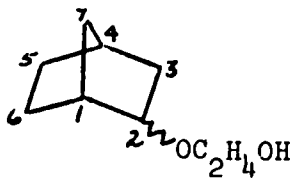
3



4

disposition of the 2-hydroxyethoxy substituents on the norbornene system in the products obtained from the reactions (i.e. either exo or endo; syn or anti) was proven by comparison of the n.m.r. spectra of the products isolated from the hydrogenolysis reactions with the n.m.r. spectra of authentic preparations.

A mixture of 2-(2-endo-5-norbornenyloxy)ethanol and 2-(2-exo-5-norbornenyloxy)ethanol was prepared from a mixture of exo- and endo-5-norbornenol by using the procedure reported by Zajac,Rhee and Brown (30) for the preparation of the saturated analogs. These materials were separated by preparative g.l.c. and the n.m.r. spectra were obtained. The exo and endo isomers were identified by comparison of the resulting spectra with the data reported by Zajac et. al. (30) for the n.m.r. spectra of the saturated analogs. These authors reported that in the n.m.r. spectrum of 2-(2-endo-norbornyloxy)ethanol (5a) the bridgehead protons on carbons 1 and 4 gave rise to two unresolved multiplets



5

a = endo isomer

b = exo isomer

centered at τ 7.63 and τ 7.87 with half widths of 8 Hz and 11 Hz respectively whereas in the exo isomer (5b) these protons gave rise to only one unresolved multiplet (2H) centered at τ 7.83 with a half width of 14 Hz. The 60 MHz n.m.r. spectra of the two unsaturated analogs synthesized in this work (Figure 11 and Figure 12) exhibited similar absorption patterns for the bridgehead protons at carbons 1 and 4. Therefore, the isomer which showed two unresolved multiplets centered at τ 6.94 and τ 7.26 with half widths of 7 Hz (Figure 11) was considered to be the endo isomer and the isomer which showed only one unresolved multiplet (2H) centered at τ 7.15 with a half width of 10 Hz (Figure 12) was designated as the exo isomer. The 60 MHz n.m.r. spectrum of the only product found from the hydrogenolysis of 5-norbornen-2-one ethylene ketal was identical to that of the n.m.r. spectrum of the compound prepared separately and considered to be 2-(2-endo-5-norbornenyloxy) ethanol.

The two possible products from the hydrogenolysis of 2-norbornen-7-one ethylene ketal were also prepared from authentic syn-7-norbornenol and authentic anti-7-norbornenol again by the procedure described by Zajac et. al. (30). The 60 MHz n.m.r. spectra of these two isomeric products (Figure 13 and Figure 14) differ in the position of the absorption of the bridgehead protons at C-1 and C-4 and also in the position of the C-7 signal. In the spectrum of the syn isomer (Figure 13) the C-7 proton absorption is obscurred by the absorption of the four methylene protons of the hydroxyethoxy substituent (τ 6.19 to τ 6.67). On the other hand,

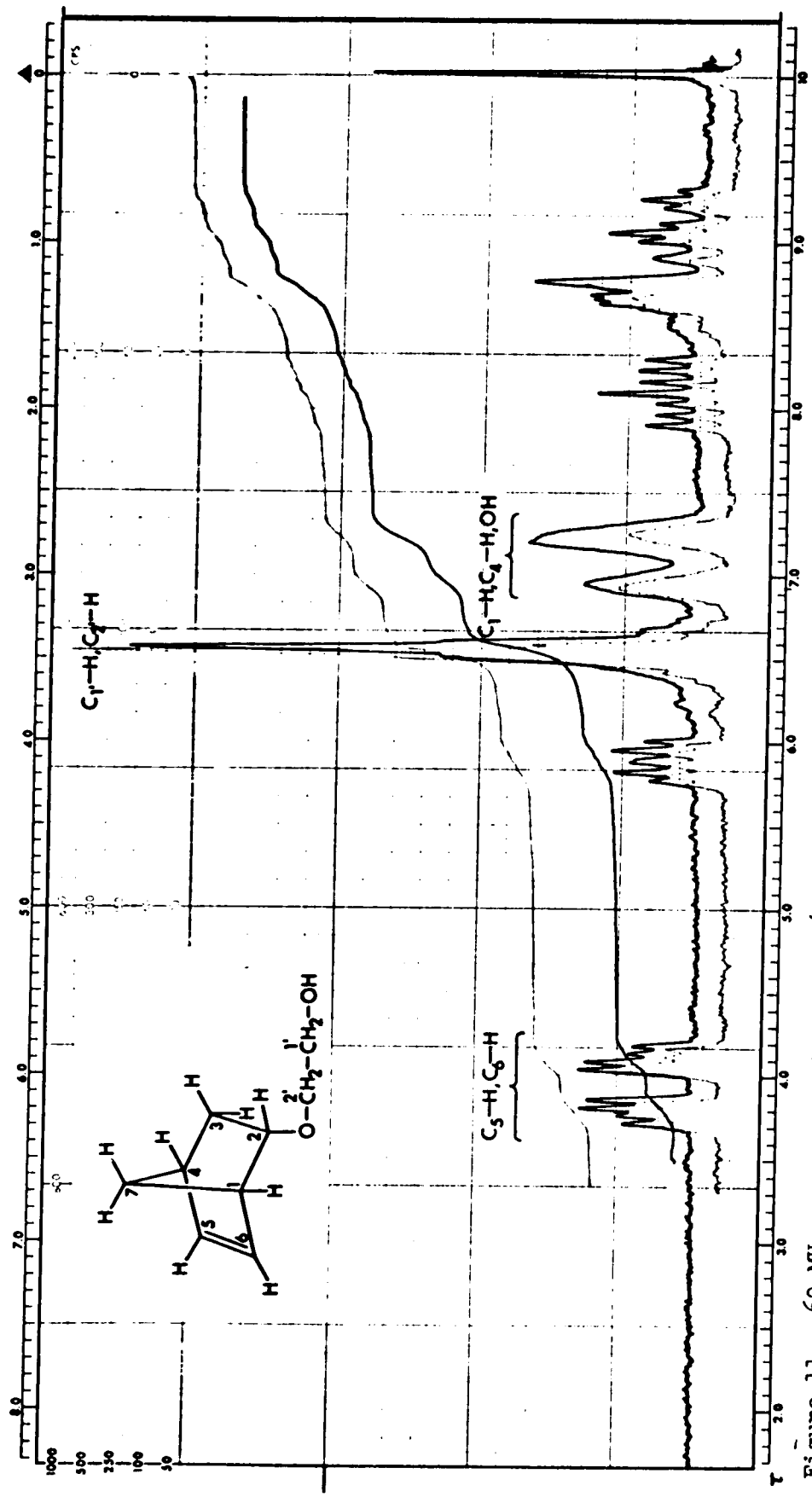


Figure 11. 60 MHz n.m.r. spectrum of 2-(2-endo-5-norbornenyloxy)ethanol in CCl_4 referred to tetramethylsilane. The lower spectrum was taken after shaking with D_2O.

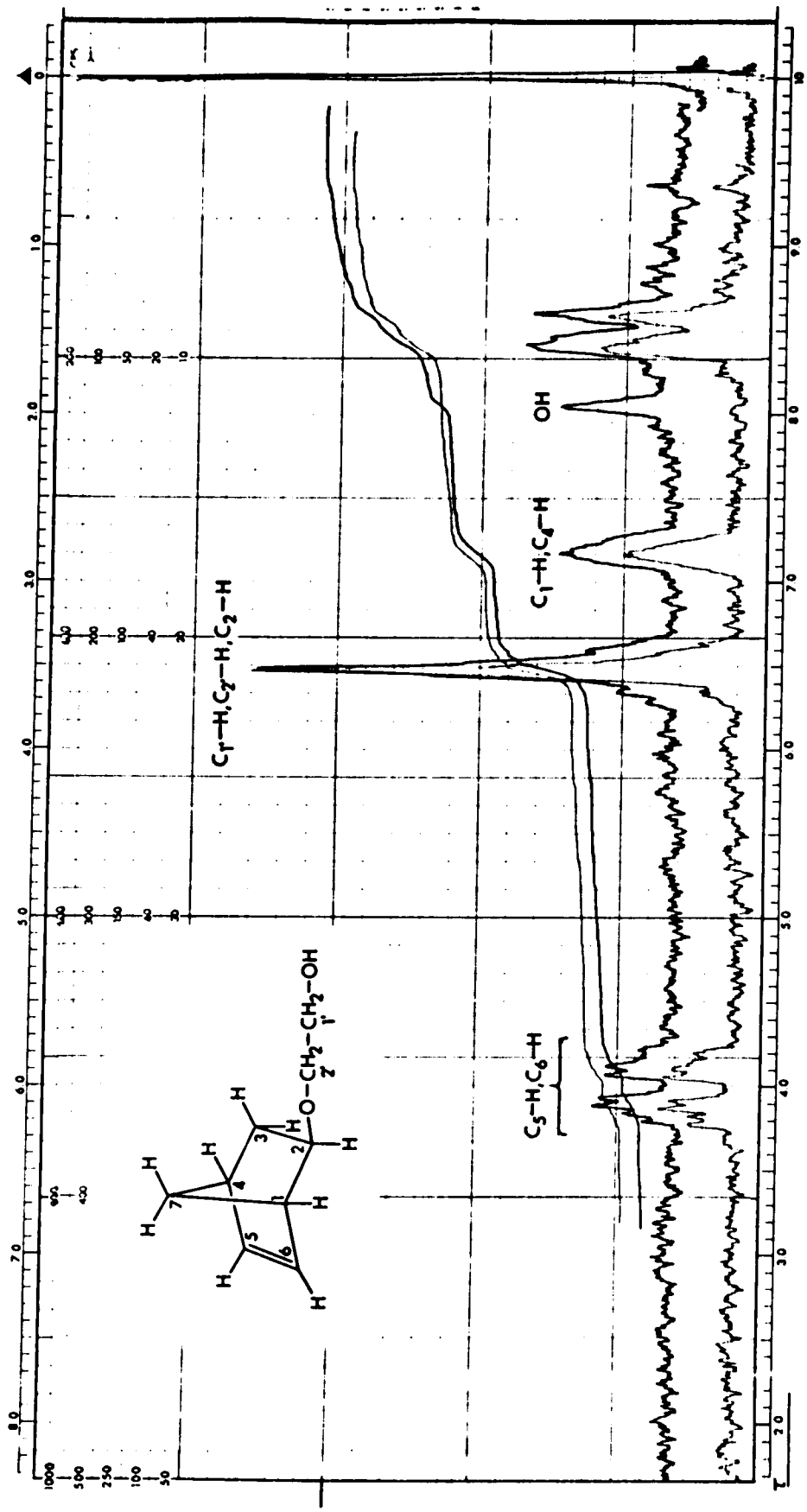


Figure 12. 60 MHz n.m.r. spectrum of 2-(2-exo-5-norbornenyloxy)ethanol in CCl_4 referred to tetramethylsilane. The lower spectrum was taken after shaking with D_2O.

the C-7 proton of the anti isomer (Figure 14) experiences a diamagnetic shielding due to the double bond (a phenomenon reported by Snyder and Frazus (31)) and hence the signal of the C-7 proton is moved upfield and occurs as a broad singlet centered at τ 6.78 with a half width of 4.5 Hz. The broad singlet centered at τ 7.11 (half width 5 Hz) attributed to the bridgehead protons at C-1 and C-4 in the syn isomer (Figure 13) were also shifted upfield slightly in the anti isomer (Figure 14) where the absorption for these two protons was evident as a broad singlet centered at τ 7.35 (half width 7 Hz). The products from the hydrogenolysis of 2-norbornen-7-one ethylene ketal were isolated by preparative g.l.c. and were identified by comparison of their respective n.m.r. spectra with those of the authentically prepared material.

The exclusive formation of 2-(2-endo-5-norbornenyloxy)ethanol from the hydrogenolysis of 5-norbornen-2-one ethylene ketal (Experiment 1, Table 10) can be ascribed to two effects. First, a steric effect and secondly an electronic effect. Zajac et. al. (30) observed that the direction of hydrogenolysis of norcamphor ethylene ketal was determined by steric approach control of the reducing species and gave total complexation with the sterically more available exo oxygen atom resulting in exclusive formation of the endo isomer (5a). In the unsaturated analog used in this work (5-norbornen-2-one ethylene ketal) steric hindrance to approach of the reducing species from the endo side of this molecule has been decreased somewhat by the formation of the C-5, C-6 double bond. Models of

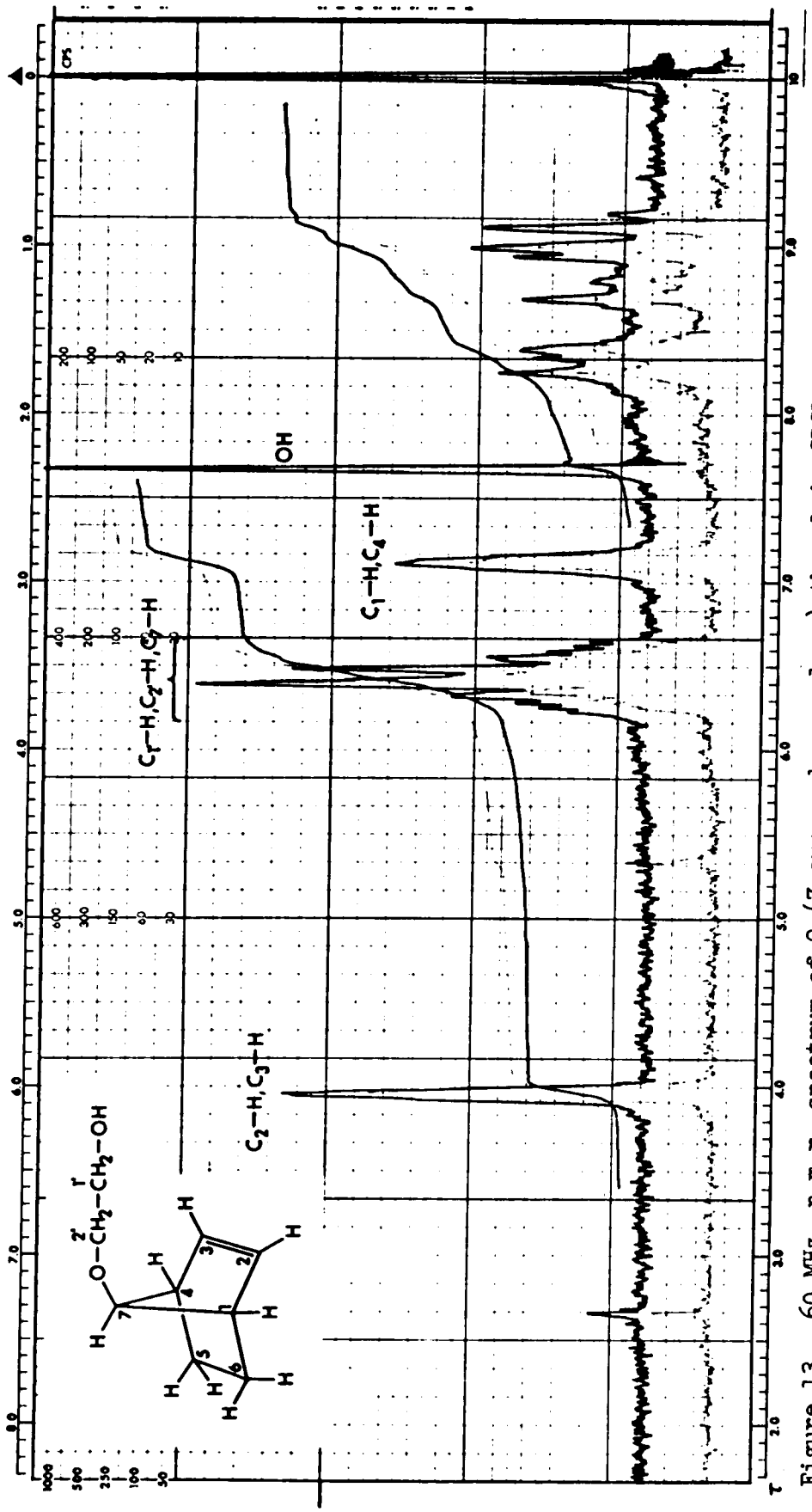


Figure 13. 60 MHz. n.m.r. spectrum of 2-(7-syn-norbornenyloxy)ethanol in $CDCl_3$ referred to tetramethylsilane. The lower spectrum was taken after shaking with D_2O.

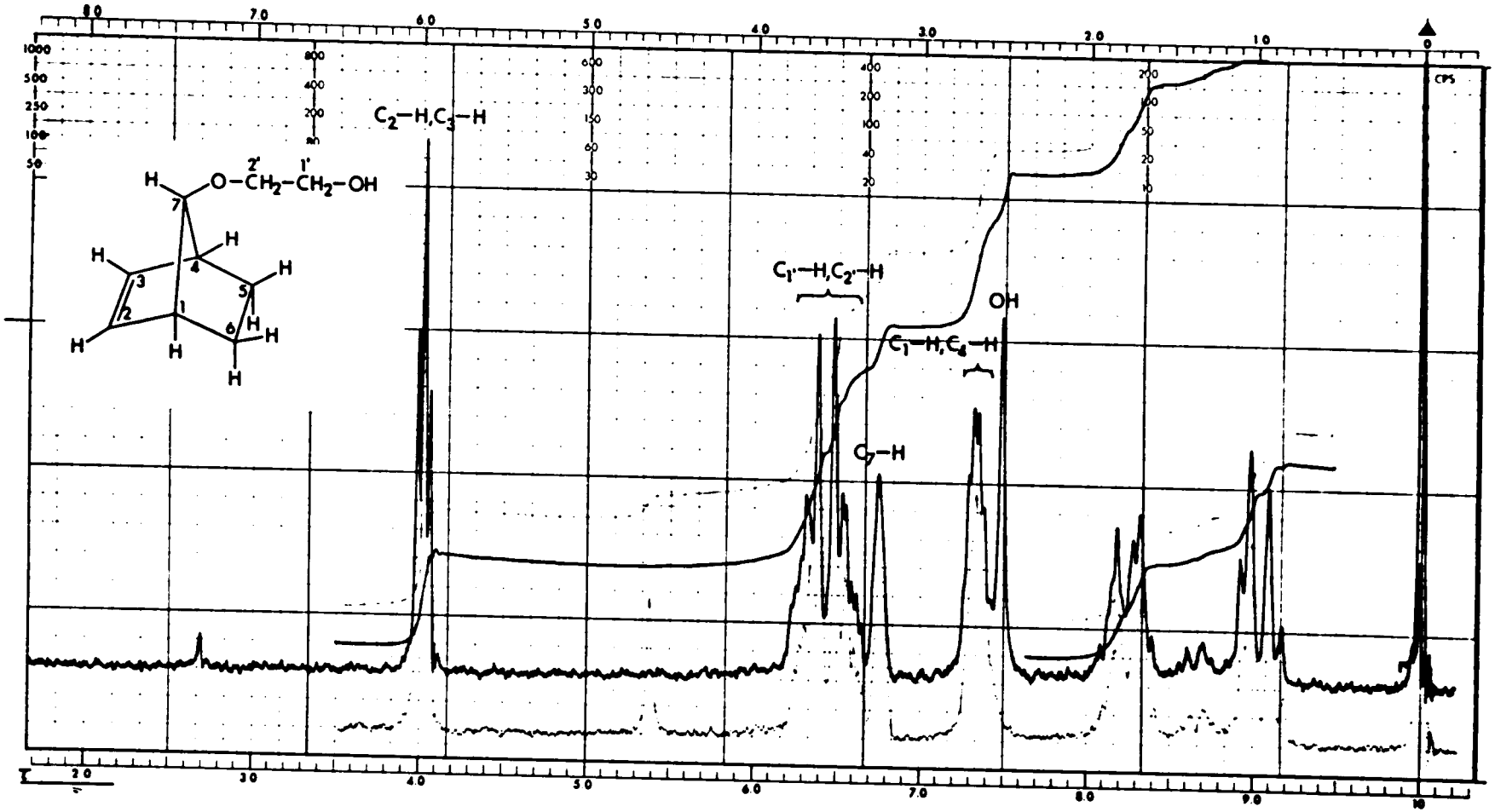


Figure 14. 60 MHz n.m.r. spectrum of 2-(7-anti-norbornenyloxy)ethanol in $CDCl_3$ referred to tetramethylsilane. The lower spectrum was taken after shaking with D_2O.

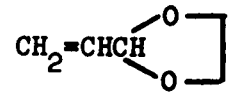
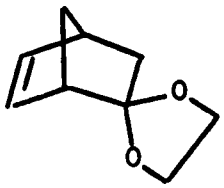
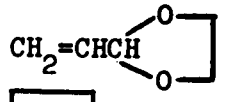
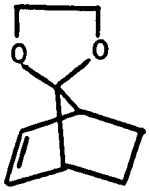
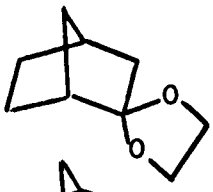
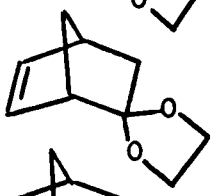
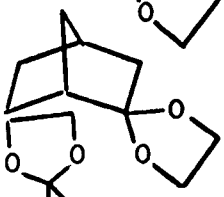
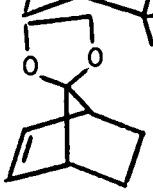
this compound, however, show that approach of the reducing species from the exo side of the molecule is still sterically favored to some extent. As to the second effect mentioned above, if participation of the C-5, C-6 double bond occurs in the formation of the carbonium ion intermediate, the cleavage of the exo C-O bond would be favored since the endo π lobes of the double bond can assist to a small extent in the leaving of the exo group. Likewise, the nearly 2:1 predominance of 2-(7-syn-norbornenyloxy)ethanol over the anti isomer from the hydrogenolysis of 2-norbornen-7-one ethylene ketal (Experiment 2, Table 10) could also be due to the participation of the π lobes of the C-2, C-3 double bond in the cleavage of the anti C-O bond.

The overall rate of hydrogenolysis of these two norbornenyl-1,3-dioxolanes, however, was observed to be much slower than the hydrogenolysis of a simple alkyl substituted compound such as 2-methyl-1,3-dioxolane (Experiment 1, Table 2) under the same conditions. Some competitive hydrogenolyses were carried out in order to determine the relative reactivity of these norbornenyl ketals as compared to the reactivity of the saturated analog, norcamphor ethylene ketal, and 2-vinyl-1,3-dioxolane. The relative reactivities were determined by the method previously used (cf. Table 9) and are reported in Table 11.

There are two striking features noticeable in the results reported in Table 11. First is the marked stability of the two

Table 11

Competitive hydrogenolysis by $AlClH_2$ of some 2-norbornenyl-1,3-dioxolanes with some other 2-substituted-1,3-dioxolanes in ether at room temperature.*

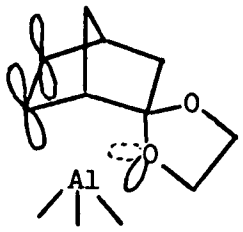
Experiment Number	Compounds	Amount of Reduction %
1		77
		trace
2		80
		trace
3		40
		trace
4		35
		trace

* Reaction time in all cases was 30 minutes.

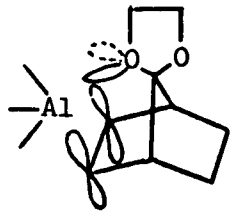
norbornenyl-1,3-dioxolanes to hydrogenolysis compared to the ease of hydrogenolysis of the saturated analog, norcamphor ethylene ketal. This is unexpected on the basis of the known anchimeric assistance which these unsaturated systems provide for carbonium ion formation in solvolysis reactions. The second feature is the decreased rate of hydrogenolysis of 2-vinyl-1,3-dioxolane when the reduction is carried out in the presence of either of the two norbornenyl-1,3-dioxolanes. Normally, 2-vinyl-1,3-dioxolane is hydrogenolyzed completely in less than 15 minutes in the presence of $AlClH_2$. The observed retardation of the rate of hydrogenolysis of these compounds may be due to the possibility that the mixed hydride can associate not only with the p electrons of the oxygen atoms but also with the π electron lobes of the carbon-carbon double bond. In order to determine the effect of the presence of a π bond on the rate of hydrogenolysis, the reduction of 2-methyl-1,3-dioxolane with $AlClH_2$ in ether was carried out in the presence of one molar equivalent of cyclohexene. Whereas the hydrogenolysis of 2-methyl-1,3-dioxolane with $AlClH_2$ is normally complete in 30 minutes, the same reaction when carried out in the presence of one molar equivalent of cyclohexene was found to be only 90% complete in 30 minutes. Thus the effect of an isolated double bond does seem to be one of retardation of the rate of hydrogenolysis.

The large rate retardation observed for the hydrogenolysis of the norbornenyl-1,3-dioxolanes as compared to the rate of hydrogenolysis of the saturated analog may also be due in part to

the geometry of these molecules. In 2-norbornen-7-one ethylene ketal the unpaired electron lobes of the syn dioxolane oxygen atom are in close proximity to the π electron lobes of the C-2, C-3 double bond. The proximity of these electron rich moieties may cause the formation of a fairly strong p-π complex with the reducing species and hence decrease the effective Lewis acidity of the reducing species and as a result, slow the overall rate of hydrogenolysis. A similar effect may be postulated for 5-norbornen-2-one ethylene ketal. These two possible coordination complexes are shown in Figure 15 A and B. Such coordination of the aluminum species could thus explain the observed slow rate of hydrogenolysis of these compounds and also the observed retarded rate of hydrogenolysis of 2-vinyl-1,3-dioxolane when carried out in the presence of the norbornenyl-1,3-dioxolanes.



A



B

Figure 15

The difference in the amount of hydrogenolysis observed in Table 10 for the two norbornenyl-1,3-dioxolanes in the same reaction time can also be explained on this basis. Again, due to the difference in geometry of these two molecules, coordination

of the aluminum species would be stronger on B (Figure 15). From the model of this compound it can be seen that the syn dioxolane oxygen atom is positioned directly between the π lobes of the C-2, C-3 double bond. Also, as has been previously mentioned, the π lobes of this double bond are closer to C-7 than to C-5 and C-6. Thus, this arrangement of electron density in 2-norbornen-7-one ethylene ketal could hold the aluminum species in a strong complex as shown in B (Figure 15). Coordination of this type with 5-norbornen-2-one ethylene ketal A (Figure 15) would be somewhat weaker due to (a) the endo dioxolane oxygen atom is positioned to one side of the carbon-carbon double bond and (b) the π electron lobes of the double bond are not as close to C-2 and C-3 as they are to C-7. As a result of the somewhat weaker p-π complex formed in this case the effective Lewis acidity of the reducing species would be greater and hence, as is observed, the rate of hydrogenolysis would be faster.

It thus appears that the rate of hydrogenolysis of 5-norbornen-2-one ethylene ketal and 2-norbornen-7-one ethylene ketal is retarded from that expected possibly due to the p-π complexation of the reducing species. This type of complexation in these molecules is due to the proximity of the p electron lobes of the oxygen atoms to the π electron lobes of the double bonds. As a result of the overall rate retardation observed for these compounds it cannot be conclusively said whether there is any assistance by the carbon-carbon double bond in the cleavage of the

dioxolane ring, however, the product proportions observed suggest that this might be a possibility.

SUMMARY

A series of experiments were carried out to determine the number of hydride ions available for hydrogenolysis of 1,3-dioxolanes by the mixed hydride $AlClH_2$. It was found that only one of the hydride ions was active in the hydrogenolysis of 1,3-dioxolanes since the Lewis acidity of the intermediate alkoxyhydridoaluminum chloride formed in these reactions was utilized by an intramolecular association and hence was not available to promote further reaction with another molecule of dioxolane. The hydride ion of the intermediate alkoxyhydridoaluminum chloride species, however, was found to be active in the reduction of compounds where no Lewis acid character was necessary.

In a study of the hydrogenolysis of some C-2 substituted 1,3-dioxolanes to determine if there was any anchimeric assistance to the formation of the carbonium ion intermediate and hence the rate of reaction, a number of dioxolanes were synthesized possessing at C-2 of the dioxolane ring substituents which are known to provide such anchimeric assistance. The hydrogenolysis of a series of dioxolanes with a heteroatom (O, N, S, Br) β to the anomeric carbon showed that the rate of hydrogenolysis of these compounds was retarded compared to the rate of reaction of a simple

C-2 alkyl-1,3-dioxolane such as 2-methyl-1,3-dioxolane under the same reaction conditions. The observed decrease in the rate of hydrogenolysis for these compounds was attributed to the electronegativity of the substituent heteroatom. This is believed to destabilize the intermediate carbonium ion and hence results in a decrease in the ease of its formation. Furthermore, the reversible association of the reducing species with the p electrons of the heteroatom would bring about a decrease in the concentration of the Lewis acid available for attack on the dioxolane moiety and this would also decrease the rate of hydrogenolysis.

The hydrogenolysis of a series of dioxolanes in which the anomeric carbon was either allylic or benzylic (e.g. 2-vinyl-1,3-dioxolane or 2-phenyl-1,3-dioxolane) was found to proceed at a much faster rate than that for simple alkyl substituted-1,3-dioxolanes. The rate enhancement observed for these compounds was attributed to the greater ease of formation of the carbonium ion intermediate in these compounds and hence the faster reaction rate. Further subtle rate enhancements were observed by substitution of electron donating groups on the phenyl or vinyl substituent. Reduction of the alkyl substituted 2-vinyl-1,3-dioxolanes was also found to occur with $LiAlH_4$ alone at elevated temperatures (no reaction was observed at room temperature) in the solvents 1,2-dimethoxyethane (DME) and di-n-propyl ether. Due to the increased rate of reaction and the product distribution observed

using $LiAlH_4$ in di-n-propyl ether as compared to the results obtained in the solvent DME, it was postulated that the lithium cation participated to some extent in the ease of ring cleavage depending on the solvent used.

The effect of the norbornenyl system at C-2 of the dioxolane ring on the rate of hydrogenolysis was also studied in order to determine if any anchimeric assistance to the formation of the carbonium ion intermediate was present in these systems. Again rate retardation was observed compared to the rate of hydrogenolysis of the saturated analog. Even the rate of hydrogenolysis of 2-vinyl-1,3-dioxolane was slowed when carried out in the presence of the two norbornenyl-1,3-dioxolanes studied. This observed rate retardation was attributed to the association of the reducing species with the π electron lobes of the double bond as well as with the p electrons of the oxygen atoms again decreasing the effective concentration of the Lewis acid reducing species ($AlClH_2$) available for hydrogenolysis.

EXPERIMENTAL

All boiling points and melting points in this work are uncorrected.

Gas liquid chromatographic analyses were made with an F and M, Model 700 instrument, equipped with 12 ft. by 1/8 in. columns packed with: (a) butanediol succinate, 20 % on Gas Chrom P (60-80 mesh), (b) silicone rubber SE 30, 20 % on Gas Chrom P (60-80 mesh). Helium was the carrier gas at a flow rate of about 40 ml per minute.

For preparative gas liquid chromatography (g.l.c.), the instrument used was an Aerograph Autoprep, Model A-700 (Wilkens Instrument and Research Co.). The column employed was 12 ft. by 1/4 in. packed with butanediol succinate, 20 % on Gas Chrom P (60-8- mesh). Helium was the carrier gas.

The column temperature and the type of column used was dependent on the boiling points of the compounds. For some analytical work on the F and M, Model 700, the temperature was linearly programmed in order to achieve better resolution. The temperature was increased at the rate of 7.5°C per minute starting from 80-100°C with the terminal temperature being dependent upon the column stability.

Infrared spectra were recorded with a Perkin-Elmer Model 21 instrument.

Nuclear magnetic resonance (n.m.r.) spectra were recorded on either a Varian Associates A-60 instrument or a Varian Associates A-56/60A instrument operated by Mr. R. Swindlehurst and his assistants. All spectra were referred to tetramethylsilane.

Elemental analyses were carried out by Mrs. Darlene Mahlow in the Chemistry Department of this University.

In the work-up procedures for the various syntheses described and the hydrogenolysis reactions, the drying agent employed was anhydrous magnesium sulfate unless otherwise stated. Solvents were removed with a rotatory evaporator under reduced pressure unless otherwise stated.

N.m.r. and i.r. spectra were obtained for all compounds reported in this work and were, in all cases, consistent with the structure assigned.

1. Preparation of 2-Substituted-1,3-dioxolanes.

Acrolein ethyleneacetal was prepared by a modification of the procedure described by Fischer and Smith (32).

To a mixture of 300 ml of pentane and 100 ml of anhydrous ether was added 123.3 g (2.2 mole) of acrolein and 126 g (2.0 mole) of ethylene glycol. p-Toluenesulfonic acid (1 g) was added and the mixture was heated under reflux using a Dean-Stark water trap. Vigorous stirring was employed in order to ensure the mixing of the two phases. After a 50-hour reflux period, 29 ml of water had been collected. The reaction mixture was then allowed to cool to room temperature, treated with 20 g of anhydrous sodium carbonate and then stirred for one hour. The solid material was then removed by suction filtration and the filtrate freed from solvent. The residue was distilled and gave a colorless liquid (45 g, 23%). B.p. 62°C at 110 mm; n_D^{28} 1.4260. Lit. b.p. 114-116°C at 760 mm; n_D^{20} 1.4327 (32).

Crotonaldehyde ethyleneacetal was prepared by the procedure of Heywood and Phillips (33).

To a mixture of 70 g (1.0 mole) of crotonaldehyde and 62 g (1.0 mole) of ethylene glycol in 500 ml of dry benzene was added 0.1 g of p-toluenesulfonic acid. This mixture was stirred and heated under reflux for 36 hours in an apparatus equipped with a water trap. At the end of this time 12 ml of water had been

collected. The reaction mixture was then allowed to cool to room temperature and 10 g of anhydrous sodium carbonate was added. Stirring was continued for 1 hour and then the solid was removed by suction filtration. The solvent was removed and the residue was distilled at reduced pressure giving 64 g (56%) of a colorless liquid. B.p. 69°C at 50 mm; n_D^{26} 1.4405. Lit. b.p. 71°C at 50 mm; n_D^{30} 1.4380 (33).

Methacrolein ethyleneacetal was prepared from methacrolein and ethylene glycol by the method of Heywood and Phillips (33) as previously described for the preparation of crotonaldehyde ethyleneacetal. The yield could not be improved by changing the concentration of reactants or the amount of catalyst used. A large amount of polymerization occurred in this preparation.

A colorless liquid was obtained in 15% yield. B.p. 61°C at 50 mm; n_D^{26} 1.4338.

Anal. Calcd. for $C_6H_{10}O_2$: C, 63.14; H, 8.83.

Found: C, 63.34; H, 9.04.

The 60 MHz n.m.r. spectrum in CCl_4 was consistent with the proposed structure, showing a multiplet centered at τ 4.92 (2H), a triplet centered at τ 5.10 (1H), J = 1.5 Hz, a multiplet centered at τ 6.17 (4H) and a doublet centered at τ 8.31 (3H), J = 1.5 Hz.

2-Pentenal ethyleneacetal was prepared as described in Part II of this thesis (Page 197).

2-Isopentenal ethyleneacetal was prepared as described in Part II of this thesis (Page 197).

Cinnamaldehyde ethyleneacetal was prepared from cinnamaldehyde and ethylene glycol by the procedure previously described for the preparation of crotonaldehyde ethyleneacetal.

A colorless liquid was obtained in 65% yield. B.p. 84°C at 0.1 mm; n_D^{24} 1.5625. This liquid crystallized on standing at room temperature for about 1 hour. Recrystallization from petroleum ether gave white needles. M.p. 29.5-31°C

Anal. Calcd. for $C_{11}H_{12}O_2$: C, 74.98; H, 6.86.

Found: C, 75.03; H, 6.94.

The 60 MHz n.m.r. spectrum in CCl_4 was consistent with the proposed structure, showing a broad multiplet between τ 2.40 and 2.81 (5H), a doublet centered at τ 3.22 for the olefinic proton adjacent to the benzene ring J = 16 Hz, a doublet of doublets for the other vinylic proton centered at τ 3.88, J = 16 Hz; J = 5 Hz, a doublet centered at τ 4.62 (1H), J = 5 Hz and a multiplet centered at τ 6.08 (4H).

2-(o-Methoxyphenyl)-1,3-dioxolane was prepared from o-methoxybenzaldehyde and ethylene glycol by the procedure previously described for the

preparation of crotonaldehyde ethyleneacetal.

A colorless liquid was obtained in 80% yield. B.p. 117°C at 2 mm; n_D^{24} 1.5325. Lit. b.p. 119.5-120.5°C at 3 mm; n_D^{20} 1.5343 (34).

2-(p-Methoxyphenyl)-1,3-dioxolane was prepared from p-anisaldehyde and ethylene glycol by the procedure previously described for the preparation of crotonaldehyde ethyleneacetal.

A colorless liquid was obtained in 83% yield. B.p. 139°C at 8 mm; n_D^{24} 1.5335. Lit. b.p. 158-160°C at 17 mm; $n_D^{19.5}$ 1.4306 (34).

2-Methyl-1,3-dioxolane was prepared according to the method of Hibbert and Timm (35).

To a mixture of 62 g (1 mole) of ethylene glycol and 44 g (0.33 mole) of paraldehyde was added 0.5 g of concentrated sulfuric acid. The resulting mixture was heated under reflux for 12 hours. During the first five hours of heating there were two layers evident but at the end of the reflux period a homogeneous solution resulted. Anhydrous sodium carbonate (10 g) was then added and the mixture was then stirred for one hour. Subsequently the solid material was removed by suction filtration and the filtrate was washed with five 100 ml portions of ether. The combined ether washings were washed with 100 ml of a saturated aqueous sodium chloride solution, dried, filtered free of drying agent and the filtrate freed from ether by fractional distillation through a four-inch Vigreaux column at atmospheric pressure. The

residue was also distilled at atmospheric pressure and gave 45 g (51%) of a colorless liquid. B.p. 72°C at 700 mm; n_D^{25} 1.3962. Lit. b.p. 83-85°C at 760 mm (35).

2-Phenyl-1,3-dioxolane was prepared from benzaldehyde and ethylene glycol by the procedure previously described for the preparation of crotonaldehyde ethyleneacetal.

A colorless liquid was obtained in 85% yield. B.p. 87°C at 5 mm; n_D^{25} 1.5248. Lit. b.p. 101°C at 10 mm (36); n_D^{20} 1.5270 (37).

2-(Bromomethyl)-1,3-dioxolane was prepared from bromoacetaldehyde diethylacetal and ethylene glycol by the procedure described by McElvain and Curry (38).

A colorless liquid was obtained in 70% yield. B.p. 60°C at 15 mm; n_D^{23} 1.4805. Lit. b.p. 175°C at 745 mm; n_D^{25} 1.4805 (38).

2-(Methylthiomethyl)-1,3-dioxolane was prepared by the following procedure.

To a stirred solution of 11.5 g (0.24 mole) of methyl mercaptan in 300 ml of dry 1,2-dimethoxyethane cooled to -10°C by means of an ice-salt bath was added 11.5 g (0.24 mole) of sodium hydride in 2 g portions. After complete addition of the sodium hydride the cooling bath was removed and the reaction mixture was stirred at room temperature for 2 hours. 2-(Bromomethyl)-1,3-dioxolane (40 g, 0.24 mole) was then added and the reaction

mixture was heated under reflux for 2 hours and then cooled to room temperature. The precipitated sodium bromide was removed by suction filtration and the filtrate was freed from solvent. The pale yellow residue was then distilled under reduced pressure and gave 15 g (47%) of a colorless liquid. B.p. 64-65°C at 15 mm; n_D^{24} 1.4820.

Anal. Calcd. for $C_5H_{10}O_2S$: C, 44.75; H, 7.46; S, 23.85.

Found: C, 44.57; H, 7.28; S, 24.00.

The 60 MHz n.m.r. spectrum in CCl_4 was consistent with the proposed structure, showing a triplet centered at τ 5.09 (1H), J = 4.5 Hz, a multiplet between τ 6.02 and 6.32 (4H), a doublet centered at τ 7.47 (2H), J = 4.5 Hz and a singlet at τ 7.89 (3H).

2-(N,N-Dimethylaminomethyl)-1,3-dioxolane was prepared according to the published procedure (39).

To 70 ml of a 33% solution of dimethylamine in dry benzene was added 25 g (0.15 mole) of 2-(bromomethyl)-1,3-dioxolane. The resulting mixture was heated in an Autoclave at 150°C for 5 hours. The reaction mixture was then allowed to cool to room temperature and the resulting dark brown oil was filtered free of solid material and the filtrate then freed from benzene. The residue was distilled under reduced pressure and gave 12 g (60%) of a colorless liquid. B.p. 59-60°C at 20 mm; n_D^{25} 1.4320. Lit. b.p. 68°C at 20 mm (39).

Anal. Calcd. for $C_6H_{13}NO_2$: C, 54.96; H, 9.92; N, 10.69.

Found: C, 54.58; H, 9.86; N, 10.51.

The 60 MHz n.m.r. spectrum in CCl_4 was consistent with the proposed structure, showing a triplet centered at τ 5.21 (1H), J = 4 Hz, a multiplet centered at τ 6.22 (4H), a doublet centered at τ 7.62 (2H), J = 4 Hz, and a singlet at τ 7.78 (6H).

2-(Methoxymethyl)-1,3-dioxolane was prepared from methoxyacetaldehyde diethylacetal and ethylene glycol by the procedure of McElvain and Curry (38).

A colorless liquid was obtained in 70% yield. B.p. 130°C at 710 mm; n_D^{24} 1.4216. Lit. b.p. 57-58°C at 18 mm; n_D^{20} 1.4209 (40).

Norcamphor ethylene ketal was synthesized from norcamphor and ethylene glycol by the procedure previously described for the preparation of crotonaldehyde ethyleneacetal.

A colorless liquid was obtained in 80% yield. B.p. 78°C at 14 mm; n_D^{25} 1.4756. Lit. b.p. 78-80°C at 14 mm; n_D^{25} 1.4319*.

5-Norbornen-2-one was prepared by the method of Bly and Bly (41).

To a mechanically stirred mixture of 20 g (0.182 mole) of 5-norbornen-2-ol (a mixture of exo and endo) and 32 g (0.296 mole) of p-benzoquinone in 300 ml of dry benzene was added 20 g (0.085 mole) of aluminum tertiary butoxide. The resulting mixture was heated under reflux for 74 hours, an additional 20 g of aluminum tertiary

* This value was found to be in error since when the value of the refractive index was determined again on the sample used by these authors (30) it was found to be n_D^{25} 1.4752.

butoxide being added in portions over the first 24 hours of reflux. At the end of the reflux period the reaction mixture was cooled to room temperature and then was diluted with 400 ml of 3N hydrochloric acid. The resulting mixture was then filtered through a Buchner funnel. The two layers present in the filtrate were separated and the aqueous layer was discarded. The benzene layer was then washed with six 150 ml portions of 3N hydrochloric acid followed by washing with four 100 ml portions of a 5% aqueous sodium hydroxide solution and two 50 ml portions of a saturated aqueous sodium chloride solution. The benzene layer was then dried, filtered free of drying agent and the filtrate freed from benzene. The residue was distilled under reduced pressure and gave 17 g (85%) of a colorless liquid. B.p. 63-64°C at 21 mm; n_D^{27} 1.4819. Lit b.p. 72-76°C at 22 mm; n_D^{25} 1.4834 (42).

5-Norbornen-2-one ethylene ketal was prepared from 5-norbornen-2-one and ethylene glycol by the procedure previously described for the preparation of crotonaldehyde ethyleneacetal.

A colorless liquid was obtained in 75% yield. B.p. 76°C at 9 mm; n_D^{24} 1.4872.

Anal. Calcd. for $C_9H_{12}O_2$: C, 71.05; H, 7.89.

Found: C, 70.92; H, 7.72.

The 60 MHz n.m.r. spectrum in CCl_4 was consistent with the proposed structure, showing a multiplet centered at τ 3.98 (2H), a singlet centered at τ 6.18 (4H), a broad singlet centered at

τ 7.22 (1H),W/2 = 7.5 Hz, a broad singlet centered at τ 7.47, W/2 = 6 Hz and a multiplet between τ 8.06 and 9.30 (4H).

exo-2-Chloro-syn-7-acetoxynorbornane was prepared according to the method of Baird (43).

To 200 ml of glacial acetic acid was added 20 g (0.21 mole) of norbornylene, 16.0 g (0.2 mole) of anhydrous sodium acetate, 50 g (0.37 mole) of anhydrous cupric chloride and 1 g of anhydrous palladium chloride. The resulting mixture was heated and stirred at 80°C for 72 hours. The cooled reaction mixture was filtered and the filter cake was washed twice with 75 ml portions of glacial acetic acid. The filtrate and the washings were combined and added to 1500 ml of water. The resulting mixture was extracted five times with 100 ml portions of pentane. The combined pentane extracts were washed twice with 25 ml of a 10% aqueous sodium carbonate solution and twice with 25 ml portions of water. The pentane solution was dried, filtered free of drying agent and the filtrate freed from pentane. The residue was distilled under vacuum and gave 25 g (73%) of a colorless liquid. B.p. 61°C at 0.1 mm; n_D^{26} 1.4849. Lit. b.p. 63-65°C at 0.1 mm; n_D^{20} 1.4833 (43).

syn-7-Norbornenol was prepared by a modification of the method of Baird (43).

To a solution of 50 g (0.265 mole) of exo-2-chloro-syn-7-acetoxynorbornane in 125 ml of dry dimethylsulfoxide was added

all at once a solution of 29.0 g (0.53 mole) of sodium methoxide in 300 ml of dry dimethylsulfoxide. The reaction mixture was stirred at room temperature overnight (14 h). To the reaction mixture was then added 300 ml of water and the resulting mixture was subjected to steam distillation until 1 liter of distillate had been collected. The distillate was extracted continuously with ether for 8 hours. The ether layer was then dried, filtered free of drying agent and the filtrate freed from ether to give 25 g (85%) of crude syn-7-norbornenol which crystallized on standing at room temperature. The product was purified for characterization by sublimation [75°C (150-200 mm)] which gave white fern-like crystals. M.p. 85.5-87°C after further purification by preparative g.l.c.. Lit. m.p. 88.5-98.5°C after purification by preparative g.l.c. (43).

2-Norbornen-7-one was prepared from syn-7-norbornenol by the method of Bly and Bly (41) as previously described for the preparation of 5-norbornen-2-one.

A colorless liquid was obtained in 80% yield. B.p. 57-59°C at 17 mm; n_D^{25} 1.4788. Lit. b.p. 54-56°C at 17 mm (41).

2-Norbornen-7-one ethylene ketal was prepared from 2-norbornen-7-one and ethylene glycol by the procedure previously described for the preparation of crotonaldehyde ethyleneacetal.

A colorless liquid was obtained in 80% yield. B.p. 73-75°C

at 6 mm; n_D^{24} 1.4904.

Anal. Calcd. for $C_9H_{12}O_2$: C, 71.05; H, 7.89.

Found: C, 70.91; H, 7.98.

The 60 MHz n.m.r. spectrum in CCl_4 was consistent with the proposed structure, showing a triplet centered at τ 3.98 (2H), J = 2.5 Hz, a triplet centered at τ 6.26 (4H), J = 3 Hz, a multiplet centered at τ 7.62 (2H), a multiplet between τ 7.94 and 8.32 (2H) and a multiplet between τ 8.97 and 9.27 (2H).

2. Preparation of Some Authentic Hydrogenolysis Products.

2-Allyloxyethanol was prepared according to the following modification of the procedure of Hurd and Pollock (44).

To a solution of 62 g (1 mole) of dry ethylene glycol in 300 ml of dry 1,2-dimethoxyethane was added 19.2 g (0.4 mole) of sodium hydride. The resulting mixture was stirred at room temperature for two hours and then 48.4 g (0.4 mole) of allyl bromide was added. This mixture was heated under reflux for two hours and was then cooled to room temperature. The solid material was removed by suction filtration and the filtrate was freed from solvent. The resulting oil was distilled under reduced pressure giving 27 g (67%) of a colorless liquid. B.p. 46°C at 5 mm; n_D^{25} 1.4333. Lit. b.p. 63-64°C at 18-19 mm; n_D^{20} 1.4356 (44).

Crotyl bromide was prepared by the method of Winstein and Young (46).

To a solution of 21.6 g (0.3 mole) of crotyl alcohol in 80 ml of dry pyridine cooled to -20°C by means of a dry ice-acetone bath was added dropwise 11.5 ml of phosphorous tribromide. The rate of addition was controlled so as to maintain the temperature between -20 to -15°C. After complete addition of the phosphorous tribromide the crude product was distilled from the solid residue under reduced pressure (3 mm) into a receiver cooled in dry ice. The distillate was then washed with 100 ml of a cold 10% aqueous sodium bicarbonate solution and then with 100 ml of ice water. The organic layer was then dried over anhydrous calcium chloride overnight in a refrigerator at -15°C. The solid material was then removed by filtration and the filtrate was distilled giving 20 g (50%) of a colorless liquid. B.p. 46-48°C at 94 mm; n_D^{23} 1.4787. Lit. b.p. 49°C at 93 mm; n_D^{25} 1.4795 (46).

2-(Crotyloxy)ethanol was prepared from crotyl bromide and ethylene glycol by the modified procedure of Hurd and Pollock (44) as previously described for the preparation of 2-allyloxyethanol.

A colorless liquid was obtained in 65% yield. B.p. 81°C at 18 mm; n_D^{27} 1.4383. Lit. b.p. 85-87°C at 21-22 mm; n_D^{20} 1.4428 (45).

2-Methylthioethanol was prepared by the following procedure.

To a solution of 39 g (0.5 mole) of 2-mercaptoethanol in 300 ml of dry 1,2-dimethoxyethane was added 12 g (0.5 mole) of sodium hydride. The resulting mixture was stirred at room temperature for two hours. Iodomethane (71 g, 0.5 mole) was then added and the reaction

mixture was left to stir overnight at room temperature. The solid materials were removed by suction filtration and the filtrate was freed from solvent. The residue was taken up in 200 ml of anhydrous ether and was again filtered to remove the precipitated solid materials and the filtrate was freed from ether. The residue was distilled at reduced pressure to give 25 g (54%) of a colorless liquid. B.p. 78°C at 30 mm; n_D^{24} 1.4869. Lit. b.p. 61°C at 10 mm; n_D^{20} 1.4930 (47).

2(2-Methylthioethoxy)ethanol was prepared by the following procedure.

To a solution of 4 g (0.044 mole) of 2-methylthioethanol in 200 ml of dry 1,2-dimethoxyethane was added 1.05 g (0.044 mole) of sodium hydride. The reaction mixture was then stirred at room temperature for two hours. Ethyl chloroacetate (5.4 g, 0.044 mole) was then added and the reaction mixture was heated under reflux overnight. The reaction mixture was then cooled to room temperature, filtered free of solid material and freed from solvent. The residue was taken up in 50 ml of anhydrous ether and was again filtered free of solid and the filtrate freed from ether.

The crude product was then added to a solution of 1.7 g (0.044 mole) of lithium aluminum hydride in 100 ml of anhydrous ether. The resulting mixture was let stir one hour and then 10 ml of a 15% aqueous potassium hydroxide solution was added. The reaction mixture was further diluted with 50 ml of water and the resulting mixture was extracted continuously with ether for 12 hours. The ether solution was then dried, filtered free of drying agent and the filtrate freed from ether. The residue was distilled under reduced pressure to give

2.3 g (52%) of a colorless liquid. B.p. 84°C at 2.5 mm; n_D^{24} 1.4837.

Anal. Calcd. for $C_5H_{12}O_2S$: C, 44.10; H, 8.83; S, 23.52.

Found: C, 44.01; H, 8.82; S, 23.40.

The 60 MHz n.m.r. spectrum in CCl_4 was consistent with the proposed structure, showing a multiplet between τ 6.20 and 6.81 (7H), a triplet centered at τ 7.35 (2H), J = 7Hz and a singlet at τ 7.88 (3H).

The i.r. spectrum (neat) showed an absorption band between 3640 cm^{-1} and 3210 cm^{-1} (O-H stretch) and a broad absorption band between 1150 cm^{-1} to 1010 cm^{-1} (C-O stretch).

Ethyl (2-N,N-dimethylaminomethoxy)acetate was prepared by a modification of the procedure of Leffler and Calkins (48).

To a solution of 30 g (0.337 mole) of 2(N,N-dimethylamino)-ethanol and 41.2 g (0.337 mole) of ethyl chloroacetate in 400 ml of dry 1,2-dimethoxyethane cooled to -10°C by means of an ice-salt bath was added in 1 g portions, 8.1 g (0.337 mole) of sodium hydride. After complete addition of the sodium hydride, the reaction mixture was allowed to warm to room temperature and was let stir 24 hours. The solids were then removed by suction filtration and the filtrate was freed from solvent. The residue was taken up in 100 ml of anhydrous ether and the precipitated solids were again removed by suction filtration. The filtrate was freed from ether and the residue was distilled under reduced pressure. Yield 25 g (42%). B.p. 64°C at 0.5 mm; n_D^{23} 1.4265.

Anal.Calcd. for $C_8H_{17}NO_3$: C, 54.86; H, 9.71; N, 8.00.

Found: C, 54.92; H, 9.66; N, 7.81.

The 60 MHz n.m.r. spectrum in CCl_4 was consistent with the proposed structure showing a quartet centered at τ 5.89 (2H), J = 7 Hz, a singlet at τ 6.08 (2H). a triplet centered at τ 6.48 (2H), J = 6 Hz, a triplet centered at τ 7.58 (2H), J = 6 Hz, a singlet at τ 7.83 (6H) and a triplet centered at τ 8.77 (3H), J = 7 Hz.

The i.r. spectrum (neat) showed an absorption band centered at 1760 cm^{-1} (C=O stretch) and a broad absorption band between 1220 cm^{-1} and 1110 cm^{-1} (C-O stretch).

2(2-N,N-Dimethylaminoethoxy)ethanol was prepared by the following procedure.

Ethyl (2-N,N-dimethylaminomethoxy)acetate (10 g, 0.06 mole) was added in a dropwise manner to a stirring solution of 2.28 g (0.06 mole) of lithium aluminum hydride in 50 ml of anhydrous ether. After complete addition of the ester, the reaction mixture was stirred one hour at room temperature and then 10 ml of a 15% aqueous potassium hydroxide solution was added. A further 50 ml of water was then added and the resulting mixture was extracted continuously with ether for 12 hours. The ether solution was dried, filtered free of drying agent and the filtrate freed from ether. The residue was distilled under reduced pressure giving 6 g (60%) of a colorless liquid. B.p. 60-61°C at 4 mm; n_D^{25} 1.4390.

Anal. Calcd. for $C_6H_{15}NO_2$: C, 54.14; H, 11.28; N, 10.53.

Found: C, 54.23; H, 11.34; N, 10.65.

The 60 MHz n.m.r. spectrum in CCl_4 was consistent with the proposed structure, showing a singlet at τ 5.31 (1H). a multiplet

centered at τ 6.54 (6H), a triplet centered at τ 7.59 (2H), J = 5.5 Hz, and a singlet at τ 7.80 (6H).

The i.r. spectrum in CCl_4 showed a broad absorption between 3600 cm^{-1} and 3050 cm^{-1} (O-H stretch) and a broad absroption between 1170 cm^{-1} and 1030 cm^{-1} (C-O stretch).

Ethyl (2-norbornenyloxy)acetate (a mixture of exo and endo) was prepared from 5-norbornen-2-ol (a mixture of exo and endo) and ethyl chloroacetate by the modified procedure of Leffler and Calkins (48) as previously described for the preparation of ethyl (2-N,N-dimethylaminomethoxy)acetate

A colorless liquid was obtained in 43% yield. B.p. 73°C at 0.6 mm; n_D^{24} 1.4701.

Anal. Calcd. for $C_{11}H_{16}O_3$: C, 67.54; H, 8.16.

Found: C, 67.43; H, 8.33.

The 60 MHz n.m.r. spectrum in CCl_4 was consistent with the proposed structure, showing a multiplet centered at τ 3.92 (2H), a triplet centered at τ 5.92 (2H), J = 7.5 Hz, a singlet at τ 6.11 (2H), a multiplet between τ 6.83 and 7.38 (2H) and a broad multiplet between τ 7.78 and 9.28 (8H).

The i.r. spectrum in CCl_4 showed an absorption 3060 cm^{-1} (vinylic C-H stretch), two bands at 1755 cm^{-1} and 1730 cm^{-1} (C=O stretch of the exo and endo compounds) and a broad absorption between 1290 cm^{-1} and 1100 cm^{-1} (C-O stretch).

2-(2—Norbornenyloxy)ethanol (a mixture of exo and endo) was prepared

by the $LiAlH_4$ reduction of ethyl (2-norbornenyloxy)acetate (a mixture of exo and endo) by the procedure previously described for the preparation of 2-(2-N,N-dimethylaminoethoxy)ethanol.

A colorless liquid was obtained in 87% yield. B.p. 63-65°C at 1 mm; n_D^{24} 1.4895.

Anal. Calcd. for $C_9H_{14}O_2$: C, 70.10; H, 9.15.

Found: C, 69.84; H, 8.73.

These two isomers were separated by preparative g.l.c. and their n.m.r. spectra and are shown in Figures 11 and 12. The assignment of the exo and endo configuration to these two isomers is discussed on page 52.

The i.r. spectrum in CCl_4 showed an absorption between 3610 cm^{-1} and 3280 cm^{-1} (O-H stretch), an absorption at 3080 cm^{-1} (vinylic C-H stretch) and a broad absorption between 1130 cm^{-1} to 1040 cm^{-1} (C-O stretch).

Ethyl (7-syn-norbornenyloxy)acetate was prepared from syn-7-norbornenol and ethyl chloroacetate by the modified procedure of Leffler and Calkins (48) as previously described for the preparation of ethyl (2-N,N-dimethylaminoethoxy)acetate.

A colorless liquid was obtained in 30% yield. B.p. 60°C at 0.1 mm; n_D^{26} 1.4768.

Anal. Calcd. for $C_{11}H_{16}O_3$: C, 67.34; H, 8.16.

Found: C, 66.78; H, 8.16.

The 60 MHz n.m.r. spectrum in $CDCl_3$ was consistent with the

proposed structure, showing a broad singlet centered at τ 3.98 (2H), W/2 = 5 Hz, a quartet centered at τ 5.79 (2H), J = 7 Hz, a singlet at τ 6.01 (2H), a broad singlet centered at τ 6.37 (1H), W/2 = 4.5 Hz, a broad singlet centerd at τ 7.11 (2H), W/2 = 7 Hz, and a multiplet between τ 8.10 and 9.23 (7H).

The i.r. spectrum (neat) showed an absorption at 3080 cm^{-1} (vinylic C-H stretch), an absorption at 1780 cm^{-1} (C=O stretch) and a broad absorption between 1290 cm^{-1} to 1110 cm^{-1} (C-O stretch).

2-(7-syn-Norbornenyloxy)ethanol was prepared by the lithium aluminum hydride reduction of ethyl (7-syn-norbornenyloxy)acetate by the procedure previously described for the preparation of 2-(2-N,N-dimethylaminoethoxy) ethanol.

A colorless liquid was obtained in 80% yield. B.p. 56°C at 0.2 mm; n_D^{26} 1.4915.

Anal. Calcd. for $C_9H_{14}O_2$: C, 70.10; H, 9.15.

Found: C, 70.28; H, 9.32.

The 60 MHz n.m.r. spectrum of this compound is shown in Figure 13.

The i.r. spectrum (neat) showed an absorption band between 3630 cm^{-1} to 3200 cm^{-1} (O-H stretch), an absorption band at 3080 cm^{-1} (vinylic C-H stretch) and a broad absorption band between 1180 cm^{-1} to 1020 cm^{-1} (C-O stretch).

anti-7-Norbornenol was prepared according to the procedure of Gassman and Pape (49).

To a solution of 8.8 g (0.232 mole) of $LiAlH_4$ in 200 ml of ether cooled to 0°C by means of an ice bath was added dropwise a solution of 7-norbornenone (25 g, 0.232 mole) in 50 ml of anhydrous ether. After total addition, the cooling bath was removed and the reaction mixture was let stir for one hour. The reduction complex was then decomposed by the dropwise addition of a 15% aqueous solution of potassium hydroxide (5 ml) and then by addition of 100 ml of water. The resulting mixture was extracted overnight with ether. The ether extract was dried, filtered free of drying agent and the filtrate freed from ether. The resulting oil was subjected to g.l.c. analysis which showed two major components in the ratio of 1:6. These materials were separated by preparative g.l.c.. The component present in the smaller amount proved to be syn-7-norbornenol by comparison with this substance prepared earlier. The component present in the larger amount exhibited a melting point of 113.5-115°C. Lit. m.p. of anti-7-norbornenol 117.5-119.5°C (49).

Ethyl (7-anti-norbornenyloxy)acetate was prepared from anti-7-norbornenol (contaminated with some syn-7-norbornenol) and ethyl chloroacetate by the modified procedure of Leffler and Calkins (48) previously described for the preparation of ethyl (2-N,N-dimethylaminoethoxy)acetate.

A colorless liquid was obtained in 45% yield. B.p. 59°C at 0.3 mm; n_D^{25} 1.4728. This material proved to be only one component by g.l.c..

Anal. Calcd. for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22.

Found: C, 67.60; H, 8.41.

The 60 MHz n.m.r. spectrum in CCl_4 was consistent with the proposed structure, showing a triplet centered at τ 4.08 (2H), J = 2 Hz, a quartet centered at τ 5.83 (2H), J = 7 Hz, a singlet at τ 6.09 (2H), a broad singlet at τ 6.75 (1H), W/2 = 4.5 Hz, a multiplet centered at τ 7.34 (2H), a multiplet between τ 8.0 to 8.37 (2H), a triplet centered at τ 8.75 (3H), J = 7 Hz and a multiplet between τ 8.94 and 9.23 (2H).

The i.r. spectrum (neat) showed an absorption at 3060 cm^{-1} (vinylic C-H stretch), an absorption at 1760 cm^{-1} (C=O stretch) and a broad absorption between 1290 cm^{-1} and 1110 cm^{-1} (C-O stretch).

2-(7-anti-Norbornenyloxy)ethanol was prepared by the $LiAlH_4$ reduction of ethyl (7-anti-norbornenyloxy)acetate by the procedure previously described for the preparation of 2-(N,N-dimethylaminoethoxy)ethanol.

A colorless liquid was obtained in 85% yield. B.p. 45°C at 0.3 mm; n_D^{26} 1.4859.

Anal. Calcd. for $C_9H_{14}O_2$: C, 70.10; H, 9.15.

Found: C, 70.07; H, 8.95.

The 60 MHz n.m.r. spectrum of this compound is shown in Figure 14.

The i.r. spectrum (neat) showed an absorption band between 3600 cm^{-1} to 3180 cm^{-1} (O-H stretc ` an absorption band at 3060 cm^{-1} (vinylic C-H stretch) and a broad absorption band between 1150 cm^{-1} to 1010 cm^{-1} (C-O stretch).

3. Hydrogenolysis of the 2-Substituted-1,3-dioxolanes.

a. Reduction using $AlClH_2$

The procedure for the reduction of all the 2-substituted-1,3-dioxolanes was that described by Diner (50) for the hydrogenolysis of the tetrahydropyranyl acetals. The reduction of 2-vinyl-1,3-dioxolane is described here as an example of the procedure.

Lithium aluminum hydride (0.57 g, 0.015 mole) was dissolved in 15 ml of dry ether and the solution was cooled to 5°C in an ice bath. To this solution was added dropwise an ether solution of aluminum chloride, prepared by adding aluminum chloride (1.99 g, 0.015 mole) in small portions to 15 ml of dry ether cooled to 5°C in an ice bath. The resulting mixed hydride solution was stirred at room temperature for 15 min and then 2-vinyl-1,3-dioxolane (3 g, 0.03 mole) was added. The resulting mixture was stirred for 30 min at room temperature and then an aqueous 15% solution of potassium hydroxide was added dropwise until no further reaction occurred and a white solid precipitated (lithium aluminate). The solid was separated by suction filtration and the ether was removed by distillation. The residue (85% recovery) was analysed by g.l.c.. Only 2-allyloxyethanol was found in the residue and was identified by comparison of the retention time with authentic material.

Other dioxolanes were stirred with the reducing species for varying lengths of time as noted in Tables 1, 2, 8, and 10.

In some cases, authentic hydrogenolysis products were prepared for comparison with those isolated from the hydrogenolysis reactions, however, isolation of the reaction products by distillation

or preparative g.l.c. was also used; the unknown products thus being characterized by their n.m.r. and i.r. spectra and their elemental analyses. The physical constants of the products isolated from these reactions are shown in Table 12.

b. Reductions using $LiAlH_4$ in ether.

The same procedure as that described above for the reductions using $AlClH_2$ was used for the reductions with $LiAlH_4$. For example, $LiAlH_4$ (1.14 g, 0.03 mole) and acrolein ethyleneacetal (3 g, 0.03 mole) were mixed in 30 ml of anhydrous ether and the mixture stirred for 48 hours.

G.l.c. analysis of the residue after work-up (85% recovery) showed 76% overall reduction and that the products were a 1:1 mixture of cis and trans-2-propenyloxyethanol. These products were identified by their n.m.r. and i.r. spectra and elemental analyses after isolation by preparative g.l.c..

Other dioxolanes were stirred with $LiAlH_4$ in ether for varying lengths of time as noted in Table 5. The physical constants of the products isolated from these reactions are shown in Table 12.

c. Reduction of cinnamaldehyde ethyleneacetal with $LiAlD_4$.

The same procedure as that described for the reductions using $LiAlH_4$ in ether was used for the reduction with $LiAlD_4$. The results of this experiment are given in Table 5 and the 60 MHz n.m.r. spectrum of the product is shown in Figure 8.

d. Reduction of cinnamaldehyde ethyleneacetal with $LiAlH_4$ followed by a D_2O work-up.

The same procedure as that described for the reductions

using $LiAlH_4$ in ether was used in this case except that at the end of the reaction time D_2O was added until no further reaction occurred. The results of this experiment are given in Table 5 and the 60 MHz n.m.r. spectrum of the product is discussed on Page 31.

e. Reductions using $LiAlH_4$ in refluxing 1,2-dimethoxyethane.

The same procedure as that described for the reductions with $LiAlH_4$ in ether was used except that after the reagents were mixed in 1,2-dimethoxyethane, the resulting solution was heated under reflux for the required reaction period. The mixture was then cooled to room temperature and worked-up as previously described except that after addition of the 15% aqueous potassium hydroxide solution, 50 ml of water was added and the resulting mixture was extracted overnight with ether. The ether extract was then dried, filtered free of drying agent and freed from solvent by fractional distillation at atmospheric pressure.

For example, $LiAlH_4$ (1.9 g, 0.05 mole) and acrolein ethylene-acetal (5 g, 0.05 mole) were mixed in 50 ml of dry 1,2-dimethoxyethane and the resulting mixture was heated under reflux for 24 hours.

G.l.c. analysis of the residue (85% recovery) showed that the residue was composed of a 1:1 mixture of cis and trans-2-propenyl-oxyethanol by comparison of retention times with previously characterized material.

Other dioxolanes were treated in the same manner for varying lengths of time as noted in Table 6. The physical constants of the products isolated from these reactions are given in Table 12.

f. Reduction of acrolein ethyleneacetal with $LiAlH_4$ in 1,2-dimethoxyethane at room temperature.

The same procedure as that described above for the reductions with $LiAlH_4$ in refluxing 1,2-dimethoxyethane was used except no heat was applied. G.l.c. analysis of the residue (90% recovery) showed only a trace of reduction. Retention time of the two reduction products agreed with the retention times exhibited by cis and trans-2-propenyloxyethanol.

g. Reductions using $LiAlH_4$ in di-n-propyl ether.

The same procedure as that described above for the reduction using $LiAlH_4$ in diethyl ether was used here. For example, $LiAlH_4$ (0.38 g, 0.01 mole) and acrolein ethyleneacetal (1 g, 0.01 mole) were mixed in 10 ml of di-n-propyl ether and the mixture stirred at room temperature at 24 hours.

G.l.c. analysis of the residue after work-up (90% recovery) showed 70% reduction and that the products were a 1:1 mixture of cis and trans-2-propenyloxyethanol by comparison of the g.l.c. retention times with authentic material.

Other dioxolanes were treated in the same manner as noted in Table 7.

h. Reductions using $LiAlH_4$ in refluxing di-n-propyl ether.

The procedure was the same as that described above for the reductions using $LiAlH_4$ in di-n-propyl ether at room temperature except that after mixing of the reagents the reaction mixture was heated under reflux for the desired reaction time. The results of

these experiments are shown in Table 7. The products were identified either by comparison of their g.l.c. retention times with authentic materials or by isolation of the products by preparative g.l.c.. The physical constants of the products so isolated are shown in Table 12.

i. Competitive hydrogenolyses using AlH_3

The competitive hydrogenolyses listed in Table 9 were carried out using the general procedure described for reductions with $AlClH_2$, however, different proportions of material were used. The general procedure is described below using the case of acrolein ethyleneacetal and crotonaldehyde ethyleneacetal as an example.

Lithium aluminum hydride (0.57 g, 0.015 mole) and aluminum chloride (0.665 g, 0.005 mole) were mixed in 40 ml of dry ether as previously described for the preparation of $AlClH_2$. The resulting mixed hydride solution was stirred at room temperature for 15 min and then a mixture of acrolein ethyleneacetal (2 g, 0.02 mole) and crotonaldehyde ethyleneacetal (2.28 g, 0.02 mole) was added. The solution was stirred at room temperature for 30 min and then an aqueous 15% potassium hydroxide solution was added dropwise until no further reaction was observed. Water (50 ml) was then added and the resulting mixture was extracted continuously with ether for 12 hours. The ether was dried, filtered free of drying agent and the ether removed by distillation. The residue (90% recovery) was analyzed by g.l.c. which showed a 1:4 ratio of

2-allyloxyethanol to 2-crotyloxyethanol by comparison of the g.l.c. retention times with authentic materials.

j. Competitive hydrogenolyses using $AlClH_2$.

The competitive hydrogenolyses reported in Tables 4 and 11 were carried out using the general procedure described for the reductions using $AlClH_2$, however, different proportions of material were used. The general procedure is descibed below using 2-methyl-1,3-dioxolane and 2-(methylthiomethyl)-1,3-dioxolane as an example.

Lithium aluminum hydride (0.143 g, 0.0037 mole) and aluminum chloride (0.5 g, 0.0037 mole) were mixed in 20 ml of anhydrous ether as previously described for the preparation of $AlClH_2$. The resulting mixed hydride solution was stirred for 15 min and a mixture of 2-methyl-1,3-dioxolane (0.66 g, 0.0075 mole) and 2-(methylthiomethyl)-1,3-dioxolane (1 g, 0.0075 mole) was added. The solution was stirred at room temperature for 30 min and an aqueous 15% solution of potassium hydroxide was added until no further reaction occurred. Water (50 ml) was then added and the resulting mixture was extracted overnight with ether. The ether extract was dried, filtered free of drying agent and the ether removed by fractional distillation at atmospheric pressure. The residue (90% recovery) was analyzed by g.l.c. and showed a 7:1 ratio of 2-ethoxyethanol to 2-(2-methylthioethoxy)ethanol by comparison of the g.l.c. retention times with authentic material.

k. Hydrogenolysis of 2-methyl-1,3-dioxolane with $AlClH_2$ in the presence of cyclohexene.

The same procedure was employed as that previously described for reductions using $AlClH_2$ except that before addition of the dioxolane, one molar equivalent of cyclohexene was added to the reducing species. For example, lithium aluminum hydride (0.43 g, 0.0113 mole) and aluminum chloride (1.5 g, 0.0113 mole) were mixed by the procedure previously descibed for the preparation of $AlClH_2$. The resulting mixed hydride was stirred 15 min and then cyclohexene (1.04 g, 0.227 mole) was added. This mixture was stirred a further 15 min and then 2-methyl-1,3-dioxolane (2 g, 0.0227 mole) was added. The solution was stirred for 30 min and then treated with a 15% aqueous potassium hydroxide solution until no further reaction occurred and a white solid precipitated. The solid material was removed by suction filtration and the ether was removed by distillation. G.l.c. analysis of the residue (87% recovery) showed 90% reduction by comparison of the g.l.c. retention times with authentic materials.

l. Hydrogenolysis using alkoxyhydridoaluminum chlorides.

The same procedure as that previously employed for the reductions using $AlClH_2$ was used except that before addition of the dioxolane one molar equivalent of the desired alcohol was added to the reducing species. For example, lithium aluminum hydride (0.645 g, 0.017 mole) and aluminum chloride (2.26 g, 0.017 mole) were mixed in 40 ml of ether as previously described for the

preparation of $AlClH_2$. The resulting mixed hydride was stirred at room temperature for 15 min and then 98% ethanol (1.56 g, 0.034 mole) was added dropwise. The resulting solution was stirred for 15 min and 2-methyl-1,3-dioxolane (3 g, 0.034 mole) was added. The reaction mixture was stirred 30 min at room temperature and an aqueous solution of potassium hydroxide was added until no further reaction occurred and a white precipitate resulted. The solid was removed by suction filtration and the ether removed by distillation. G.l.c. analysis of the residue (90% recovery) showed 100% reduction of the dioxolane by comparison of the g.l.c. retention times with those of authentic material.

This general procedure was used for all hydrogenolyses with the alkoxyhydridoaluminum chlorides and hydrides by changing the alcohol used to give the desired reducing species.

Table 12

Physical constants of the products isolated from the hydrogenolysis reactions.

Product	Boiling Point °C	n_D (T°C)	Analysis Calcd.	Found
$CH_3CH{=}CHOC_2H_4OH$ (cis)	66-72 at 22 mm (1:1 mixture of cis and trans)	1.4408 (25)	C, 58.80	C, 58.61
			H, 9.87	H, 10.17
$CH_3CH{=}CHOC_2H_4OH$ (trans)		1.4391 (25)	C, 58.80	C, 58.51
			H, 9.87	H, 9.85
$C_2H_5CH{=}CHOC_2H_4OH$ (cis)		1.4417 (25)	C, 62.04	C, 62.20
	72-79 at 20 mm (1:1 mixture of cis and trans)		H, 10.41	H, 10.84
$C_2H_5CH{=}CHOC_2H_4OH$ (trans)		1.4413 (25)	C, 62.04	C, 62.26
			H, 10.41	H, 10.17
$CH_2{=}C(CH_3)CH_2OC_2H_4OH$	69-71 at 20 mm	1.4382 (25)	C, 62.04	C, 62.15
			H, 10.41	H, 10.67
$(CH_3)_2C{=}CHOC_2H_4OH$	74 at 18 mm	1.4449 (25)	C, 62.04	C, 61.80
			H, 10.41	H, 9.83
$C_2H_5CH{=}CHCH_2OC_2H_4OH$	68 at 4 mm	1.4434 (22)	C, 64.58	C, 64.38
			H, 10.84	H, 10.40

Table 12-Continued

Product	Boiling Point °C	n_D(T°C)	Analysis Calcd.	Found
$C_3H_7CH=CHOC_2H_4OH$ (cis)	60-68 at 10 mm (1:1 mixture of cis and trans)	1.4414 (26)	C, 64.58	C, 64.43
			H, 10.84	H, 10.66
$C_3H_7CH=CHOC_2H_4OH$ (trans)		1.4446 (25)	C, 64.58	C, 64.60
			H, 10.84	H, 10.93
$(CH_3)_2C=CHCH_2OC_2H_4OH$	69 at 4.5 mm	1.4502 (22)	C, 64.58	C, 64.52
			H, 10.84	H, 10.73
$(CH_3)_2CHCH=CHOC_2H_4OH$	74-75 at 5 mm	1.4532 (24)	C, 64.58	C, 64.29
			H, 10.84	H, 10.71
$C_6H_5CH_2CH_2CH$(O, O)	60 at 0.1 mm	1.5617 (24)	C, 74.13	C, 73.94
			H, 7.92	H, 7.72
$C_6H_5CHDCH_2CH$(O, O)	60 at 0.1 mm	1.5170 (24)	C, 73.74	C, 73.84
			H, 8.37	H, 8.17
$C_6H_5CH=CHCH_2OC_2H_4OH$	92 at 0.05 mm	1.5553 (27)	C, 74.13	C, 74.10
			H, 7.92	H, 7.72

Table 12-Continued

Products	Boiling Point °C	$n_D(T^oC)$	Analysis Calcd.	Found
m-$CH_3OC_6H_4CH_2OC_2H_4OH$	102 at 0.5 mm	1.5300 (21)	C, 65.92	C, 65.66
			H, 7.74	H, 7.67
p-$CH_3OC_6H_4CH_2OC_2H_4OH$	109 at 0.5 mm	1.5285 (23)	C, 65.92	C, 65.97
			H, 7.74	H, 8.00

Table 13

Pertinent spectral data for the compounds reported in Table 12.

Compound	N. M. R.				I. R.	
	Proton	Multiplicity	Chemical Shift τ	Coupling(Hz)	Absorption cm^{-1}	Assignment
$CH_3CH=CHOR$ (cis) 3 2 1	H-1	2 quartets	4.10	$J_{1,2}=7; J_{1,3}=1.5$	3650-3150	O-H
	H-2	multiplet	5.68	$J_{2,1}=J_{2,3}=7$	1670(s)	vinyl ether
					3040	vinyl C-H
$CH_3CH=CHOR$ (trans) 3 2 1	H-1	2 quartets	3.80	$J_{1,2}=13; J_{1,3}=1.5$	3650-3150	O-H
	H-2	multiplet	5.28	$J_{2,1}=13; J_{2,3}=7$	1650(s)	vinyl ether
					3060	vinyl C-H
$CH_3CH_2CH=CHOR$ (cis) 3 2 1	H-1	2 quartets	4.13	$J_{1,2}=5.5; J_{1,3}=1$	3650-3150	O-H
	H-2	quartet	5.70	$J_{2,1}=5.5; J_{2,3}=7$	1660(s)	vinyl ether
					3030	vinyl C-H
$CH_3CH_2CH=CHOR$ (trans) 3 2 1	H-1	2 triplets	3.78	$J_{1,2}=12.5; J_{1,3}=1.5$	3650-3150	O-H
	H-2	multiplet	5.23	$J_{2,1}=12.5; J_{2,3}=7$	1650(s)	vinyl ether
					3050	vinyl C-H

Table 13-Continued

Compound	N. M. R.				I. R.	
	Proton	Multiplicity	Chemical Shift τ	Coupling(Hz)	Absorption cm^{-1}	Assignment
$CH_2=C(CH_3)CH_2OR$ (3 2 1)	H-1	singlet	6.12		3650-3150	O-H
	H-2	singlet	8.28		1650(w)	C=C
	H-3	multiplet	5.12			
$(CH_3)_2C=CHOR$ (2 1)	H-1	multiplet	4.22		3600-3100	O-H
	H-2	broad singlet	8.46	W/2=5	1685(s)	vinyl ether
$C_2H_5CH=CHCH_2OR$ (2 1)	H-1,H-2	multiplet	4.48		3650-3250	O-H
					1675(w)	C=C
$C_2H_5CH_2CH=CHOR$ (cis) (2 1)	H-1	2 triplets	4.09	$J_{1,2}=6.5; J_{1,3}=1$	3650-3100	O-H
	H-2	multiplet	5.70	$J_{2,1}=6.5$	3050	vinyl C-H
					1680(s)	vinyl ether
$C_2H_5CH_2CH=CHOR$ (trans) (2 1)	H-1	2 triplets	3.80	$J_{1,2}=12.5; J_{1,3}=1$	3650-3150	O-H
	H-2	multiplet	5.30	$J_{2,1}=12.5; J_{2,3}=7$	3070	vinyl C-H
					1655(s)	vinyl ether

Table 13-Continued

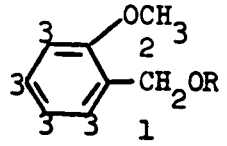
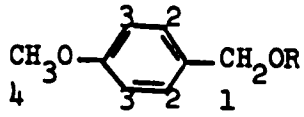
Compound	N. M. R.				I. R.	
	Proton	Multiplicity	Chemical Shift τ	Coupling(Hz)	Absorption cm^{-1}	Assignment
$(CH_3)_2C=CHCH_2OR$ (2 1)	H-1	doublet	6.03	$J_{1,2}=7$	3650-3100	O-H
	H-2	multiplet	4.70		1680(w)	C=C
$(CH_3)_2CHCH=CHOR$ (4 3 2 1)	H-1	doublet	3.80	$J_{1,2}=12.5$	3650-3100	O-H
	H-2	multiplet	5.05-5.55	$J_{2,1}=12.5; J_{2,3}=7$	1650(s)	vinyl ether
	H-3	multiplet	7.50-8.12	$J_{3,2}=7; J_{3,4}=7$		
	H-4	doublet	9.00	$J_{4,3}=7$		
$C_6H_5CH=CHCH_2OR$ (3 2 1)	H-1	doublet	5.96	$J_{1,2}=5$	3650-3120	O-H
	H-2,H-3	multiplet	3.62-3.91			
	H-1	singlet	5.50		3650-3150	O-H
	H-2	singlet	6.27			
	H-3	multiplet	2.58-3.37			

Table 13-Continued

Compound	N. M. R.				I. R.	
	Proton	Multiplicity	Chemical Shift τ	Coupling(Hz)	Absorption cm^{-1}	Assignment
	H-1	singlet	5.70		3650-3150	O-H
	H-2	doublet	2.90	$J_{2,3}=8$		
	H-3	doublet	3.34	$J_{3,2}=8$		
	H-4	singlet	6.35			

R = CH_2CH_2OH

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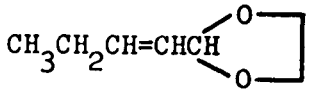
PART II

DEHYDROBROMINATION OF SOME α-BROMO ACETALS

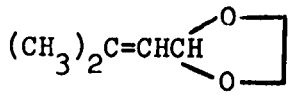
INTRODUCTION

A. The Problem

For some of the hydrogenolysis experiments described in Part I of this thesis, the two α,β-unsaturated acetals, 2-pentenal ethyleneacetal 1 and 2-isopentenal ethyleneacetal 2 were required.



1



2

Their preparation by base catalyzed removal of hydrogen bromide from the corresponding α-bromo acetal precursors gave results which were unexpected on the basis of literature reports. McElvain, in a review article (1), has reported a number of results on the dehydrohalogenation reaction of many α-halo acetals in basic solution, particularly with potassium t-butoxide in t-butyl alcohol.

Those α-halo acetals which had no hydrogen atoms available on an adjacent carbon atom for abstraction by the base other than the anomeric hydrogen were found to give ketene acetals exclusively (Scheme 1). On the other hand, α-bromo dialkylacetals having one or more hydrogen atoms on the β carbon atom gave, upon

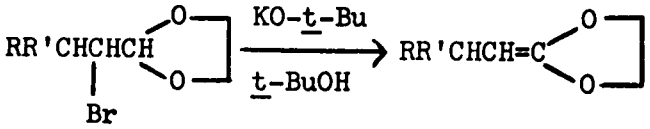
dehydrobromination, apparently only the dialkyl acetals of the corresponding α,β-unsaturated aldehydes.

$$RR'\underset{\underset{X}{|}}{C}\text{-}CH(OR")_2 \xrightarrow[\underline{t}\text{-BuOH}]{KO\text{-}\underline{t}\text{-}Bu} RR'C{=}C(OR")_2$$

R, R' = H, halogen, C_6H_5
R" = CH_3, C_2H_5, $\underline{n}$-C_3H_7, $\underline{i}$-C_4H_9, $\underline{i}$-C_5H_{11}, C_6H_5
X = Br, I
Bu = C_4H_9

Scheme 1

In the present work it was found that application of these reactions to α-bromo ethyleneacetals with hydrogen atoms on the β carbon gave, in most cases, the corresponding substituted ketene ethyleneacetals as the major product (Scheme 2).



R = R' = H
R = CH_3, R' = H
R = C_2H_5, R' = H
Bu = C_4H_9

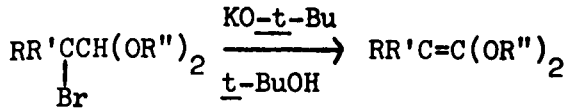
Scheme 2

Accordingly a series of experiments were devised to determine the factors influencing the direction of the dehydrohalogenation of α-bromo acetals in both the dialkyl and the ethylene series. A second objective was to devise a route which would provide the desired α,β-unsaturated ethyleneacetals, 1 and 2 , required for the hydrogenolysis experiments.

B. Literature Survey

1. The Dehydrohalogenation of α-Halo Acetals

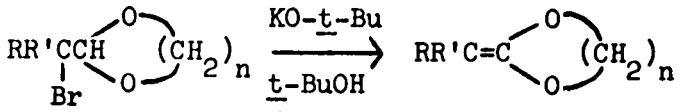
A considerable amount of work has been reported by McElvain (1) on the reaction of α-halo acetals under basic conditions. In most cases the base employed was potassium t-butoxide in t-butyl alcohol. McElvain has used this method to prepare dichloro- and dibromoketene dialkylacetals, the ketene di-n-propyl-, diisobutyl-, and diisoamylacetals, as well as phenylketene dimethylacetal (Scheme 3) and a number of 2-methylene-1,3-dioxolanes and 2-methylene-1,3-dioxanes (Scheme 4). The use of a tertiary alcohol as solvent in these reactions



R = H, Cl, Br, C_6H_5
R'= H, Cl, Br
R"= CH_3, C_2H_5, C_3H_7, i-C_4H_9, i-C_5H_{11}
Bu= C_4H_9

Scheme 3

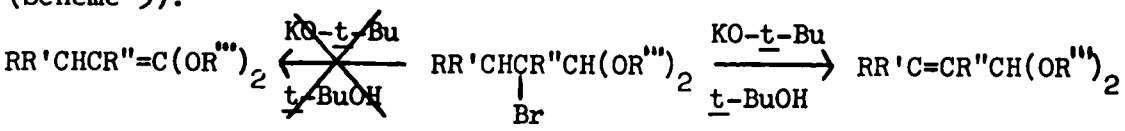
was found necessary due to the tendency of primary and secondary alcohols to add to the ketene acetal product to form the corresponding mixed orthoester.



n = 2, 3
R = H, Cl, Br, C_6H_5
R'= H, Cl, Br
Bu= C_4H_9

Scheme 4

Upon extension of the dehydrohalogenation reaction with the aim of producing alkylketene diethylacetals, McElvain (2) found the course of the reaction to be altered (Scheme 5). For example, treatment of such acetals as α-bromo-n-butyraldehyde diethylacetal 3, α-bromo-isobutyraldehyde diethylacetal 4 and α-bromo-isovaleraldehyde diethylacetal 5 under the basic conditions led to the formation of the corresponding α,β-unsaturated acetals in yields of 64, 41 and 62 per cent respectively. There was no evidence found to show that any of the expected ketene acetals were formed in these reactions (Scheme 5).



α-bromo acetal

3 R = H, R'= CH_3, R"= H

4 R = R'= H, R"= CH_3

5 R = R'= CH_3, R"= H

R"" = C_2H_5 in each case

Bu= C_4H_9

Scheme 5

McElvain and coworkers made a brief kinetic study of these reactions. They found that the data obtained gave approximately a straight line when plotted using the second order rate equation $\frac{1}{a-x} = k_2t$. It was shown that the rate was first order with respect to the α-bromo acetal and first order with respect to base. In order to explain the results obtained, these workers considered two points: (i) the mode of removal of the elements of hydrogen bromide from the α-bromo acetal and (ii) the possibility that the ketene

acetal actually was formed initially and then was isomerized under the reaction conditions to the observed α,β-unsaturated acetal.

Concerning the first point, the finding that the reaction was second order ruled out any scheme whereby the bromide ion is first separated by solvation in a rate controlling step followed by rapid proton removal. The alternative, favored by McElvain, was that involving the removal of the proton as the rate controlling step followed by a rapid elimination of the bromide ion. The displacement of the bromide ion by the alkoxide group followed by elimination of a molecule of alcohol from the resulting alkoxy product was also considered. It was found, however, that the reaction occurred much faster with potassium t-butoxide in t-butyl alcohol than with sodium ethoxide in ethyl alcohol thus showing this latter route was not valid. This must be based on the assumption (which was not stated by McElvain) that the rate controlling step was the displacement by the alkoxide group which would be faster for the sterically smaller and more nucleophilic ethoxide ion than for the t-butoxide ion.

Concerning the second point, that of isomerization of the ketene acetal, it was found that the ketene acetals expected in Scheme 5, which were synthesized by another method, were found to be unchanged when subjected to the alkaline reaction conditions.

McElvain (2) had initially expected that the electronegative character of the two geminal oxygen atoms of the acetal group would enhance the acidity of the anomeric hydrogen atom. However,

when it was observed that the base preferentially abstracted the hydrogen atoms on the β carbon, McElvain concluded that such an inductive effect was overpowered by an electromeric effect in these cases, i.e. the ethoxyl groups function in resonance structures such as is shown in Figure 1, which promote the separation of the anomeric hydrogen as a hydride ion rather than as a proton. The

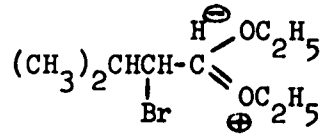
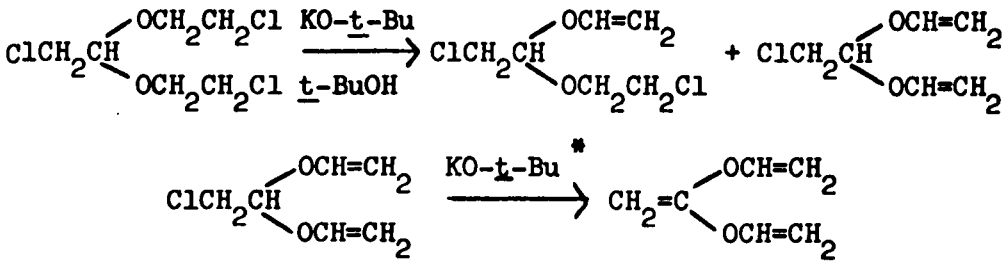


Figure 1

observed lack of reactivity of the anomeric hydrogen in these molecules may be due, more simply, to the destabilization of any carbanion character at the anomeric carbon atom by electronic repulsion between the carbanion and the electrons of the oxygen atoms. This repulsion would make the abstraction of the anomeric hydrogen a much less favorable path compared to the abstraction of a proton from the β carbon atom if the reaction exhibited any carbanion character.

In the preparation of ketene divinylacetal, McElvain (3) attempted the stepwise dehydrochlorination of chloroacetaldehyde di-(β-chloroethyl)acetal (Scheme 6). Upon treatment of chloroacetaldehyde di-(β-chloroethyl)acetal with potassium t-butoxide in t-butyl alcohol, the usual dehydrohalogenation conditions, there was obtained a mixture of two products which arose from the removal of one and of two molecules of hydrogen chloride from the

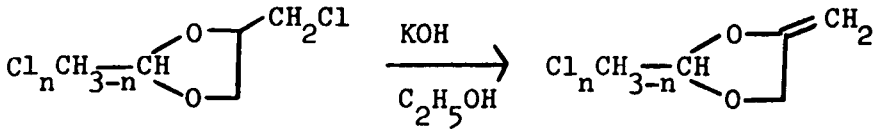
β-chloroethyl groups. Completion of the dehydrochlorination was



Scheme 6

effected by distilling the chloroacetaldehyde divinylacetal from sublimed potassium t-butoxide.

Dietrich, Raynor and Karabinos (4) carried out the ethanolic potassium hydroxide dehydrochlorinations of 2,4-bis-chloromethyl-1,3-dioxolane, 2-dichloromethyl-4-chloromethyl-1,3-dioxolane and 2-trichloromethyl-4-chloromethyl-1,3-dioxolane and have observed high selectivity in proton abstraction at the 4-position to give the corresponding 4-methylene products (Scheme 7).



n = 1, 2, 3

Scheme 7

These results were contrary to their expectations that proton removal at C-2 should be favored by the following two factors known to control orientation in base promoted E2 reactions when steric influences are equal. These are (i) stability of the olefin (more resonance structures possible) and (ii) enhancement of the acidity of the α hydrogen atom by attached electronegative groups

* Sublimed

(3 electronegative groups around C-2 and 2 electronegative groups around C-4). Dietrich and coworkers (4) concluded that the reason the base did not preferentially remove the hydrogen from C-2 to form the 2-methylene products may be related to the stability of an intermediate anion-proton complex. It was speculated that the stability of such a complex at C-2 was decreased, perhaps owing to the electrostatic repulsion of the resulting anion at C-2 by O-1 and O-3.

A steric effect was also observed by Dietrich et. al. (4) in these reactions. The dehydrochlorination of 2-trichloromethyl-4-chloromethyl-1,3-dioxolane (Scheme 7, n = 3) stopped when only a portion of the starting material had been converted to the monoolefin. Both the original starting material and the recovered unreacted starting material were found to be mixtures of cis and trans isomers but the recovered starting material was found to be greatly depleted in the amount of cis isomer. The greater stability of the trans isomer to the dehydrochlorination reaction was attributed to the steric hindrance encountered by the base as it approached C-4 on the same side of the molecule as the bulky trichloromethyl group. This steric hindrance was not observed for the 2-dichloromethyl-, and the 2-monochloromethyl- compounds (Scheme 7, n = 2, 1).

The lack of reactivity of the anomeric hydrogen in the above cases (Scheme 7) is somewhat surprising especially since McElvain and Curry (5) had found that in the preparation of cyclic ketene acetals (Scheme 4) the elements of hydrogen bromide could be

removed relatively easily from the α-bromo precursors. Also, in the preparation of 2,4-dimethylene-1,3-dioxolane by the base catalyzed dehydrohalogenation of 2,4-bis-chloromethyl-1,3-dioxolane, Yasnitskii, Sarkisyants and Ivanyuk (6) reported that the only product obtained was the 2,4-dimethylene-1,3-dioxolane. No monoolefin was isolated. In both of the above cases (5, 6) the alkaline conditions used were potassium t-butoxide in t-butyl alcohol.

2. Dehydrohalogenation of β-Halo Ethers

The removal of the elements of hydrogen halide from a β-halo ether (Scheme 8) appears to require more stringent conditions that the removal of hydrogen halide from an α-halo acetal. Lauer and Spielman (7) in the attempted preparation of some α,β-unsaturated

$$\underset{\underset{Br}{|}}{RCHCH_2OR'} \xrightarrow{base} RCH{=}CHOR'$$

Scheme 8

ethers by the dehydrobromination of the β-bromo ether precursors found these materials to be remarkably stable to base. Complete dehydrobromination was effected only after two or three successive distillations from powdered potassium hydroxide. McElvain and Fajardo-Pinzon (8) have prepared phenyl vinyl ether in 69 per cent yield from β-phenoxyethyl bromide by heating the precursor with powdered potassium hydroxide at temperatures of 160 to 200 °C. Swallen and Boord (9) have also commented on the remarkable stability towards base of β-halogenated ethers and describe some β-bromo ethers which could be distilled from solid potassium

hydroxide without appreciable decomposition.

3. Dehydrohalogenation of β-Halo Sulfides and Thioacetals

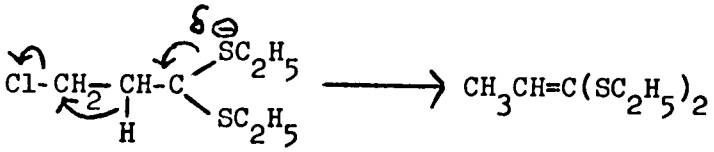
Contrary to the apparent lack of chemical reactivity of the anomeric hydrogen atom in acetals towards base, the anomeric hydrogen atom of thioacetals is readily removed by bases.

Rothstein (10) reported that the treatment of β-chloropropionaldehyde diethylthioacetal with potassium t-butoxide in t-butyl alcohol gave methylketene diethylthioacetal (Scheme 9).

$$ClCH_2CH_2CH(SC_2H_5)_2 \xrightarrow[t\text{-}BuOH]{KO\text{-}t\text{-}Bu} CH_3CH{=}C(SC_2H_5)_2$$

Scheme 9

The formation of this product was attributed to a hydride shift and displacement of chloride ion from an intermediate stabilized carbanion (A in Scheme 10) to provide the product shown. Rothstein



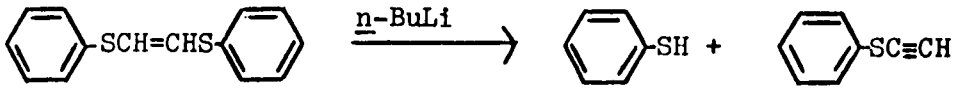
A Scheme 10

also found that methylketene diethylthioacetal and acrolein diethylthioacetal were stable under the reaction conditions thus showing that the product did not arise from any isomerizations. The existence of an intermediate such as A (Scheme 10) was attributed to the ability of sulfur to accommodate electrons in its outer d orbitals and this would promote the formation of a carbanion on the anomeric carbon.

The ability of sulfur to stabilize an adjacent negative

charge has been utilized by Arens (11 and references cited therein) in synthetic work. For example, when treated with sodium amide in liquid ammonia, formaldehyde diethylthioacetal loses a proton from the anomeric carbon and the resulting carbanion is easily alkylated with an alkyl halide to give the homologous thioacetal.

The participation of sulfur in stabilizing adjacent negative charges has also been reported for sulfides. Doumani (12) and Arens (13) both observed the formation of methyl vinyl sulfide from the base catalyzed dehydration of 2-methylthioethanol at 250°C. Parham and Stright (14) effected the elimination of thiophenol from cis and trans-1,2-bis-(phenylthio)ethene with n-butyl lithium at 0°C (Scheme 11). In an analagous reaction Arens and coworkers (11)



Scheme 11

found that ethanol can be eliminated from enol ethers if a β-alkylthio group is present (Scheme 12). These observations again were

$$C_2H_5OCH{=}CHSC_2H_5 \xrightarrow{n\text{-BuLi}} C_2H_5OH + C_2H_5SC{\equiv}CH$$

Scheme 12

attributed to the stability of the carbanion formed in the sulfur containing compounds.

4. Elimination Reactions in Dimethylsulfoxide

a. Mode of Removal of HX

Parker (15, 16) has reported that reactions which involve the separation of ions by solvent participation, such as SN1 reactions,

are suppressed or converted into the SN2 type reaction in dipolar aprotic solvents. SN1 ionizations in dipolar aprotic solvents are not common as neither of the resulting ions will be stabilized by solvation in these solvents. This is because the resulting anion cannot form a hydrogen bond with the solvent and the cation (carbonium ion) usually has a highly shielded charge preventing effective solvation. Also, in dipolar aprotic solvents, there is less solvent assistance to the departure of the leaving group than there is in protic solvents. Pyridine and butyl bromide react together at substantially the same rate in dipolar aprotic solvents as in methanol-water mixtures of the same dielectric constant and ionic strength as the dipolar aprotic solvent (17). Although the pyridine is not solvated by hydrogen bonding in the dipolar aprotic solvent, the rate enhancement expected from the increase in basicity of the pyridine is nullified by the fact that in the transition state, the leaving bromide ion is less assisted in the dipolar aprotic solvent than in the protic solvent.

Froemsdorf and coworkers (18, 19) in a study of the formation of olefinic products from base catalyzed eliminations in various solvents including dimethylsulfoxide have provided some information on the mechanism of elimination reactions in general. An El_{CB}-type * mechanism was considered a possibility for base catalyzed eliminations in dimethylsulfoxide but, since only trans

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* El_{CB}: unimolecular elimination in the conjugate base of the substrate is a two step process involving the intermediate formation of a carbanion that subsequently looses the leaving group to give the olefin.

elimination was observed from the reaction of trans-2-methylcyclohexyl tosylate with potassium t-butoxide in dimethylsulfoxide, these results seemed to discount this possibility. An increase in the predominance of the 1-ene product was observed in the base catalyzed elimination reactions carried out on a number of 2-alkyl tosylates and 2-alkyl bromides in the solvent dimethylsulfoxide as compared to that found for these reactions in the protic solvents used (Scheme 13). The increase in the amount of the 1-ene product by

$$RCH_2\underset{X}{\underset{|}{C}}HCH_3 \xrightarrow{\text{base}} RCH{=}CHCH_3 + RCH_2CH{=}CH_2$$

$R = CH_3,\ C_2H_5,\ C_3H_7$
$X = OSO_2C_6H_4CH_3\text{-}p\ ,\ Br$

Scheme 13

using the solvent dimethylsulfoxide was postulated (18, 19) not to be a manifestation of the steric requirements of the attacking base or leaving group by comparing the data for the potassium ethoxide catalyzed elimination in the two solvents ethyl alcohol and dimethylsulfoxide. This is shown below in Table 1, Experiments 1 and 2, and 7 and 9. In these two pairs of experiments the size of the alkoxide and the leaving group remains the same but the basicity of the solution is increased in dimethylsulfoxide over that in ethyl alcohol. Froemsdorf and coworkers (18, 19) state that the data are consistent with a transition state that involves a great deal of heterolysis of the carbon-hydrogen bond and a lesser amount of heterolysis of the carbon-oxygen or carbon-bromine bonds. This type of transition state is also concordant with the observation that

Table 1

Products from the elimination reactions of 2-alkyl tosylates and 2-alkyl bromides [1].

Experiment Number	Compound	Solvent	Base	1-ene %
1	2-butyl OTs [2]	C_2H_5OH	KOC_2H_5	35
2	2-butyl OTs	DMSO [3]	KOC_2H_5	54
3	2-butyl OTs	DMSO	KO-t-C_4H_9	61
4	2-pentyl OTs	C_2H_5OH	KOC_2H_5	42
5	2-pentyl OTs	DMSO	KOC_2H_5	66
6	2-pentyl OTs	DMSO	KO-t-C_4H_9	72
7	2-butyl Br	C_2H_5OH	KOC_2H_5	19
8	2-butyl Br	t-C_4H_9OH	KOC_2H_5	38
9	2-butyl Br	DMSO	KOC_2H_5	25
10	2-butyl Br	t-C_4H_9OH	KO-t-C_4H_9	53
11	2-butyl Br	DMSO	KO-t-C_4H_9	31

1 Taken from the work of Froemsdorf et. al. (18, 19)

2 OTs = $OSO_2C_6H_4CH_3$-p

3 DMSO = dimethylsulfoxide

eliminations in dimethylsulfoxide are many times more rapid than they are in hydroxylic solvents (20) and that the carbanion character of the transition state in the β-phenylethyl system is increased with an increase in base strength in the same solvent (21). Froemsdorf and coworkers (18, 19) concluded that it was reasonable to assume that, as more 1-ene is produced, carbon-hydrogen bond stretching becomes more important in the transition state. The increase in 1-ene produced by replacing potassium ethoxide by potassium t-butoxide as the base was postulated as a manifestation of base

strength and not the bulkiness of the base, i.e. carbon-hydrogen bond stretching is so pronounced that steric effects of the attacking base are of little importance. An increase in base strength, therefore, whether it results from a decrease in the energy of solvation of the base brought about by a change of solvent or a change of base in the same solvent should increase the C-H stretching in the transition state.

b. Rate Increases and Base Strength in Dimethylsulfoxide.

A large number of organic reactions involve the breaking of a carbon-hydrogen bond. The rates of many of these reactions such as base catalyzed eliminations and prototropic rearrangements have been shown to be increased upon changing the medium from a protic solvent to a dipolar aprotic solvent (20, 22). Cram, Rickborn, Kingsbury and Haberfield (23) have shown that the potassium methoxide catalyzed H-D exchange at a carbon α to a CN, $CONR_2$ or CO_2R group is 10^9 times faster in dimethylsulfoxide than in methyl alcohol. The observed rate increase was attributed to the difference in solvation of the base in the two solvents. In methyl alcohol, the methoxide ion is highly solvated by hydrogen bonding and hence is less basic than in dimethylsulfoxide where similar solvation cannot occur and thus the alkoxide ion is more basic. Anions of alkoxide bases are much less solvated in dipolar aprotic media than in protic solvents whereas the metal cations are solvated well in both solvents through coordination with the electronegative oxygen of either the alcohol (protic solvent) or dimethylsulfoxide (aprotic

solvent) (16). Alkoxides are, therefore, more basic in dipolar aprotic solvents.

The usual pKa values for alcohols of from 16 to 18 are only valid in solvents containing hydroxyl groups. Upon increasing the dimethylsulfoxide content of the solution, the pKa values of n-butyl and t-butyl alcohols have been shown to decrease to a limiting value of about 30 in pure dimethylsulfoxide (24, 25). This means that the alkoxides are 10^{12} to 10^{14} times more basic in pure dimethylsulfoxide than in pure alcohol. This is true, however, only of potassium and cesium alkoxides as the sodium and lithium alkoxides are less basic owing to ion pair formation.

Solutions of potassium t-butoxide in dimethylsulfoxide are among the most strongly basic systems of organic chemistry. Their basicity is equivalent to that of the sodium salt of dimethylsulfoxide ($NaCH_2SOCH_3$) (26, 27) and is surpassed only by that of the potassium salt of dimethylsulfoxide. An important use of these basic systems in dimethylsulfoxide is, therefore, the deprotonation of weakly acidic compounds.

The quantity of the methylsulfinyl carbanion in equilibrium with potassium t-butoxide has been shown to be sufficient for its quantitative interception as the benzophenone adduct (Scheme 14). This has been carried out by Ledwith and McFarland (25) and confirms the rapid equilibrium between base and solvent in these systems.

Estimates of the relative acidity of t-butyl alcohol

$$KO\text{-}\underline{t}\text{-}Bu + CH_3SOCH_3 \rightleftharpoons KCH_2SOCH_3 + HO\text{-}\underline{t}\text{-}Bu$$

$$KCH_2SOCH_3 + (C_6H_5)_2C{=}O \longrightarrow (C_6H_5)_2\underset{\underset{OH}{|}}{C}CH_2SOCH_3$$

Scheme 14

and dimethylsulfoxide have been determined (24, 25) but differ by a factor of 10^3. Ledwith and McFarland (25) state that t-butyl alcohol is 7×10^6 times more acidic than dimethylsulfoxide whereas Steiner and Gilbert (24) state the difference is only 7×10^3 in favor of the acidity of t-butyl alcohol. Both of these results suggest, however, that the relative acidities of t-butyl alcohol and dimethylsulfoxide are sufficiently different so that the possibility that the anion derived from dimethylsulfoxide in the presence of potassium t-butoxide is the attacking base in elimination reactions using this solvent base combination is at best only remote due to its small concentration.

c. Prototropic Rearrangements.

A solution of potassium t-butoxide in dimethylsulfoxide has been shown to be an excellent medium for the isomerization of olefins. Schriesheim et. al. (22) have shown that simple olefins such as butenes, pentenes and hexenes can be isomerized at measurable rates in this medium at moderate temperatures. In these cases, the high basicity and high solvent power of this system act in the same direction to promote facile isomerization. The rate determining step in the base catalyzed isomerization of olefins has been postulated to be the formation of a carbanion by proton abstraction followed by allylic rearrangement and reprotonation to give the isomerized olefin (22).

RESULTS AND DISCUSSION

1. Dehydrobromination in t-Butyl Alcohol as Solvent.

The work of McElvain, Clarke and Jones (2) showed that the treatment of the diethylacetals of some α-bromo aldehydes (Scheme 5), which possess a proton on the β carbon, with a solution of potassium t-butoxide in t-butyl alcohol gave exclusive formation of the diethyl acetals of the corresponding α,β-unsaturated aldehydes. Accordingly we applied the same reaction conditions to the ethylene acetals of several α-bromo aldehydes in order to prepare the ethylene acetals of the corresponding α,β-unsaturated aldehydes. The results obtained were contrary to those predicted by McElvain's work and therefore the work of McElvain was reinvestigated with the aid of modern techniques in order to explain our findings.

In our repetition of a portion of the work of McElvain, Clarke and Jones (2), it was found that the compounds α-bromo-n-butyraldehyde diethylacetal and α-bromoisovaleraldehyde diethylacetal both were converted to the diethyl acetals of the corresponding α,β-unsaturated aldehydes as had been reported. Also, in agreement with the published work (2), α-bromo-n-valeraldehyde diethylacetal when treated in the same manner gave exclusively 2-pentenal diethylacetal. No evidence could be found for the formation of any of the corresponding ketene acetals in the above mentioned dehydrobrominations, again in agreement with McElvain's results (2). These results are shown in Table 2.

Table 2

Base catalyzed dehydrobromination of some α-bromo diethyl acetals using potassium t-butoxide in t-butyl alcohol [a,b]

Experiment Number	Compound	Time, Hours	Products	Yield %
1[c]	$C_2H_5CHBrCH(OC_2H_5)_2$	5	$CH_3CH=CHCH(OC_2H_5)_2$	40
2[c]	$(CH_3)_2CHCHBrCH(OC_2H_5)_2$	5	$(CH_3)_2C=CHCH(OC_2H_5)_2$	60
3[c]	$C_3H_7CHBrCH(OC_2H_5)_2$	5	$C_2H_5CH=CHCH(OC_2H_5)_2$	60
4[d]	$CH_3CH=CHCH(OC_2H_5)_2$	20	$CH_3CH=CHCH(OC_2H_5)_2$	100
5[d]	$(CH_3)_2C=CHCH(OC_2H_5)_2$	20	$(CH_3)_2C=CHCH(OC_2H_5)_2$	100
6[d]	$C_2H_5CH=CHCH(OC_2H_5)_2$	20	$C_2H_5CH=CHCH(OC_2H_5)_2$	100

a. A repetition of a portion of the work of McElvain (2).

b. Temperature in all cases was 80°C.

c. The total time and temperature in these experiments depended on the time required to remove the solvent and product from the residual base as will be described below.

d. These experiments were worked up with a modified procedure to be described on page 127.

The details of the published reaction conditions (28) which were used initially in the present work are of considerable importance. The reactions were carried out under completely anhydrous conditions. Following the addition of the α-bromo acetal to the stirred solution of the potassium t-butoxide in t-butyl alcohol, and a subsequent period of reflux, the solvent, t-butyl alcohol, was removed by fractional distillation at atmospheric pressure. The pressure was then lowered in order to allow the remaining material to distill. By following the above procedure the total reaction time was dependent on the rate of distillation of the solvent and of the product. Also, the temperature was raised above 80°C in the final distillation in order to remove the products from the solid residue.

McElvain (2) also synthesized the ketene acetals n-propylketene diethylacetal 6 and isopropylketene diethylacetal 7, which were the other expected products from the dehydrobromination reactions, and found them to be recovered unchanged after having been subjected to the same reaction conditions. The stability of

$C_3H_7CH=C(OC_2H_5)_2$ (6) $(CH_3)_2CHCH=C(OC_2H_5)_2$ (7)

the α,β-unsaturated acetals obtained as products from the dehydrobromination reaction was investigated in our work and these materials were also found to be recovered unchanged after they had been subjected to the reaction conditions (Experiments 4, 5, 6, Table 2).

The yields obtained by following the procedure of McElvain

(28) for the dehydrohalogenation reaction were only fair ($\leqslant 60\%$) and hence it was felt that other products which may have been formed, as well as the α,β-unsaturated acetals, may have been lost as a result of decomposition due to the high temperatures necessary to remove the reaction products from the solid residues during the distillation. For subsequent work, in order to increase the amount of material recovered from the dehydrobromination reactions, the following modification of McElvain's procedure was used.

At the completion of the reflux period, the reaction mixture was not subjected to distillation directly, but was allowed to cool to approximately 50^{o}C and then was mixed with an equal volume of distilled water. This mixture was then continuously extracted with ether for 12 hours and in this way total recoveries of material in excess of 80 per cent were obtained consistently. This procedure was also advantageous in that any ketene acetal which might be formed as a product from the dehydrobromination could be trapped by its facile reaction with water to form the corresponding ester.

The reaction of ketene acetals with water has been studied by McElvain and Curry (5). All ketene dialkylacetals react with water to form an ester and an alcohol or, in the case of cyclic ketene acetals such as 1,3-dioxolanes or 1,3-dioxanes, to form a β or γ hydroxy ester. These reactions are shown below. The rate of reaction of the

$$RR'C{=}C(OR'')_2 + H_2O \longrightarrow RR'CHCOOR'' + R''OH$$

$$RR'C{=}C\!\left\langle\begin{matrix}O\\O\end{matrix}\right\rangle\!(CH_2)_n + H_2O \longrightarrow RR'CHCOO(CH_2)_nOH$$

$n = 2$ or 3

ketene acetals with water have been found to vary over a wide range depending on the nature of R and R'. McElvain and Curry (5) have

reported, however, that dialkyl and cyclic acetals where R and R' are H, alkyl or aryl have a strong affinity for water as shown by a decrease in the value of the refractive index of these compounds approaching that of the corresponding ester upon exposure of the ketene acetal to the moisture of the air. It has thus been possible in this work to estimate by gas liquid chromatography (g.l.c.) the relative amounts of the products formed in the dehydrobromination reaction by measuring the peaks corresponding to the ester and the α,β-unsaturated acetal. Conversion of the ketene acetals to the esters also resulted in simplification of the g.l.c. analysis since quite often the peaks for the ketene acetal and the α,β-unsaturated acetal were coincident and in some cases the ketene acetal decomposed on the column. The corresponding esters exhibited retention times quite different from those of the α,β-unsaturated acetals and were stable on the column used. The relative peak areas of the dehydrohalogenation products found on g.l.c. were used to determine the product ratios with no corrections applied. The relative peak size for the α,β-unsaturated acetal and the corresponding ester, resulting from the hydrolysis of the ketene acetal, was checked using equimolar amounts of the two authentic products (for example 2-pentenal ethyleneacetal and ethyl n-valerate). In the cases checked there was found to be at most a 10 per cent difference in peak size and usually the difference was well within this limit. Hence correction of peak size to give a more exact indication of the molar ratios of the products was not necessary as the differences

found in product proportions were greater than the error due to uncorrected peak areas, hence there was no doubt as to the direction of reaction.

When the work of McElvain, Clarke and Jones (2) was again repeated but this time with the modified procedure, evidence for simultaneous formation of ketene acetals was obtained since the corresponding esters were found in the relative amounts of 6-26 per cent depending on the structure of the starting acetal. These results are reported in Table 3 along with those of the dehydrobromination of some other α-bromo acetals.

From the results in Table 3 it can be seen that there is a decrease in the amount of the ketene acetal formed as the size of the alkyl group R in the OR moiety is increased (Experiments 1-3). This suggests that there might be a steric effect preventing the approach of the base to the anomeric hydrogen and thus reaction of the base with the hydrogen atoms on the β-carbon becomes more important. On the other hand, if an electromeric effect controls the direction of dehydrobromination as had been suggested by McElvain (2), then one would observe a decrease in the amount of ketene acetal formed with increasing electron donating power of the alkyl group R in the OR moiety of the acetal. Since the electron donating power of the alkyl groups is known to decrease in the order isopropyl>ethyl>methyl, the observations noted in Table 3 might also be explained on this electromeric basis.

Using the conformational free energy difference (A values)

Table 3

Base catalyzed dehydrobromination of α-bromo dialkylacetals using potassium t-butoxide in t-butyl alcohol [a,b]

Experiment Number	Compound	Total Recovery %	Products	Relative Amounts %	Reaction %
1	$C_3H_7CHBrCH(OCH_3)_2$	85	$C_2H_5CH{=}CHCH(OCH_3)_2$	74	53
			$C_4H_9\overset{O}{\overset{\|}{C}}OCH_3$	26	
2	$C_3H_7CHBrCH(OC_2H_5)_2$	90	$C_2H_5CH{=}CHCH(OC_2H_5)_2$	88	45
			$C_4H_9\overset{O}{\overset{\|}{C}}OC_2H_5$	12	
3	$C_3H_7CHBrCH[OCH(CH_3)_2]_2$	85	$C_2H_5CH{=}CHCH[OCH(CH_3)_2]_2$	100	42
			$C_4H_9\overset{O}{\overset{\|}{C}}OCH(CH_3)_2$	0	
4	$(CH_3)_2CHCHBrCH(OC_2H_5)_2$	90	$(CH_3)_2C{=}CHCH(OC_2H_5)_2$	94	40
			$(CH_3)_2CHCH_2\overset{O}{\overset{\|}{C}}OC_2H_5$	6	
5	$CH_3CHBrCH(OC_2H_5)_2$	80	$CH_2{=}CHCH(OC_2H_5)_2$	100	48
			$CH_3CH_2\overset{O}{\overset{\|}{C}}OC_2H_5$	0	

a. The modified aqueous work-up procedure was used.
b. In all cases the reaction time was 20 hours and the temperature was 80°C.

of the alkoxy groups determined in the cyclohexane system as a criterion of steric size, an increase is observed from 0.7 k. cal./mole for methoxy to 0.9 k. cal./mole for ethoxy (29). A value for the isopropoxy group was not available, however, it would be expected to be larger than 0.9 k. cal./mole. This increase in the size of the freely rotating OR groups of the acetal would increase the steric hindrance of the approach of the base to the anomeric centre but would not have as large an effect about the β carbon atom.

Although steric and/ or electronic effects could explain the results found in Table 3 it is apparent that their relative effectiveness is difficult to ascertain. However, the results of the dehydrobromination of some α-bromo-2-alkyl-1,3-dioxolanes and dioxanes shown in Table 4 provide some assistance in this regard.

Dehydrobromination of α-bromo-n-valeraldehyde ethyleneacetal under the conditions described by McElvain, Barnes and Johnson (28) led to the formation of only n-propylketene ethyleneacetal (Experiment 1, Table 4). No evidence for the formation of the corresponding α,β-unsaturated acetal could be found. Furthermore, this ketene acetal was found to be stable under the reaction conditions. The α,β-unsaturated isomer, which was the product that had been expected but was not obtained, was synthesized by another route and was found to undergo some rearrangement under the same reaction conditions but only to the β,γ-unsaturated acetal. This isomerization occurred at a much slower rate than the original dehydrobromination as was determined by comparing the amounts of the respective products

Table 4

The dehydrobromination of some α-bromo-2-alkyl-1,3-dioxolanes and dioxanes with potassium t-butoxide in t-butyl alcohol [a].

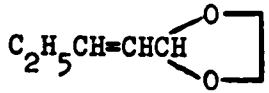
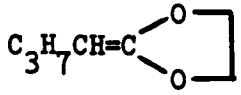
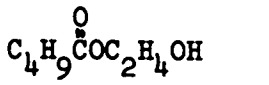
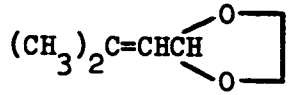
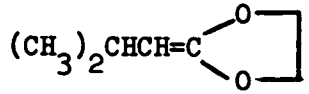
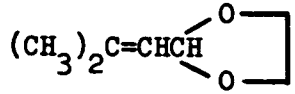
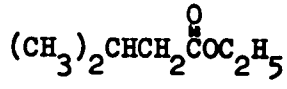
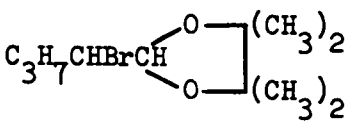
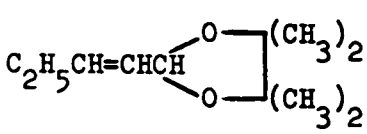
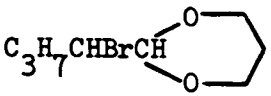
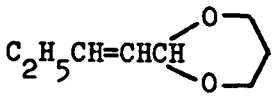
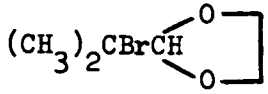
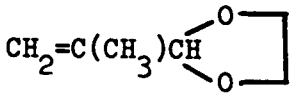
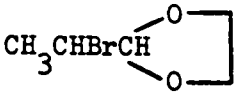
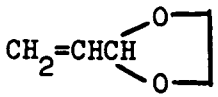
Experiment Number	Compound	Time, Hours	Total Recovery %	Products	Relative Amounts %	Reaction %
1		5	70		0	70
					100	
2		5	90		0	42
					100	
3		5	70		14[b]	70
					86[b]	
4		5	75		15	49
					85	

Table 4-Continued

Experiment Number	Compound	Time, Hours	Total Recovery %	Product	Relative Amount %	Reaction %
5		24	90		100	20
6		20	90	 $C_4H_9\overset{O}{\overset{\|}{C}}O(CH_2)_3OH$	40 60	53
7		5	90	 $(CH_3)_2CH\overset{O}{\overset{\|}{C}}OC_2H_4OH$	0 100	40
8		3	85	 $C_2H_5\overset{O}{\overset{\|}{C}}OC_2H_4OH$	0 100	50

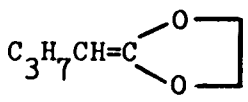
a. Temperature in each case was 80°C.

b. These relative amounts were determined by the relative areas of the signals of the methyl groups protons in the 60 MHz n.m.r. spectrum as no separation could be obtained on g.l.c.

formed in the two reactions in a given time. In the usual dehydrobromination time of 5 hours (Table 4) little isomerization could be detected. After 25 hours of reflux in the usual basic solution there was observed 20 per cent isomerization of the 2-isopentenal ethyleneacetal and 25 per cent isomerization of the 2-pentenal ethyleneacetal to the respective β,γ-unsaturated isomers.

These results found for the dehydrobromination of α-bromo-n-valeraldehyde ethyleneacetal were also checked by the modified procedure (Experiment 2,Table 4) which involved the addition of water. By this method, after extraction, the dehydrobromination mixture gave the ketene acetal exclusively as shown by the isolation of only one substance other than unreacted starting material. This single substance proved to be the monohydroxyester of ethylene glycol and n-valeric acid.

The n-propylketene ethyleneacetal 8 isolated from Experiment 1, Table 4 was characterized by its 60 MHz n.m.r. spectrum and by conversion of this substance into some derivatives. The 60 MHz n.m.r. spectrum in CCl_4 referred to tetramethylsilane exhibited a singlet (4H) at τ 5.92 assigned to the four protons of the ethylene bridge on C-4 and C-5 of 8. A triplet (1H) centred at



8

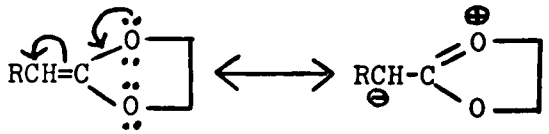
τ 6.51, J_{obs}=7.5 Hz was assigned to the olefinic proton. The multiplets between τ 7.90 and τ 9.30 could be attributed to the

remaining protons. The triplet at τ 6.51, obviously due to the single olefinic proton, is at unusually high field compared to that at which most olefinic protons are found. The usual absorption range for olefinic protons given by Jackman (30) is from τ 2.0 to τ 5.5. This unusual shift to higher field is also observed for the signals of the two olefinic protons of the compound ketene diethylacetal 9. They appear as a singlet at τ 6.90. The position

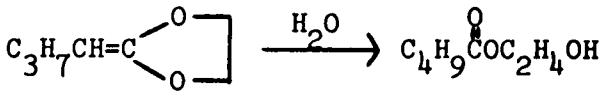
$$CH_2=C(OC_2H_5)_2$$

9

of these olefinic protons is believed to be due to the shielding effect experienced at the α carbon atom caused by the mesomeric shift of electron density from the oxygen atoms towards the double bond as is shown below.



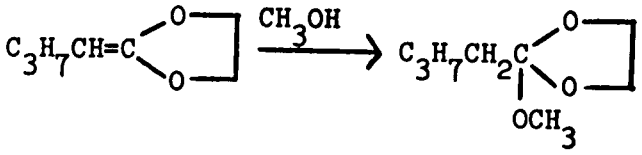
The n-propylketene ethyleneacetal 8 was converted by treatment with water into the monohydroxyester of ethylene glycol and n-valeric acid which was isolated and characterized (Scheme 15).



Scheme 15

Also, the addition of one molecular equivalent of methyl alcohol to the n-propylketene ethyleneacetal provided the expected mixed orthoester of n-valeric acid with ethylene glycol and methyl alcohol

(Scheme 16). This orthoester was also isolated and characterized.



Scheme 16

The exclusive formation of n-propylketene ethyleneacetal observed in the dehydrobromination of α-bromo-n-valeraldehyde ethyleneacetal is indicative that the factor controlling the direction of removal of hydrogen bromide might well be a problem of physical approach of the base to the anomeric hydrogen atom and not due to the unfavorable removal of the anomeric hydrogen as a proton as had been suggested by McElvain (2). The change in the magnitude of the inductive electron donation of the acetals' alkoxy groups towards the anomeric carbon on going from the dimethylacetal to the ethyleneacetal would be expected to be negligible. On the otherhand, models show that the anomeric hydrogen is sterically more unencumbered in the ethyleneacetal than it is in the dimethylacetal. The Stuart model of the dimethylacetal of α-bromo-n-valeraldehyde shows that the freely rotating methoxy groups sweep out a considerable volume around the anomeric carbon thus creating steric hindrance to the approach of a bulky base such as the t-butoxide anion to that centre. This effect becomes progressively greater for the diethoxy- and diisopropoxyacetals. On the other hand, the Stuart model of the ethyleneacetal of α-bromo-n-valeraldehyde shows that the anomeric

hydrogen is quite exposed. This is the result of the fixed position of the two methylene groups in the 5-membered 1,3-dioxolane ring.

The increase in the amount of ketene acetal obtained from the dehydrobromination of α-bromo-n-valeraldehyde ethyleneacetal (Experiment 2,Table 4) compared to the amount of ketene acetal formed from the dehydrobromination of α-bromo-n-valeraldehyde dimethylacetal (Experiment 1, Table 3) is too large to be explained on the basis of the difference in electron donor ability of the alkoxy moieties of the two acetals.

It was of interest to determine if a change would occur in the proportion of α,β-unsaturated acetal to ketene acetal on increasing the ease of proton removal at the β carbon by decreasing steric hindrance to approach of the base at this position and also by increasing the number of hydrogen atoms on the β carbon available for removal. Accordingly, α-bromopropionaldehyde ethyleneacetal and α-bromoisobutyraldehyde ethyleneacetal were subjected to the usual dehydrobromination conditions. Both of these compounds gave exclusively the corresponding ketene acetal isolated as the ester (Experiments 7 and 8, Table 4). Thus, in spite of the decrease in steric crowding about the β carbon atom when it is changed from a secondary to a primary state, reaction still occurs only at the anomeric centre in the ethylene acetals. Also, changing the ratio of the number of β hydrogen atoms to the single anomeric hydrogen from 2 to 1 in α-bromo-n-valeraldehyde ethyleneacetal to 3 to 1 in α-bromopropionaldehyde ethyleneacetal

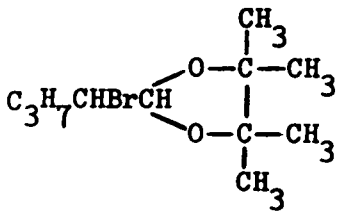
and to 6 to 1 in α-bromoisobutyraldehyde ethyleneacetal did not change the fact that the corresponding ketene acetals were still formed exclusively from the dehydrobromination of these compounds. The methylketene ethyleneacetal isolated from the dehydrobromination of α-bromopropionaldehyde ethyleneacetal was found to be unchanged when subjected to the same reaction conditions. The expected isomeric product, acrolein ethyleneacetal, was synthesized and was also found to be recovered unchanged when subjected to the dehydrobromination conditions.

The effect of decreasing the steric hindrance about the β carbon in the diethylacetals does seem to exhibit some effect on the direction of reaction in contrast to what has been found for the ethyleneacetals. In the dehydrobromination of α-bromopropionaldehyde diethylacetal (Experiment 5, Table 3) no evidence could be found for the formation of any of the corresponding ketene acetal whereas with α-bromo-n-valeraldehyde diethylacetal (Experiment 2, Table 3), 12 per cent of the product isolated was the ketene acetal. It thus appears that decreasing the steric hindrance to approach of the base to the β carbon in the diethylacetals does change the proportion of products to give a larger amount of the product resulting from attack of the base on the hydrogen atoms of the β carbon atom. The fact that this effect was not observed in the ethyleneacetals possibly means that either the anomeric hydrogen is so exposed in the ethyleneacetal series

that it is the easiest to approach by the base, or that the anomeric hydrogen in the ethyleneacetal series is more acidic than it is in the diethylacetals. It is most likely that the steric availability of the anomeric hydrogen is the controlling factor. The change in inductive effect of the alkoxyl group towards the anomeric carbon on changing the acetal function from the ethyleneacetal to the diethylacetal would not be expected to be large enough so as to alter the lability of the anomeric hydrogen by such an extent as is observed in the complete reversal of the proportion of products from the dehydrobromination of α-bromopropionaldehyde diethylacetal and α-bromopropionaldehyde ethyleneacetal. In the first case (Experiment 5, Table 3) the α,β-unsaturated acetal was the only product and in the latter case (Experiment 8, Table 4) the ketene acetal was the only product formed. It thus appears that reaction at the anomeric carbon of the ethyleneacetals is most favorable due to the steric availability of the anomeric hydrogen and the direction of reaction in the ethyleneacetal series is not effected by steric changes at the β carbon. Reaction at the anomeric carbon of diethylacetals is, however, not favored as the anomeric hydrogen is sterically shielded and therefore any decrease in the steric hindrance at the β carbon will cause approach of the base to the hydrogen atoms on the β carbon to become more favored.

Further evidence to support the view that steric factors are more important than are electronic in controlling the direction

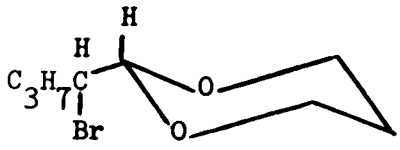
of dehydrobromination in these reactions was obtained from the results of the reaction of α-bromo-n-valeraldehyde tetramethylethyleneacetal under the usual basic conditions. The only product, other than recovered starting material, isolated from this reaction was 2-pentenal tetramethylethyleneacetal (Experiment 5, Table 4). The Stuart model of α-bromo-n-valeraldehyde tetramethylethyleneacetal 10 shows that the introduction of the four methyl groups on C-4 and



10

C-5 of the 1,3-dioxolane ring causes increased steric interaction to approach of the base (t-butoxide anion) to the anomeric hydrogen. The result of this increase in steric hindrance to attack at the anomeric hydrogen would be to favor removal of one of the hydrogens on the β carbon and this is exactly what is observed.

The reaction of the acetal 2-(1-bromo-n-butyl)-1,3-dioxane 11 under the usual basic conditions also demonstrates the effect of steric hindrance to approach of the base on the direction of removal of the hydrogen bromide. Eliel and Knoeber (31) have shown



11

that 1,3-dioxane rings substituted in the 2 position by an alkyl

group prefer the conformation in which the alkyl substituent is equatorially disposed. Thus the anomeric hydrogen in the 2-alkylated-1,3-dioxanes is preferably in the axial position. The Stuart model of 11 clearly shows that approach of a bulky base such as the t-butoxide anion to the axially disposed anomeric hydrogen may be hindered due to the interactions which develop between the axial C-4 and C-6 hydrogen atoms and the approaching base. Such steric hindrance to abstraction of the anomeric hydrogen would again favor removal of a hydrogen atom from the β carbon atom. The result of steric hindrance to reaction at the anomeric hydrogen site is demonstrated by the fact that in the dehydrobromination of 2-(1-bromo-n-butyl)-1,3-dioxane 11 the α,β-unsaturated acetal is obtained to the extent of 40 per cent of the product while the remaining 60 per cent is the ketene acetal. The steric hindrance to approach of the base to the anomeric hydrogen is not as great in 2-substituted-1,3-dioxanes as in dialkylacetals since in the 1,3-dioxane ring, the three methylene groups are held in a fixed position compared to the freely rotating alkoxyl groups of the dialkylacetals.

H. C. Brown and coworkers (32, 33) considered the role of steric effects in bimolecular elimination reactions and suggested that the direction of elimination would be influenced by: (a) the steric requirements of the groups on the incipient double bond, (b) the steric requirements of the attacking base, and (c) the steric requirements of the leaving group. In all the eliminations discussed

so far in this work the attacking base and the leaving group have been consistently the t-butoxide and bromide ions respectively.

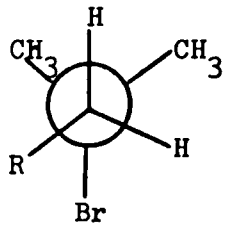
Brown (32) showed in a study of the base catalyzed dehydrobromination of a series of tertiary bromides (Scheme 17) that as the size of the alkyl group R increased from methyl to t-butyl, the proportion of 1-olefin (A in Scheme 17) to 2-olefin (B in Scheme 17) increased from 0.43:1 to 6.14:1 respectively. The increase in the ratio of A to B as R was changed from methyl to t-butyl was attributed to changes in the steric interactions

$$RCH_2\underset{\underset{Br}{|}}{C}(CH_3)_2 \longrightarrow \underset{A}{RCH_2C{=}CH_2} + \underset{B}{RCH{=}C(CH_3)_2}$$

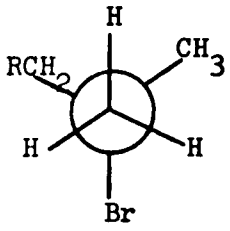
$R = CH_3$, $t\text{-}C_4H_9$

Scheme 17

in the two respective transition states (Figure 2, A and B). As the size of the alkyl group R is increased, greater steric interactions will occur in the transition state leading to the 2-olefin (Figure 2-A)



A



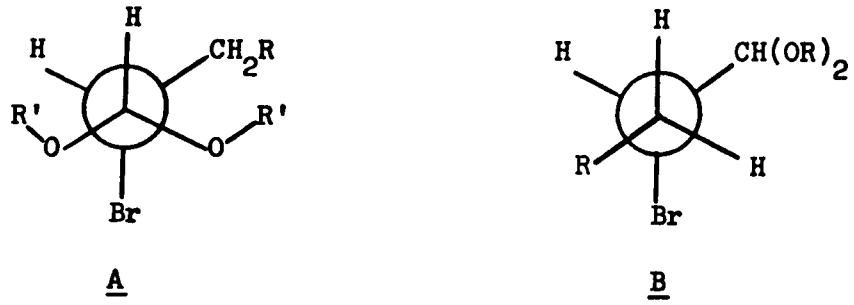
B

Figure 2

as compared to the interactions in the transition state leading to the 1-olefin (Figure 2-B) thus causing formation of the 1-olefin to be favored.

In the base catalyzed dehydrobromination of the α-bromo dialkyl acetals, similar transition states occur and are shown in

Figure 3 A and B. In the transition state Figure 3-A which leads



A B

Figure 3

to the formation of the ketene acetal, as the size of the R' group is increased greater interactions occur between the OR' group and the CH_2R group as well as between the OR' group and the bromine atom. Also in this same transition state the OR' groups effectively shield the anomeric hydrogen from attack by a bulky base. In the transition state leading to the formation of the α,β-unsaturated acetal (Figure 3-B), such interactions do not occur between the substituents on the incipient double bond. Although in this transition state (Figure 3-B) the approach of the base to the hydrogen atoms on the β carbon is somewhat hindered by the freely rotating acetal moiety ($-CH(OR)_2$), the interactions in the transition state leading to the ketene acetal (Figure 3-A) are more serious.

In the corresponding transition state for the dehydrobromination of the α-bromo-2-alkyl-1,3-dioxolanes (Figure 4, A and B) the extent of interactions in the transition state leading to the formation of the ketene acetal (Figure 4-A) are decreased due to the restricted nature of the 1,3-dioxolane ring. In transition state Figure 4-A the two methylene groups of the 1,3-dioxolane ring are held away from the CH_2R group and the bromine atom and

consequently provide less steric interaction with these substituents.

A B

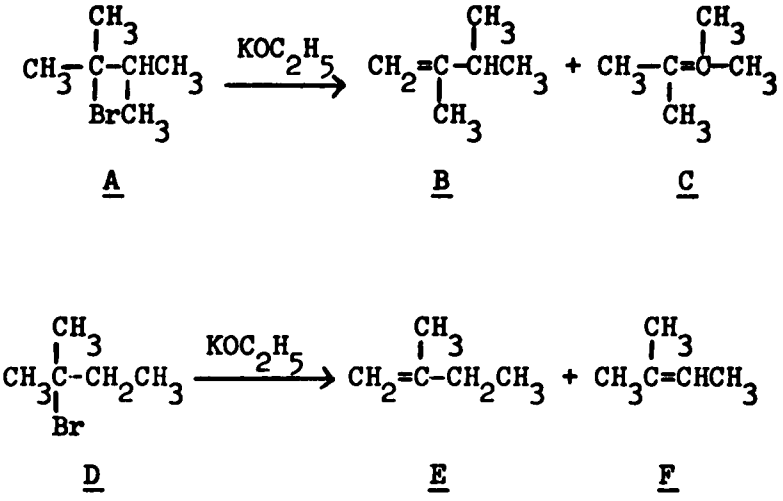
Figure 4

Also, in transition state Figure 4-A, the two methylene groups cannot effectively shield the anomeric hydrogen from approach of the base. In transition state Figure 4-B which is similar to transition state Figure 3-B the approach of the base to the hydrogen atoms on the β carbon is again somewhat hindered due to the freely rotating acetal moiety. The decreased steric interaction in transition state Figure 4-A as compared to those in transition state Figure 3-A greatly favors formation of the ketene acetal in the dehydrobromination of the ethylene acetals. Thus an increase in the steric requirements of the R' groups in the dialkyl acetals (Figure 3) should result in a decreased tendency for the formation of the ketene acetal, a situation which has been found to be true in this study.

In the elimination of hydrogen bromide from α-bromo-isovaleraldehyde diethylacetal (Experiment 4, Table 3) and α-bromoisovaleraldehyde ethyleneacetal (Experiment 3, Table 4) the formation of 94 and 14 per cent respectively of the corresponding α,β-unsaturated acetals was surprising on the basis of the results

for the corresponding n-valeraldehyde acetals where 88 and 0 per cent of the α,β-unsaturated acetals had been formed under the same conditions (Experiment 2, Table 3) and (Experiment 2, Table 4). A smaller proportion of the α,β-unsaturated acetals was expected from the dehydrobromination of the two α-bromoisovaleraldehyde acetals than from the two α-bromo-n-valeraldehyde acetals because the steric hindrance to approach of the base to the hydrogen on the β carbon has been increased due to the fact that the β carbon is tertiary in the isovaleraldehyde acetals. That more of the α,β-unsaturated acetal was formed than expected on the basis of the apparently greater steric interference which exists in the two isovaleraldehyde acetals is probably due to the possibility that formation of the α,β-unsaturated acetal intermediates in these cases can be stabilized by hyperconjugation to a greater extent than is possible for the formation of the α,β-unsaturated acetals of n-valeraldehyde.

This effect has also been observed by H. C. Brown (33). He reported that in the elimination of hydrogen bromide with potassium ethoxide from 2,3-dimethyl-2-bromobutane (Scheme 18-A) and 2-methyl-2-bromobutane (Scheme 18-D) there is obtained 79 per cent of 2,3-dimethyl-2-butene from the former (Scheme 18-C) and 70 per cent of 2-methyl-2-butene from the latter (Scheme 18-F). These results are based on total olefin yield equalling 100 per cent. The 1-olefins (B and E of Scheme 18) are quite similarly structured and must be of similar stability. The greater yield



Scheme 18

of the 2-olefin in the case of 2,3-dimethyl-2-bromobutane must be the result of greater hyperconjugative stabilization of the incipient olefin by the four methyl groups compared to the lesser stabilization afforded by the three methyl groups in the transition state leading to the 2-methyl-2-butene (Scheme 18-F). Thus in the elimination of hydrogen bromide from α-bromoisovaleraldehyde diethylacetal compared to hydrogen bromide elimination from α-bromo-n-valeraldehyde diethylacetal and from the two corresponding ethyleneacetals, more α,β-unsaturated acetal than ketene acetal is obtained from the isovaleraldehyde acetals than from the n-valeraldehyde acetals due to greater hyperconjugative stabilization of the transition state leading to the α,β-unsaturated isomer in the case of the isovaleraldehyde acetals. These results are in agreement with the theoretical basis of the Saytzeff rule as proposed by Hughes, Ingold and coworkers (34).

It has thus been shown in our investigation that the

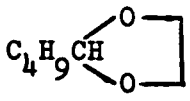
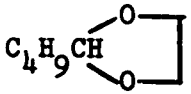
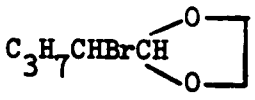
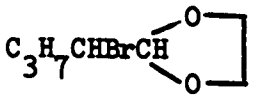
anomeric hydrogen in acetals does exhibit some lability towards base, however, this lability is not great as the site of proton removal can be influenced by changes in the steric availability of the anomeric hydrogen and by changes in steric interactions in the transition states leading to the formation of the ketene acetals.

Further investigation into the ease of removal of the anomeric hydrogen was carried out by attempting deuterium exchange at the anomeric carbon. The results of these experiments are shown in Table 5. The saturated acetal, n-valeraldehyde ethyleneacetal, was subjected to the basic conditions previously used for the dehydrobromination but in the solvent t-butyl alcohol OD. The starting material was recovered with no deuterium incorporation. α-Bromo-n-valeraldehyde ethyleneacetal was also subjected to the deuterium exchange conditions using one-half a molecular equivalent of potassium t-butoxide in the deuterated solvent in order to ensure incomplete reaction and therefore the recovery of at least some starting material. The recovered α-bromo-n-valeraldehyde ethyleneacetal contained no deuterium. The attempted measurement of the amount of deuterium incorporation was carried out using n.m.r. techniques by comparing the area of the signal attributed to the anomeric hydrogen with the area of the signal attributed to the four methylene hydrogens on C-4 and C-5 of the 1,3-dioxolane ring. The ratio of these two areas did not change after attempted deuterium exchange from that found before the exchange was attempted.

The fact that the anomeric hydrogen did not exchange is

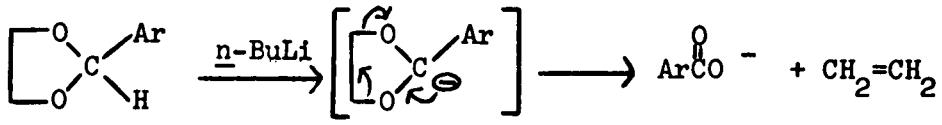
Table 5

Attempted deuterium exchange [a]

Experiment Number	Compound	Total Recovery %	Product	Relative Amount %	% D Incorporation
1		95		100	0
2		90		25	0
				75	

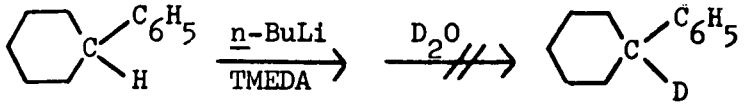
a. The reflux temperature and time were 80°C and 20 hours in both experiments

not surprising in the light of other work that has been done in attempting to generate a carbanion at the anomeric centre. Berlin, Rathore and Peterson (35) attempted to metalate a series of 2-aryl-1,3-dioxolanes using such strong bases as organolithium reagents and found that an exothermic reaction occurred at room temperature in ether between the 2-aryl-1,3-dioxolanes and the base. The products of the reaction suggest that the reaction passes through the carbanion stage (Scheme 19). In an attempt to



Scheme 19

generate a carbanion which cannot fragment in this manner, a similar reaction was tried on 2-phenyl-1,3-dioxane (36). Treatment of this molecule with the very effective metalating agent n-butyl lithium/N,N,N',N'—tetramethylethylene diamine (TMEDA) at -70°C to +20°C still did not give any evidence for the carbanion which should be stabilized by conjugation with the aromatic ring (Scheme 20). These findings are in agreement with the postulate



Scheme 20

of McElvain et. al. (2) that the removal of the anomeric hydrogen as a proton in an El_{CB} type process, is difficult. The removal of the anomeric hydrogen by base in a concerted process, however,

whereby an adjacent group is lost as in the dehydrobromination reactions or in the fragmentation of the dioxolane ring should not be as disfavored as the formation of a discrete negative charge on the anomeric carbon as in an El_{CB} process.

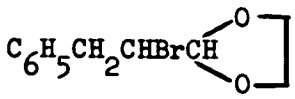
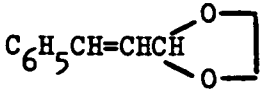
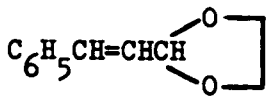
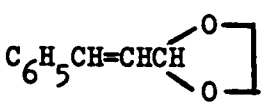
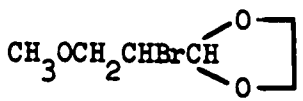
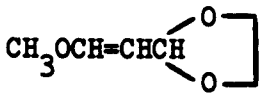
An investigation was also carried out in the course of our work in order to compare the ease of removal of the anomeric hydrogen with the ease of removal of the hydrogen atoms at the β carbon when the β carbon is attached to an electronegative group. The electronegative groups chosen were of necessity limited to the ether oxygen and the phenyl units since other groups might suffer displacement. The results of these experiments are shown in Table 6.

The dehydrobromination of α-bromo-β-phenlypropionaldehyde diethylacetal with potassium t-butoxide in t-butyl alcohol gave only cinnamaldehyde diethylacetal (Experiment 1, Table 6). This was the product expected on the basis of the conclusions drawn by McElvain (2) for the dehydrobromination of α-bromo acetals with a hydrogen atom on the β carbon. The increased yield of product in a shorter reaction time than had before been used (see Table 3) and the fact that no evidence for the formation of the corresponding ketene acetal could be found can be attributed to the more facile abstraction of the benzylic protons by the base than abstraction of the anomeric hydrogen atom.

Dehydrobromination of α-bromo-β-phenylpropionaldehyde ethyleneacetal also gave the corresponding α,β-unsaturated acetal

Table 6

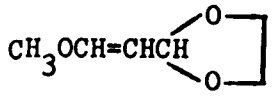
Dehydrobromination of some α-bromo acetals with an electronegative group adjacent to the β carbon [a].

Experiment Number	Compound	Time, Hours	Total Recovery %	Products	Relative Amount %	Reaction %
1	$C_6H_5CH_2CHBrCH(OC_2H_5)_2$	5	90	$C_6H_5CH{=}CHCH(OC_2H_5)_2$	100	80
				$C_6H_5CH_2CH_2COC_2H_5$	0	
2		8	85		100	85
				$C_6H_5CH_2CH_2COC_2H_4OH$	0	
3		8	80		100	0
4		20	80		30	69
				$CH_3OCH_2CH_2COC_2H_4OH$	70	

a. The temperature was 80°C in all the above experiments.

cinnamaldehyde ethyleneacetal, as the lone product (Experiment 2, Table 6). Although this is the first case in which the α,β-unsaturated acetal has been formed exclusively from an α-bromo ethyleneacetal, this was not unexpected, again due to the greater reactivity of the benzylic hydrogen atoms. The product obtained, cinnamaldehyde ethyleneacetal, was found to be stable under the reaction conditions (Experiment 3, Table 6). The synthesis of the corresponding ketene acetal was attempted but failed to give any of the desired product so the stability of this compound could not be determined under the dehydrobromination conditions, however, by analogy with the stability of the alkylketene acetals, the benzylketene ethyleneacetal might also be expected to be stable to base. It thus appears that the anomeric hydrogen atom is less reactive towards base than are the benzylic hydrogen atoms.

A comparison of the reactivity towards base of the anomeric hydrogen atom of an ethyleneacetal and a hydrogen atom on a carbon α to an ether linkage was carried out by attempting the potassium t-butoxide catalyzed dehydrobromination of α-bromo-β-methoxypropionaldehyde ethyleneacetal. The results of this dehydrobromination (Experiment 4, Table 6) show that 70 per cent of the proton removal occurred at the anomeric carbon giving rise to the ketene acetal isolated as the ester obtained by the modified aqueous work-up procedure. The other 30 per cent of proton abstraction occurred at the carbon atom α to the ether linkage giving the product β-methoxyacrolein ethyleneacetal 12.

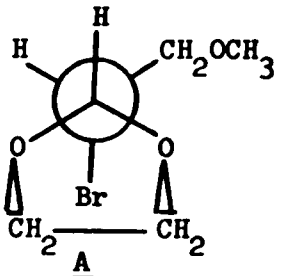


12

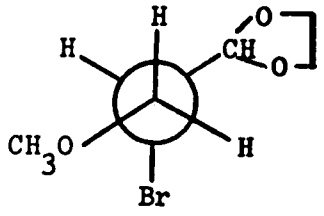
McElvain (3) had attempted the stepwise removal of hydrogen chloride from chloroacetaldehyde di-(β-chloroethyl)acetal (Scheme 6) with potassium t-butoxide in t-butyl alcohol and found that hydrogen chloride was first removed from the chloroethyl groups of the acetal. The steric hindrance to approach of the base to the anomeric hydrogen would be greater in chloroacetaldehyde di-(β-chloroethyl) acetal than in chloroacetaldehyde diethylacetal because in the former, the size of the freely rotating β-chloroethoxy groups is larger than the ethoxy groups in the latter. The increased steric hindrance to approach of the base to the anomeric hydrogen in chloroacetaldehyde di-(β-chloroethyl)acetal would cause preferential removal of the hydrogen atoms of the dichloroethyl groups by the bulky t-butoxide anion.

Examination of the Stuart model of α-bromo-β-methoxy-propionaldehyde ethyleneacetal used in Experiment 4, Table 6 shows that there is no large difference in the steric availability of the anomeric hydrogen and the hydrogen atoms on the β carbon to approach by the bulky t-butoxide anion as there was in the case of chloroacetaldehyde di-(β-chloroethyl)acetal. Examination of the two possible transition states for elimination of hydrogen bromide from α-bromo-β-methoxypropionaldehyde ethyleneacetal (Figure 5) also shows that there are no large steric interactions

which favor one transition state over the other. In the transition



A



B

Figure 5

state leading to the formation of the ketene acetal (Figure 5-A) the two methylene groups of the 1,3-dioxolane ring are held away from the methoxymethyl group because of the more rigid structure of the 5-membered 1,3-dioxolane ring. Also in the transition state leading to the formation of the α,β-unsaturated acetal (Figure 5-B), no serious interactions occur between groups when the double bond is being formed. This analysis indicates that the two possible transition states A and B (Figure 5) can be formed with nearly equal ease. Accordingly, steric effects should not determine the direction of proton removal in α-bromo-β-methoxypropionaldehyde ethyleneacetal. The direction of proton removal should then be solely a function of the lability of the respective protons governed by the adjacent electronegative groups. The observation that 30 per cent of the proton abstraction occurs at the β carbon in α-bromo-β-methoxy-propionaldehyde ethyleneacetal whereas no proton abstraction occurred at the β carbon in α-bromo-n-valeraldehyde ethyleneacetal suggests that substitution of the methoxy group on the β carbon does enhance the acidity of the two hydrogen atoms on the β carbon.

The fact that 70 per cent of the proton abstraction still occurs at the anomeric carbon inspite of the ratio of 2:1 for the number of hydrogen atoms on the β carbon to the single anomeric hydrogen and the enhancement of acidity of the hydrogen atoms on the β carbon in α-bromo-β-methoxypropionaldehyde ethyleneacetal suggests that the addition of a second alkoxyl group to a carbon, as in an acetal, does increase the lability of the so formed anomeric hydrogen over that of a hydrogen atom α to an ether linkage.

2. Dehydrobromination of Some α-Bromo ethyleneacetals in Dimethylsulfoxide.

In an attempt to find a method for the production of the two desired α,β-unsaturated acetals 1 and 2 , required for the hydrogenolysis experiments in Part I of this thesis, the dehydrobromination of the corresponding α-bromo acetal precursors was attempted in the solvent dimethylsulfoxide. The results of these experiments are shown in Table 7.

In Experiments 1 and 2, Table 7 a procedure similar to that of McElvain (28) was employed. After addition of the α-bromo acetal precursor to the base in dimethylsulfoxide, which was observed to produce an exothermic rection, the solution was stirred for one hour at room temperature. The reaction vessel was then fitted for downward distillation. The distillation from the crude reaction mixture was carried out under reduced pressure and the distillate was collected in a dry ice-acetone cooled receiver. The products expected from the dehydrobromination reaction have

Table 7

Dehydrobromination of some α-bromo ethyleneacetals in dimethylsulfoxide

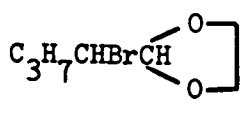
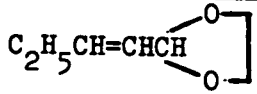
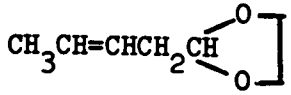
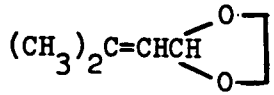
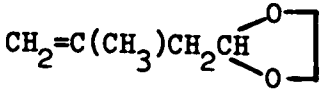
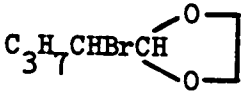
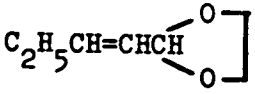
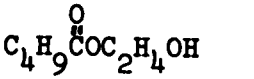
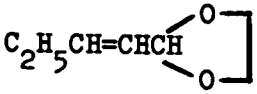
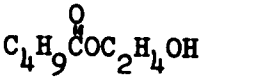
Experiment Number	Product	Base	Time, Hours	Total Recovery %	Products	Relative Amounts %	Reaction %
1[a,c]		$NaOCH_3$	1[b]	45		95-2 [d]	45
						5-98 [d]	
2[a,c]		$NaOCH_3$	1[b]	47		95-50	47
						5-50	
3[e]		$NaOCH_3$	1	90		70	95
						30	
4[e]		$NaOCH_3$	20	90		70	100
						30	

Table 7-Continued

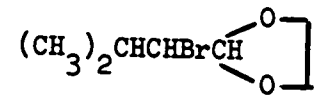
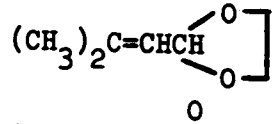
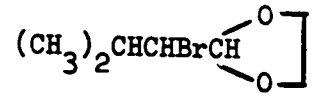
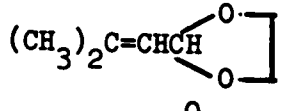
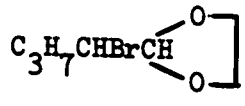
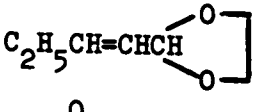
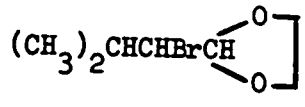
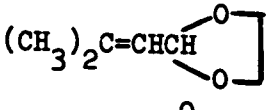
Experiment Number	Compound	Base	Time, Hours	Total Recovery%	Products	Relative Amounts%	Yield %
5[e]		$NaOCH_3$	1	90		98	98
					$(CH_3)_2CHCH_2COC_2H_4OH$	2	
6[e]		$NaOCH_3$	20	90		98	100
					$(CH_3)_2CHCH_2COC_2H_4OH$	2	
7[e]		KO-t-Bu	1	90		33	100
					$C_4H_9COC_2H_4OH$	67	
8[e]		KO-t-Bu	1	90		72	100
					$(CH_3)_2CHCH_2COC_2H_4OH$	28	

Table 7-Continued

Experiment Number	Compound	Base	Time, Hours	Total Recovery%	Products	Relative Yield % Amount%	
9[e]	$C_3H_7CHBrCH\begin{matrix}O\\O\end{matrix}$	$NaCH_2\overset{O}{\overset{\|}{S}}CH_3$	1	90	$C_2H_5CH{=}CHCH\begin{matrix}O\\O\end{matrix}$	60	100
					$C_4H_9\overset{O}{\overset{\|}{C}}OC_2H_4OH$	40	

a. These two experiments were done with a nonaqueous work-up to be described below.

b. This time does not include the time required to complete the distillation.

c. The temperature of these reactions was raised to that required to effect distillation of the products.

d. These values depend on the total time of exposure to the basic solution and the temperature of the reaction mixture.

e. The temperature of these reaction was not allowed to go above 40°C.

boiling points lower than that of dimethylsulfoxide, therefore, once the temperature of the distillation had reached that of the boiling point of dimethylsulfoxide at the pressure used, the distillation was terminated. The distillate obtained from this step always contained dimethylsulfoxide as a contaminant and therefore was redistilled on a spinning band column, a procedure which provided the product free of dimethylsulfoxide. The product obtained from these dehydrobromination reactions was always found to be a mixture of the α,β- and β,γ-unsaturated acetals corresponding to the α-bromo acetal used. The ratio of the α,β- to β,γ-unsaturated acetals was dependent on the time of exposure to the basic solution and the temperature necessary to distill the products from the reaction mixture (Experiments 1 and 2, Table 7). A study of the stability of the olefinic products under the dehydrobromination conditions will be discussed later. Since the total recoveries were low by this method, the modified procedure involving the addition of water was again employed.

In experiments 3 to 9 of Table 7 the addition of the α-bromo acetal to the basic solution was controlled so as not to allow the temperature of the solution to rise above 40°C. The temperature of the solution was found to rise quickly with rapid addition of the α-bromo acetal and this increase in temperature caused isomerization of the desired α,β-unsaturated acetal to the undesired β,γ-unsaturated acetal. After addition of the α-bromo acetal was completed and a period of time allowed in which the resulting solution was stirred at room temperature, the solution

was mixed with an equal volume of saturated aqueous sodium chloride solution. The sodium chloride solution, rather than distilled water, was used in these reactions to decrease the solubility of the products in the dimethylsulfoxide-water mixture. Continuous extraction with ether was again employed to remove the products from the aqueous solution. In this way, material recoveries of approximately 90 per cent were obtained. As well, evidence was found for the simultaneous formation of some ketene acetal from both of the α-bromo acetal precursors used in this study by the isolation of the esters expected from hydrolysis of the ketene acetals.

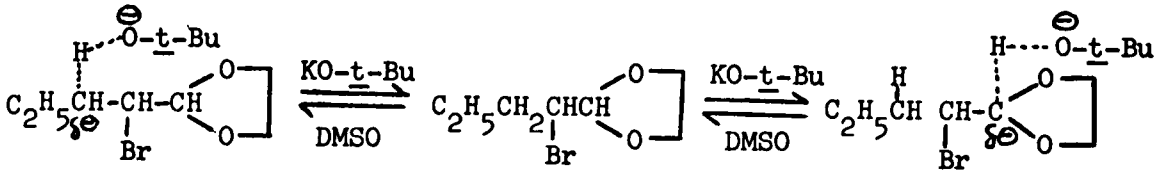
In the sodium methoxide catalyzed dehydrobromination of α-bromo-n-valeraldehyde ethyleneacetal (Experiments 3 and 4, Table 7) it was found that only two compounds, the corresponding α,β-unsaturated acetal and ketene acetal, were found. No evidence for the corresponding β,γ-unsaturated acetal could be found. The ratio of products remained constant as the reaction time was increased from one hour to twenty hours, a fact which demonstrates the stability of the two products in the basic solution, certainly at temperatures less than 40°C. The dehydrobromination of α-bromoisovaleraldehyde ethyleneacetal under the same conditions also gave only the corresponding α,β-unsaturated acetal and ketene acetal. These products were also found to be stable under the reaction conditions over a twenty hour period (Experiments 5 and 6, Table 7) at less than 40°C. The potassium t-butoxide catalyzed elimination of hydrogen bromide from both α-bromo-n-valeraldehyde ethyleneacetal

and α-bromoisovaleraldehyde ethyleneacetal also gave the same two products respectively with no evidence for the formation of either of the corresponding β,γ-unsaturated acetals (Experiments 7 and 8, Table 7).

The change in the 100:0 proportion of ketene acetal to α,β-unsaturated acetal in the potassium t-butoxide catalyzed elimination of hydrogen bromide from α-bromo-n-valeraldehyde ethyleneacetal in t-butyl alcohol as solvent (Experiment 2, Table 4), to 67:33 in the potassium t-butoxide catalyzed elimination from the same α-bromo acetal in dimethylsulfoxide as solvent (Experiment 7, Table 7) could be a result of an alteration in the mechanism of the elimination reaction brought about by the change in both the base strength and effective size of the base caused by a change in the solvation of the anion.

Froemsdorf, McCain and Wilkinson (18, 19) have postulated that in base catalyzed elimination reactions, as the strength of the base is increased, either by a change of the base in the same solvent or by a change of solvent, carbon-hydrogen bond stretching becomes so pronounced in the transition state that steric effects of the attacking base are of little importance. The use of the strongly basic system, potassium t-butoxide in dimethylsulfoxide, thus may increase the carbon-hydrogen bond stretching in the transition state leading to the elimination of hydrogen bromide from an α-bromo acetal. The two possible transition states are shown in Scheme 21. Such an increase in the carbon-hydrogen bond

stretching would give more El_{CB} character to the transition state, i.e. more carbanion character would be developed at the carbon atom adjacent to the carbon bearing the bromine atom. The development



A B

Scheme 21

of carbanion character at the anomeric carbon as in B of Scheme 21 would be hindered by the repulsion of a partial negative charge at this position by the p electrons of the two adjacent oxygen atoms. Such a partial negative charge is not developed in the elimination reactions in t-butyl alcohol as solvent because the system is less basic and therefore the carbon-hydrogen bond stretching is not as great in the transition state in this solvent. Also in t-butyl alcohol the reaction is concerted in nature due to the hydrogen bonding ability of this solvent which would assist the bromide ion to leave. Such assistance is not possible in dimethylsulfoxide. The development of carbanion character at the β carbon is also slightly hindered by the fact that the β carbon is a secondary carbon. It is felt, however, that the carbanion which tends to develop in transition state B (Scheme 21) is destabilized to a greater extent by the two adjacent oxygen atoms than is the developing carbanion of transition state A (Scheme 21) where the only destabilizing effect is that due to its formation on a secondary carbon atom. Thus in the equilibrium shown in

Scheme 21, transition state B is less stable than transition state A and therfore the equilibrium will be shifted in favor of A. If this is so, then the preference for the transition state A predicts increased formation of the α,β-unsaturated acetal, a result which is actually observed. The observation that the amount of the α,β-unsaturated acetal formed increased to only 33 per cent of the product from the dehydrobromination of α-bromo-n-valeraldehyde ethyleneacetal in the solvent dimethylsulfoxide whereas it is not formed at all if the solvent is t-butyl alcohol suggests there may still be a large steric factor due to the size of the t-butoxide anion which prevents the formation of even a greater proportion of the α,β-unsaturated acetal.

The effect of the size of the base on the direction of dehydrobromination in dimethylsulfoxide is shown by the results of Experiments 3, 4, 5, and 6 (Table 7) where the base employed was sodium methoxide. In the sodium methoxide catalyzed dehydrobromination of α-bromo-n-valeraldehyde ethyleneacetal in the solvent dimethylsulfoxide, the ratio of α,β-unsaturated acetal to ketene acetal has increased to 70:30 (Experiments 3 and 4, Table 7). The decrease in the proportion of α,β-unsaturated acetal when potassium t-butoxide rather than sodium methoxide is used as the base (a drop from 70 % to 33 %) (Experiment 7, Table 7) supports the view that there is a steric effect in these dehydrobromination reactions. This steric effect of a bulky base is further illustrated by comparison of Experiments 5 and 6 with Experiment 8 (Table 7) where again a

greater proportion of the α,β-unsaturated acetal is obtained using the sterically smaller sodium methoxide as base.

By using the strongly basic medium of sodium methoxide in dimethylsulfoxide, the transition states shown in Scheme 21 may still be formed. This view is based on the finding of Froemsdorf et. al. (18, 19) that the enhancement of basicity of potassium ethoxide by changing the solvent from ethyl alcohol to dimethylsulfoxide was sufficient to cause a significant increase in the proportion of 1-ene product formed (Experiments 1 and 2, Table 1) and thus was indicative of greater carbon-hydrogen bond stretching in the transition state. Thus in the elimination with sodium methoxide in dimethylsulfoxide, transition state A (Scheme 21) is again favored on the basis of the electronic considerations suggested above. The production of more α,β-unsaturated acetal in the presence of sodium methoxide in dimethylsulfoxide than with potassium t-butoxide thus clearly demonstrates that although carbon-hydrogen bond stretching is increased in these strongly basic media and thus the mechanism involves some El_{CB} character, the steric effect of the attacking base is a highly important factor in determining the direction of removal of hydrogen bromide.

The solvent may also play a part in determining the direction of elimination due to the increase or decrease in the effective size of the anion by solvation. In t-butyl alcohol, the effective size of the t-butoxide anion is increased due to hydrogen bonding with the solvent and thus will favor abstraction of the sterically most available hydrogen atom. In the solvent

dimethylsulfoxide, where such hydrogen bonding is not possible, the effective size of the base is decreased compared to that in t-butyl alcohol and thus some proton abstraction may occur at more sterically hindered positions. This effect was demonstrated by the results reported by Froemsdorf et. al. (19) in the elimination of hydrogen bromide from 2-bromobutane with potassium t-butoxide in the two solvents t-butyl alcohol and dimethylsulfoxide (Experiments 10 and 11, Table 1). In t-butyl alcohol 53 per cent of the 1-ene was formed, but in dimethylsulfoxide where the carbon-hydrogen bond stretching would be increased in the more strongly basic medium, only 31 per cent of the 1-ene was formed. This observed decrease in the amount of 1-ene formed where an increase was expected could be due to the decrease in effective size of the base in dimethylsulfoxide as mentioned above. This information emphasizes the previous conclusion that the effective size of the base is an important factor in determining the direction of dehydrohalogenation. This solvent influence on the effective size of the base with its resulting effect on the dehydrobromination reaction is also illustrated by the following observations. By changing the solvent from t-butyl alcohol to dimethylsulfoxide in the potassium t-butoxide catalyzed dehydrobromination of α-bromoisovaleraldehyde ethyleneacetal, the proportion of α,β-unsaturated acetal produced was increased from 14 per cent in t-butyl alcohol (Experiment 3, Table 4) to 72 per cent in dimethylsulfoxide (Experiment 8, Table 7). The increase of 58 per cent (i.e. 72-14) in the proportion of α,β-unsaturated

acetal produced by only changing the solvent is again less than the increase observed when sodium methoxide is used as the base in the solvent dimethylsulfoxide. In the sodium methoxide catalyzed elimination in dimethylsulfoxide, the α,β-unsaturated acetal is produced to the extent of 98 per cent of the olefinic products. The fact that more α,β-unsaturated acetal is formed from the dehydrobromination of α-bromoisovaleraldehyde ethyleneacetal than from α-bromo-n-valeraldehyde ethyleneacetal is again probably due at least in part to the possibility that formation of the α,β-unsaturated acetal from the former is stabilized by hyperconjugation more than is possible in the latter case.

The finding that more α,β-unsaturated acetal than ketene acetal is found when dimethylsulfoxide is used as solvent can thus be explained on the basis of the change in the mechanism of the elimination reaction due to the change in base strength of the medium and also to a change in the effective size of the base caused by a change of the degree of solvation of the anion.

The possibility that the attacking base in these reactions might be the dimethyl sulfoxonium anion, which would be present in a small concentration in the presence of an alkoxide base as was shown by Ledwith and McFarland (25), was also investigated. This anion was generated specifically by the action of sodium hydride on dimethylsulfoxide and was used as the base in the dehydrobromination of α-bromo-n-valeraldehyde ethyleneacetal (Experiment 9, Table 7). The different product proportions observed using the sodium salt

of dimethylsulfoxide as base compared with the product proportions using either sodium methoxide or potassium t-butoxide as base is indicative that in these latter reactions the attacking base is primarily the alkoxide anion. The observed increase in the amount of α,β-unsaturated acetal produced using the sodium salt of dimethylsulfoxide as base is also in accord with the postulate that there is a directive effect in these eliminations depending on the size of the base. The amount of α,β-unsaturated acetal produced is greater when using the sodium salt of dimethylsulfoxide than when using potassium t-butoxide but, however, is not as great as when sodium methoxide is the base used. These results are in accord with the relative size of these three bases. Froemsdorf and McCain (18) also stated that the possibility of the dimethyl sulfoxonium anion existing as the attacking base is remote since if this anion were the attacking species then the ratio of olefinic products would be the same when ethoxide was replaced with t-butoxide. This was not observed. It is felt, therefore, in this work that although the possibility of dehydrobromination occurring due to the equilibrium concentration of the dimethyl sulfoxonium ion cannot be discounted entirely, the primary reaction is catalyzed by the alkoxide base as shown by the changes observed in product proportions by changing the base.

3. Attempted Base Catalyzed Isomerization of Some Olefinic Acetals in Dimethylsulfoxide.

The stability of the α,β-unsaturated acetals, the

β,γ-unsaturated acetals and n-propylketene ethyleneacetal under the dehydrobromination conditions was also investigated and these results are reported in Table 8. The results of the reaction of n-propylketene ethyleneacetal with potassium t-butoxide and sodium methoxide in dimethylsulfoxide are shown in Table 8 (Experiments 1 and 2). The stability of n-propylketene ethyleneacetal to these bases in dimethylsulfoxide and to potassium t-butoxide in t-butyl alcohol (as reported on page 131) may be due to the electronic nature of the ketene acetal double bond. Due to the mesomeric shift of electrons from the oxygen atoms towards the double bond, a feature which was suggested to be the reason for the highfield position of the olefinic protons in the n.m.r. spectrum, a higher concentration of negative charge exists at the α carbon atom. This type of electronic delocalization involving oxygen and the two sp^2 hybridized carbon atoms in 3,4-dihydro-2H-pyran has been postulated to be the reason for the significantly higher barrier to conformational isomerism (6.6 ± 0.3 k. cal./mole at -140°C) in this compound as compared to that for cyclohexene (5.2 k. cal./mole at -165°C) (37). McElvain (1) also postulated this type of polarization as the reason for the abnormally high boiling points of ketene acetals and the extraordinary reactivity of these compounds. Also, alkylation with reactive alkyl halides such as allyl and benzyl bromide occur with displacement of the halogen by the negatively polarized α carbon atom (Scheme 22). Because of this type of polarization of the ketene acetal, abstraction of a proton from the allylic carbon

Table 8

The attempted isomerization of various unsaturated acetals in dimethylsulfoxide using the modified dehydrohalogenation procedure [a].

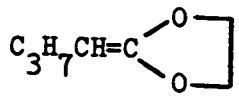
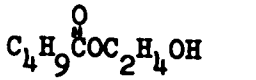
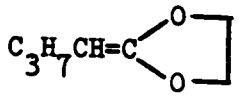
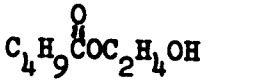
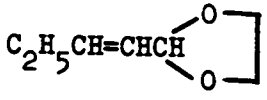
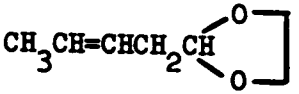
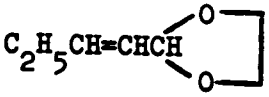
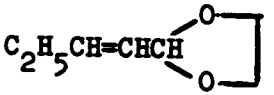
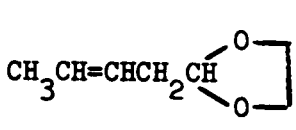
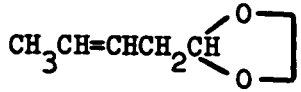
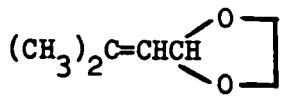
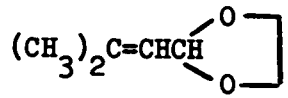
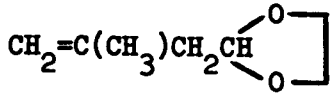
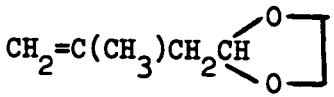
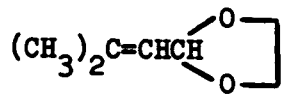
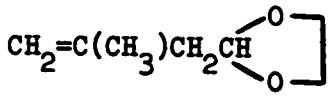
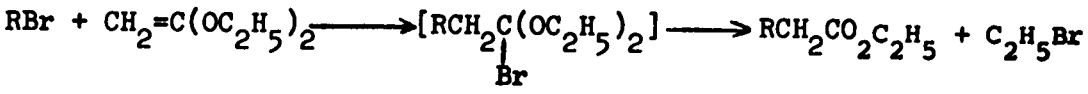
Experiment Number	Compound	Base	Time, Hours	Total Recovery%	Products	Relative Amount%
1		$NaOCH_3$	18	90		100
2		KO-t-Bu	18	90		100
3		$NaOCH_3$	12	80		2
						98
4		KO-t-Bu	12	78		2
						98

Table 8-Continued

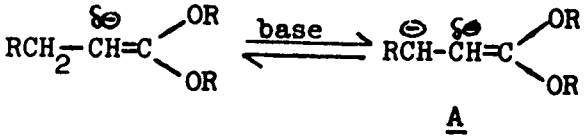
Experiment Number	Compound	Base	Time, Hours	Total Recovery%	Products	Relative Amount %
5		$NaOCH_3$	12	85		2
						98
6		$NaOCH_3$	20	80		45
						55
7		$NaOCH_3$	20	80		50
						50

a. The temperature in all the above reactions was 80°C.



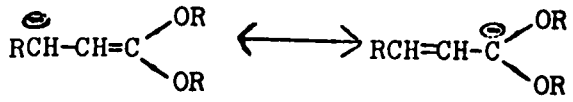
Scheme 22

to initiate isomerization would be difficult as this would involve the formation of adjacent negative charges (Scheme 23). Also, if the intermediate A in Scheme 23 were formed, little if any resonance stabilization would occur in this anion since the negative charge,



Scheme 23

in the extreme, would be transfered to the anomeric carbon which, as has been postulated, is an unfavorable situation (Scheme 24). These points are therefore suggested as an explanation of the stability of n-propylketene ethyleneacetal to the alkaline dehydrobromination conditions. These same reasons could thus



Scheme 24

provide an explanation for the stability of other ketene acetals found by McElvain (2) to resist rearrangement under alkaline conditions.

As seen in Experiments 3 and 4 (Table 8), 2-pentenal ethyleneacetal is easily isomerized to 3-pentenal ethyleneacetal by

either sodium methoxide or potassium t-butoxide in dimethylsulfoxide. No isomerization of the α,β-unsaturated acetal to the corresponding ketene acetal was observed, again due to the unfavorable formation of a carbanion at the anomeric carbon. Such preliminary carbanion formation, according to Schriesheim et. al. (22), is a necessary step for the isomerization of olefins. 2-Pentenal ethyleneacetal was converted almost exclusively under the reaction conditions at 80°C (Experiments 3 and 4, Table 8) to 3-pentenal ethyleneacetal but was found to be stable in the same basic solution at temperatures below 40°C (Experiment 4, Table 7). Also it was found that 3-pentenal ethyleneacetal rearranged back to 2-pentenal ethyleneacetal to the extent of only two per cent under the same conditions and in the same period of time. The explanation of the apparently greater thermodynamic stability of 3-pentenal ethyleneacetal over 2-pentenal ethyleneacetal in the equilibrium mixture of 98:2 respectively has eluded us.

The isomerization of 2-isopentenal ethyleneacetal was also carried out (Experiment 6, Table 8) with sodium methoxide in dimethylsulfoxide. It was found that this compound isomerized to 3-isopentenal ethyleneacetal to the extent of 55 per cent in 20 hours. The isomerization of 3-isopentenal ethyleneacetal under the same conditions was also attempted. This compound was found to isomerize to 2-isopentenal ethyleneacetal to the extent of 50 per cent in the same time. Although an equilibrium was not reached in the 20 hour reaction period for the isomerization of the two

*iso*pentenal ethyleneacetals, from the nearly equal amounts of both isomers formed from either side of the equilibrium the two isomers appear to be of nearly equal thermodynamic stability. It was expected that 2-*iso*pentenal ethyleneacetal would be more stable than 3-*iso*pentenal ethyleneacetal but again an explanation of the greater than expected thermodynamic stability of the β,γ-isomer has eluded us. Again no ketene acetal was observed in these isomerizations. The greater ease of isomerization of the α,β- to β,γ-unsaturated acetals and *vice versa* in the solvent dimethylsulfoxide is in accord with the work of Schriesheim *et. al.*(22) where it was found that the ease of olefin isomerizations is greater in dimethylsulfoxide than in a protic solvent.

SUMMARY

In the course of this study on the direction of removal of hydrogen bromide from α-bromo dialkyl- and ethyleneacetals which possess a hydrogen atom on the β carbon, it has been found that the anomeric hydrogen does exhibit some reactivity towards base in these reactions. The reactivity of the anomeric hydrogen towards base is not, however, as great as initially expected on the basis of the expected electron withdrawal by the two adjacent oxygen atoms. In fact, the inductive electron withdrawing power of the two adjacent oxygen atoms seems to be of secondary importance to the steric availability of the anomeric hydrogen to the approaching

t-butoxide anion in the solvent t-butyl alcohol. In all of the elimination reactions carried out with potassium t-butoxide in t-butyl alcohol the direction of removal of hydrogen bromide seemed to be governed by the relative steric availability of the anomeric hydrogen and the hydrogen atoms on the β carbon as well as the interactions developed in the transition state leading to the formation of the double bond. There was no evidence found for the isomerization of the α,β-unsaturated acetals to the corresponding ketene acetals or vice versa in any of the compounds studied and therefore the product distributions reported are those of both thermodynamic and kinetic control.

All the elimination reactions in t-butyl alcohol were presumed to be of a concerted nature due to the second order kinetic analysis reported by McElvain (2) and by the fact that no evidence could be found by deuterium exchange experiments for the production of a carbanion intermediate.

A study of the reactivity of the anomeric hydrogen towards base showed that the anomeric hydrogen is less reactive than is a benzylic hydrogen atom but more reactive than a hydrogen atom α to an ether linkage providing that the steric availability of the hydrogen at the two sites is nearly equal and crowding effects in the transition state are also nearly equal. Thus in the elimination reactions carried out with potassium t-butoxide in t-butyl alcohol the direction of removal of hydrogen bromide seems to be governed by the ease of steric approach of the base to the reaction site

unless the acidity of the hydrogen atoms on the β carbon is increased by a neighboring electronegative group.

When the solvent used for the dehydrobromination is changed from t-butyl alcohol to dimethylsulfoxide, the direction of removal of hydrogen bromide still seems to be governed somewhat by the ease of steric approach of the base to the reaction sites but the magnitude of this effect is diminished by an electronic factor brought about by a change in the mechanism of the reaction. This change is due to the greater basicity of alkoxides in dimethylsulfoxide. In this solvent, carbon-hydrogen bond stretching becomes more important in the transition state lending El_{CB} character to the reaction. The effect of this change in the mode of the reaction is to destabilize the transition state leading to the formation of the ketene acetal in favor of the transition state leading to the α,β-unsaturated acetal. Again no interconversion of these two olefinic products was observed. Also, in this dipolar aprotic solvent no hydrogen bonding to the base is possible and therefore the effective size of the base is reduced. Such a decrease in the effective size of the base would also decrease the selectivity exhibited in approach to the two reaction sites. The relative importance of the change in mechanism (brought about by the change in basicity of the medium) and the change in the effective size of the base, however, is not known.

Thus it has been shown possible to produce preferentially, either the α,β-unsaturated acetal or the ketene acetal from α-bromo ethyleneacetals by choosing the proper conditions of solvent and base.

EXPERIMENTAL

All boiling points and melting points in this work are uncorrected.

Gas liquid chromatographic analyses were made with an F and M, Model 700 instrument, equipped with 12 ft. by 1/8 in. columns packed with: (a) butanediol succinate, 20 % on Gas Chrom P (60-80 mesh), (b) silicone rubber SE 30, 20 % on Gas Chrom P (60-80) mesh and (c) carbowax 20M, 20 % on Gas Chrom P (60-80 mesh). Helium was the carrier gas at a flow rate of about 40 ml per minute.

For preparative gas liquid chromatography (g.l.c.), the instrument used was an Aerograph Autoprep, Model A-700 (Wilkens Instrument and Research Co.). The column employed was 12 ft. by 1/4 in. packed with butanediol succinate, 20 % on Gas Chrom P (60-80 mesh). Helium was the carrier gas.

The column temperature and type of column used was dependent upon the boiling points of the compounds. For some analytical work on the F and M, Model 700, the temperature was linearly programmed in order to achieve better resolution. The temperature was increased at the rate of 7.5 ^{o}C per minute starting from 80-100 ^{o}C with the terminal temperature being dependent upon the column stability.

The quantitative analyses were made by measuring the areas corresponding to the peaks involved. In a number of cases these

areas were compared with those obtained from known and weighed artificial mixtures. However, it was found that equimolar mixtures of dehydrobromination products gave peaks of nearly equal area for the components (within 10 %).

Infrared spectra were recorded with a Perkin-Elmer Model 21 instrument.

Nuclear magnetic resonance (n.m.r.) spectra were recorded on either a Varian Associates A-60 instrument or a Varian Associates A-56/60A instrument operated by Mr. R. Swindlehurst and his assistants. All spectra were referred to tetramethylsilane.

Elemental analyses were carried out by Mrs. Darlene Mahlow in the Chemistry Department of this University.

In the work-up procedures for the various syntheses described and the dehydrobromination reactions, the drying agent employed was anhydrous magnesium sulfate unless otherwise stated. Solvents were removed with a rotatory evaporator under reduced pressure unless otherwise stated.

N.m.r. and i.r. spectra were obtained for all compounds reported in this work and were, in all cases, consistent with the structure assigned.

1. Preparation of α-Bromo Acetals

n-Valeraldehyde dimethylacetal was prepared by a modification of the procedure described by Bachman (39) for the preparation of the diethylacetal of hexanal.

To a stirred suspension of magnesium turnings (22.6 g, 0.94 mole) in 100 ml of anhydrous ether was added dropwise, 20 ml of a solution of 129 g (0.94 mole) of n-butyl bromide in 100 ml of anhydrous ether. The addition was carried out cautiously until the Grignard reagent was formed and then at such a rate as to maintain gentle reflux of the ether. After 20 ml of the solution of n-butyl bromide had been added, the reaction mixture was diluted with a further quantity (400 ml) of anhydrous ether and then the remainder of the n-butyl bromide solution was added in a dropwise manner. After the addition was completed the resulting ether solution was heated under reflux for four hours. The solution was then cooled to room temperature and 100 g (0.94 mole) of trimethyl orthoformate was added dropwise and then the solution was heated under reflux overnight.

The solution was then cooled to room temperature and was poured on to 500 ml of a stirred ice-water mixture. The ether layer was separated and the aqueous layer washed twice with 200 ml portions of ether. The combined ether layers were washed first with 100 ml of water and then with 100 ml of saturated aqueous sodium chloride solution. The ether layer was then dried, filtered free of solid and the filtrate freed from ether. The residue was distilled and

gave a clear liquid (45 g, 36 %). B.p. 51-53°C at 30 mm; n_D^{24} 1.3969. Lit. b.p. 120-129°C at 760 mm (40).

α-Bromo-n-valeraldehyde dimethylacetal was prepared by a modification of the procedure of Hartung and Adkins (41).

To a stirred solution of n-valeraldehyde dimethylacetal (42 g, 0.32 mole) in 300 ml of dry chloroform was added dropwise 51 g (0.32 mole) of bromine. The rate of addition was controlled so as to maintain the temperature of the reaction mixture between 30-35°C. When the addition was complete, the solution was stirred at room temperature for 2 hours and was then cooled to -10°C by means of an ice-salt bath. Potassium hydroxide (18 g, 0.32 mole) in 150 ml of methanol was then added in a dropwise manner to the cooled solution. After this was added the resulting solution was allowed to warm to room temperature with stirring and was left overnight. The precipitated potassium bromide was then separated by filtration and the solvents removed by fractional distillation through a 4 inch Vigreaux column at atmospheric pressure. The residue was then taken up in 400 ml of ether and this solution was washed first with four 100 ml portions of saturated aqueous sodium carbonate solution and then with 100 ml of saturated aqueous sodium chloride solution. The ether layer was dried, filtered free of drying agent and the filtrate freed from ether. The residue was distilled and gave 40 g (59%) of a colorless liquid. B.p. 78-80°C at 12 mm; n_D^{23} 1.4559.

Anal. Calcd. for $C_7H_{15}BrO_2$: C, 39.80; H, 7.12; Br, 37.90.

Found: C, 39.58; H, 7.04; Br, 38.08.

The 60 MHz n.m.r. spectrum in CCl_4 was consistent with the proposed structure, showing a doublet centred at τ 5.70 (1H), J = 6 Hz, a multiplet between τ 6.0 and 6.32 (1H), two singlets at τ 6.66 and 6.68 (6H), and a multiplet between τ 8.0 and 9.25 (7H).

n-Valeraldehyde diethylacetal was prepared from n-butyl bromide and triethyl orthoformate by the modified method of Bachman (39) as previously described for the preparation of n-valeraldehyde dimethylacetal.

A colorless liquid was obtained in 80% yield. B.p. 60°C at 11 mm; n_D^{23} 1.4019. Lit. b.p. 162.5-163.5°C; n_D^{20} 1.4021 (42).

α-Bromo-n-valeraldehyde diethylacetal was prepared from n-valeraldehyde diethylacetal and bromine by the modified procedure of Hartung and Adkins (41) as previously described for the preparation of α-bromo-n-valeraldehyde dimethylacetal except that the potassium hydroxide was added in an ethanol solution in this case.

A colorless liquid was obtained in 70% yield. B.p. 80°C at 7 mm; n_D^{23} 1.4453. Lit. b.p. 92-96°C at 12 mm (43).

α-Bromo-n-valeraldehyde ethyleneacetal was prepared by the trans-acetalization of α-bromo-n-valeraldehyde diethylacetal with ethylene glycol according to the following modification of the procedure of

McElvain and Curry (5).

α-Bromo-n-valeraldehyde diethylacetal (41 g, 0.17 mole) was added to a solution of ethylene glycol (11 g, 0.17 mole) in 200 ml of dry toluene. The flask was set up for fractional distillation through a four-inch Vigreaux column. p-Toluenesulfonic acid (0.1 g) was added to the reaction mixture and the mixture was then heated to 110°C. A mixture of ethanol and toluene distilled between 75-110°C. The distillation was continued until the temperature remained constant at 110°C and only toluene was being collected. The solution was then cooled to room temperature and washed with two 100 ml portions of saturated aqueous sodium carbonate solution and then with 100 ml of saturated aqueous sodium chloride solution. The toluene layer was then dried, filtered free of drying agent and the filtrate freed from toluene. The residue was distilled to give a colorless liquid (30 g, 85%). B.p. 81°C at 5 mm; n_D^{24} 1.4734.

Anal. Calcd. for $C_7H_{13}BrO_2$: C, 40.02; H, 6.23; Br, 38.25.

Found: C, 40.13; H, 6.10; Br, 38.15.

The 60 MHz n.m.r. spectrum in CCl_4 was consistent with the proposed structure, showing a doublet centered at τ 5.15 (1H), J = 4 Hz, a multiplet centered at τ 6.1 (4H), a multiplet between τ 8.0 and 8.75 (4H), and a multiplet between τ 8.91 and 9.25 (3H).

isovaleraldehyde diethylacetal was prepared from 1-bromo-2-methylpropane and triethyl orthoformate by the modified procedure of Bachman (39) as previously described for the preparation of n-valeraldehyde dimethyl-

acetal.

A colorless liquid was obtained in 75% yield. B.p. 71°C at 50 mm; n_D^{24} 1.3974. Lit. b.p. 158°C (2).

α-Bromoisovaleraldehyde diethylacetal was prepared from isovaleraldehyde diethylacetal and bromine by the modified procedure of Hartung and Adkins (41) as previously described for the preparation of α-bromo-n-valeraldehyde diethylacetal.

A colorless liquid was obtained in 60% yield. B.p. 90°C at 15 mm; n_D^{23} 1.4426. Lit. b.p. 92-93°C at 14 mm; n_D^{25} 1.4438 (2).

α-Bromoisovaleraldehyde ethyleneacetal was prepared from α-bromoisovaleraldehyde diethylacetal and ethylene glycol by the modified procedure of McElvain and Curry (5) as previously described for the preparation of α-bromo-n-valeraldehyde ethyleneacetal.

A colorless liquid was obtained in 75% yield. B.p. 75°C at 4.5 mm; n_D^{24} 1.4747.

Anal. Calcd. for $C_7H_{13}BrO_2$: C, 40.02; H, 6.23; Br, 38.25.

Found: C, 40.09; H, 6.22; Br, 38.39.

The 60 MHz n.m.r. spectrum in CCl_4 was consistent with the proposed structure, showing a doublet centered at τ 5.08 (1H), J = 5 Hz, a multiplet centered at τ 6.10 (4H), a broad multiplet between τ 7.70 and 8.24 (1H) and two doublets centered at τ 8.98 and τ 9.00 (6H).

α-Bromo-n-valeraldehyde was prepared by the modification of the procedure of Erlenmeyer and Jung (44).

To a stirred solution of n-valeraldehyde (86 g, 1 mole) in 300 ml of chloroform, maintained at -15°C by means of a dry ice-acetone bath, was added bromine (160 g, 1 mole) in a dropwise manner. After complete addition of the bromine, a red color persisted. The solution was then allowed to warm to room temperature and to stir overnight by which time the red color had disappeared and a yellow solution resulted. Sodium bicarbonate (90 g, 1.07 mole) was then added in 10 g portions so as to control the evolution of carbon dioxide. After complete addition of the sodium bicarbonate, the solution was stirred for 1 hour and then was filtered free of solid. The chloroform was removed by fractional distillation at atmospheric pressure and the residue was distilled under vacuum from 10 g of solid sodium carbonate. Yield, 49.5 g (30%) of a colorless liquid that yellowed upon standing. B.p. 52-56°C at 15 mm; n_D^{24} 1.4702. Lit. b.p. 54°C at 13 mm (44); n_D^{20} 1.4640 (45).

α-Bromo-n-valeraldehyde diisopropylacetal was prepared by the following procedure.

To a stirred solution of α-bromo-n-valeraldehyde (66 g, 0.4 mole) in 200 ml of isopropyl alcohol was added 100 g of anhydrous magnesium sulfate and 0.5 g of p-toluenesulfonic acid. This mixture was heated under reflux for 24 hours and was then cooled to room temperature and filtered free of solid. The excess isopropyl alcohol was removed by fractional distillation at atmospheric pressure and then the residue was distilled at reduced pressure giving 35 g (34%) of a colorless liquid. B.p. 85°C at 8 mm; n_D^{23} 1.4398.

Anal. Calcd. for $C_{11}H_{23}BrO_2$: C, 49.44; H, 8.61; Br, 29.96.

Found: C, 49.23; H, 8.31; Br, 29.67.

The 60 MHz n.m.r. spectrum in CCl_4 was consistent with the proposed structure, showing a doublet centered at τ 5.40 (1H), J = 3.5 Hz, a multiplet between τ 5.94 and 6.44 (3H), and a multiplet between τ 8.00 and 9.15 (19H).

Propionaldehyde diethylacetal was prepared from ethyl bromide and triethyl orthoformate by the modified method of Bachman (39) as previously described for the preparation of n-valeraldehyde dimethylacetal.

A colorless liquid was obtained in 73% yield. B.p. 121-124°C at 705 mm; n_D^{26} 1.3861. Lit. b.p. 123°C at 760 mm; n_D^{20} 1.3897 (46).

α-Bromopropionaldehyde diethylacetal was prepared from propionaldehyde diethylacetal and bromine by the modified method of Hartung and Adkins (41) as previously described for the preparation of α-bromo-n-valeraldehyde diethylacetal.

A colorless liquid was obtained in 65% yield. B.p. 76-79°C at 19 mm; n_D^{23} 1.4375. Lit b.p. 82-85°C at 30 mm; n_D^{20} 1.4371 (47).

α-Bromopropionaldehyde ethyleneacetal was prepared from α-bromopropionaldehyde diethylacetal and ethylene glycol by the modified procedure of McElvain and Curry (5) as previously described for the preparation of α-bromo-n-valeraldehyde ethyleneacetal.

A colorless liquid was obtained in 67% yield. B.p. 72°C at 10 mm; n_D^{22} 1.4769.

Anal. Calcd. for $C_5H_9BrO_2$: C, 33.15; H, 4.97; Br, 44.10.

Found: C, 33.49; H, 5.03; Br, 43.87.

The 60 MHz n.m.r. spectrum in CCl_4 was consistent with the proposed structure, showing a doublet centered at τ 5.18 (1H), J = 4 Hz, a multiplet centered at τ 6.1 (5H), and a doublet centered at τ 8.38 (3H), J = 7 Hz.

n-Butyraldehyde diethylacetal was prepared by the method of Salmi (48) except a Dean-Stark water trap was employed.

To a stirred mixture of n-butyraldehyde (72 g, 1 mole) and 98% ethyl alcohol (92 g, 2 mole) in 250 ml of dry benzene was added 0.5 g of p-toluenesulfonic acid. This mixture was heated under reflux for 14 hours in an apparatus equipped with a Dean-Stark water trap after which time 18 ml of water had been collected. The solution was then cooled to room temperature and 10 g of anhydrous sodium carbonate was added. The mixture was stirred for 1 hour and then filtered free of solid and the filtrate freed from benzene. The residue was distilled and gave 32 g (20%) of a colorless liquid. B.p. 77-78°C at 100 mm; n_D^{24} 1.3943. Lit. b.p. 144-145°C at 760 mm; n_D^{20} 1.3965 (46).

α-Bromo-n-butyraldehyde diethylacetal was prepared by the method of Hartung and Adkins (41).

To a stirred mixture of 29.2 g (0.2 mole) of n-butyraldehyde diethylacetal and 50 g (0.5 mole) of anhydrous calcium carbonate in 300 ml of dry carbon tetrachloride was added dropwise 32 g (0.2 mole)

of bromine. The rate of addition of the bromine was adjusted so as to maintain the temperature of the reaction mixture between 40-50°C. After complete addition of the bromine, the mixture was stirred 1 hour at room temperature and was then filtered free of solid. The filtrate was then washed first with eight 100 ml portions of a saturated aqueous sodium carbonate solution and then with 100 ml of a saturated aqueous sodium chloride solution. The carbon tetrachloride layer was then dried over anhydrous sodium carbonate, filtered free of solid and the filtrate freed from carbon tetrachloride. The residue was distilled and gave 10 g (26%) of a colorless liquid. B.p. 81°C at 10 mm; n_D^{25} 1.4398. Lit. b.p. 74-77°C at 15 mm; n_D^{20} 1.4418 (47).

α-Bromoisobutyraldehyde ethyleneacetal was prepared by the following procedure.

To a stirred solution of isobutyraldehyde (43 g, 0.5 mole) in 400 ml of dry chloroform, maintained at 0°C by means of an ice bath, was added dropwise 80 g (0.5 mole) of bromine. After complete addition of the bromine the solution was stirred one hour at room temperature. Sodium bicarbonate (42 g, 0.5 mole) was then added to the reaction mixture in 5 g portions so as to control the formation of carbon dioxide and the resulting mixture was stirred overnight. The reaction mixture was then filtered free of solid and the filtrate was washed first with two 100 ml portions of a saturated aqueous sodium bicarbonate solution and then with 100 ml of a saturated aqueous sodium chloride solution. The chloroform

layer was then dried, filtered free of drying agent and the filtrate freed from chloroform.

The residue was then taken up in 200 ml of dry benzene. To this solution was added 31 g (0.5 mole) of ethylene glycol and 0.5 g of p-toluenesulfonic acid. This mixture was heated under reflux for 16 hours in an apparatus equipped with a Dean-Stark water trap. The solution was then cooled to room temperature and was washed first with two 100 ml portions of a saturated aqueous sodium carbonate solution and then with 100 ml of saturated aqueous sodium chloride solution. The benzene layer was dried, filtered free of drying agent and the filtrate freed from benzene. The residue was distilled and gave 35 g (36%) of a colorless liquid. B.p. 66°C at 8 mm; n_D^{23} 1.4731.

Anal. Calcd. for $C_6H_{11}BrO_2$: C, 36.90; H, 5.74; Br, 41.00.

Found: C, 36,52; H, 5.95; Br, 41.00.

The 60 MHz n.m.r. spectrum in CCl_4 was consistent with the proposed structure, showing a singlet at τ 5.18 (1H), a multiplet centered at τ 6.0 (4H) and a singlet at τ 8.35 (6H).

β-Phenylpropionaldehyde diethylacetal was prepared from β-phenylethyl bromide and triethyl orthoformate by the modified method of Bachman (39) as previously described for the preparation of n-valeraldehyde dimethylacetal.

A colorless liquid was obtained in 80% yield. B.p. 90°C at 1.5 mm; n_D^{24} 1.4765.

Anal. Calcd. for $C_{13}H_{20}O_2$: C, 75.00; H, 9.61.

Found: C, 74.93; H, 9.30.

The 60 MHz n.m.r. spectrum in CCl_4 was consistent with the proposed structure, showing a singlet at τ 2.85 (5H), a triplet centered at τ 5.62 (1H), J = 5 Hz, a multiplet centered at τ 6.50 (4H), a multiplet between τ 7.20 and 7.54 (2H), a multiplet between τ 7.95 and 8.38 (2H) and a triplet centered at τ 8.84 (6H), J = 7 Hz.

α-Bromo-β-phenylpropionaldehyde diethylacetal was prepared from β-phenylpropionaldehyde diethylacetal and bromine by the modified procedure of Hartung and Adkins (41) as previously described for the preparation of α-bromo-n-valeraldehyde diethylacetal.

A colorless liquid was obtained in 80% yield. B.p. 100-102°C at 0.4 mm; n_D^{28} 1.5066.

Anal. Calcd. for $C_{13}H_{19}BrO_2$: C, 54.35; H, 6.62; Br, 27.87.

Found: C, 53.80; H, 6.56; Br, 28.13.

The 60 MHz n.m.r. spectrum in CCl_4 was consistent with the proposed structure showing a singlet at τ 2.84 (5H), a doublet centered at τ 5.51 (1H), J = 5 Hz, a multiplet between τ 5.83 and 7.32 (5H) and two triplets centered at τ 8.79 and 8.82 (6H), J = 7 Hz.

α-Bromo-β-phenylpropionaldehyde ethyleneacetal was prepared from α-bromo-β-phenylpropionaldehyde diethylacetal and ethylene glycol by the modified procedure of McElvain and Curry (5) as previously

In a 5 litre round bottom flask were placed 80 g of magnesium turnings and 800 ml of dry benzene. To this stirred solution was added gradually, over a period of 10-15 min, 90 g of mercuric chloride dissolved in 400 g of dry acetone. An exothermic reaction resulted and the addition was adjusted to maintain the solution at gentle reflux. When this solution of mercuric chloride was added, a further quantity of acetone (200 g) and benzene (200 ml) was added. When the reaction began to subside, heat was applied until no further reaction was evident. By this time, a solid had filled about half of the flask thus interfering with the effective stirring of the mixture.

When the reaction was completed, 200 ml of water was added. The solution was heated under reflux for 1 hour, then cooled to 50°C and the solid was removed by filtration under vacuum through a Buchner funnel. The solid was washed with 500 ml of benzene and the combined filtrate and washings were evaporated to one-half the volume, after which 300 ml of water was added. The solution was cooled to 10-15°C in a refrigerator for 6-12 hours while the pinacol hydrate crystallized.

The white, flaky precipitate was collected by filtration under vacuum. Since it was subjected without further purification to the next step of the preparation of anhydrous pinacol, no yield was determined.

Anhydrous pinacol (2,3-dimethyl-2,3-butanediol) was prepared by the

method described by Vogel (50).

A mixture of pinacol hydrate and 200 ml of benzene was heated in a flask set up for downward distillation. After approximately 100 ml of distillate had been collected the two layers in the distillate were separated and the upper, benzene layer was returned to the distillation flask while the lower water layer was discarded. This process was repeated until the benzene distillate was observed to be clear and all the water had been removed by the azeotropic distillation. The benzene was then removed by distillation at atmospheric pressure and the residue was also distilled at atmospheric pressure giving a colorless liquid. B.p. 160-163°C at 710 mm. Lit. b.p. 169-173°C at 760 mm (50).

2-(1-Bromo-n-butyl)-1,3-dioxane was prepared from α-bromo-n-valeraldehyde diethylacetal and propane-1,3-diol by the modified procedure of McElvain and Curry (5) as previously described for the preparation of α-bromo-n-valeraldehyde ethyleneacetal.

A colorless liquid was obtained in 90% yield. B.p. 89-91°C at 4.5 mm; n_D^{23} 1.4770.

Anal. Calcd. for $C_8H_{15}BrO_2$: C, 43.09; H, 6.73; Br, 35.83.

Found: C, 43.06; H, 7.15; Br, 35.75.

The 60 MHz n.m.r. spectrum in CCl_4 was consistent with the proposed structure, showing a doublet centered at τ 5.43 (1H), J=4 Hz, a multiplet between τ 5.68 and 6.53 (5H) and a multiplet between τ 7.52 and 9.28 (9H).

n-Valeraldehyde ethyleneacetal was prepared from n-valeraldehyde diethylacetal and ethylene glycol by the modified procedure of McElvain and Curry (5) as previously described for the preparation of α-bromo-n-valeraldehyde ethyleneacetal.

A colorless liquid was obtained in 75% yield. B.p. 81°C at 60 mm; n_D^{22} 1.4189.

Anal. Calcd. for $C_7H_{14}O_2$: C, 64.58; H, 10.84.

Found: C, 64.39; H, 11.24.

The 60 MHz n.m.r. spectrum in CCl_4 was consistent with the proposed structure, showing a triplet centered at τ 5.28 (1H), J = 5 Hz, a multiplet centered at τ 6.22 (4H), and a multiplet between τ 8.38 and 9.25 (9H).

α-Bromo-β-methoxypropionaldehyde ethyleneacetal was prepared by the general bromomethoxylation technique of van de Sande and Kopecky (51).

To a stirred solution of 20 g (0.2 mole) of acrolein ethyleneacetal in a mixture of 100 ml of anhydrous ether and 100 ml of anhydrous methanol, cooled to -50°C by means of a dry ice-acetone bath, was added 28.6 g (0.1 mole) of 1,3-dibromo-5,5-dimethylhydantoin in 2 g portions. During this addition the temperature of the reaction mixture was maintained between -55 to -50°C. After all of the hydantoin had been added, the mixture was allowed to warm to room temperature and was then poured into 250 ml of ice cold saturated aqueous sodium bicarbonate solution. This mixture was extracted with four 100 ml portions of ether and then the combined

ether extracts were washed first with 100 ml of a saturated aqueous sodium sulfite solution and then with 100 ml of a saturated aqueous sodium bicarbonate solution. The ether layer was then dried, filtered free of drying agent and the filtrate freed from ether. The residue was distilled under reduced pressure and gave a colorless liquid. Yield 30 g (71%). B.p. 80-81°C at 2.7 mm; n_D^{24} 1.4792.

Anal. Calcd. for $C_6H_{11}BrO_2$: C, 34.14; H, 5.21; Br, 37.88.

Found: C, 33.88; H, 5.21; Br, 37.94.

The 60 MHz n.m.r. spectrum in CCl_4 was consistent with the proposed structure, showing a doublet centered at τ 5.0 (1H), J = 3 Hz, a multiplet between τ 5.92 and 6.45 (7H), and a singlet at τ 6.67 (3H).

2. Dehydrobromination of α-Bromo Acetals.

a. Dehydrobromination using the procedure of McElvain (28).

The procedure used for the dehydrobromination of some α-bromo acetals in the initial part of this work was that described by McElvain, Barnes and Johnson (28) for the preparation of ketene diethylacetal. The dehydrobromination of α-bromoisovaleraldehyde diethylacetal is described here as an example of the procedure.

To a stirred solution of potassium t-butoxide (10 g, 0.084 mole) in 100 ml of dry t-butyl alcohol was added 20 g (0.084 mole) of α-bromoisovaleraldehyde diethylacetal. This mixture was heated to 80°C for 5 hours after which time the reaction flask was

fitted for downward distillation through a four-inch Vigreaux column. The excess t-butyl alcohol was then removed by fractional distillation at atmospheric pressure without previous separation of the potassium bromide formed. When the bulk of the t-butyl alcohol had been removed the pressure was lowered and the products were distilled. A receiver cooled in a dry ice-acetone bath was used in our work at this stage to prevent the volatile products from being lost into the vacuum system. After all of the volatile products had been collected, the distillation was terminated and the distillate allowed to warm to room temperature. This distillate was found by g.l.c. analysis to be contaminated with some t-butyl alcohol and was therefore redistilled from a flask equipped with an ordinary Claisen head. A colorless liquid was obtained in 60% yield.

B.p. 65°C at 14 mm; n_D^{22} 1.4196.

Anal. Calcd. for $C_9H_{18}O_2$: C, 68.31; H, 11.47.

Found: C, 68.50; H, 11.02.

In all cases where this procedure was employed the dehydrobromination products were isolated and identified by their respective n.m.r. and i.r. spectra and their elemental analyses. The physical constants of the products obtained by this method are given in Table 9.

b. Dehydrobromination using the modified aqueous work-up procedure.

The procedure used for the dehydrobromination of the α-bromo acetals in the major portion of this work involved the addition of water in the work-up procedure and was found to give

better total material recoveries. The dehydrobromination of α-bromoisobutyraldehyde ethyleneacetal is described here as an example of the procedure.

To a stirred solution of potassium t-butoxide (2.87 g, 0.0256 mole) in 25 ml of dry t-butyl alcohol was added 5 g (0.0256 mole) of α-bromoisobutyraldehyde ethyleneacetal. This mixture was heated to 80°C for 5 hours after which time the reaction mixture was allowed to cool to approximately 50°C and was then mixed with approximately 50 ml of water. This mixture was extracted continuously with ether for 12 hours. The ether layer was then dried, filtered free of drying agent and the filtrate freed from ether and t-butyl alcohol by fractional distillation at atmospheric pressure through a four-inch Vigreaux column. The residue was subjected to g.l.c. analysis before distillation and was found to show one peak other than the peak corresponding to unreacted starting material. No evidence for the presence of methacraldehyde ethyleneacetal (the preparation of which is described in Part I of this thesis) could be found in the residue as was shown by comparing the retention time of an authentic sample of methacraldehyde ethyleneacetal with the g.l.c. trace of the crude residue. The residue was then subjected to distillation. A colorless liquid, other than recovered starting material, was obtained in 40% yield. B.p. 78-79°C at 8 mm; n_D^{25} 1.4224.

Anal. Calcd. for $C_6H_{12}O_2$: C, 54.53; H, 9.15.

Found: C, 54.13; H, 9.17.

This material was identified by its n.m.r. and i.r. spectra as well as its elemental analysis.

The general procedure described above was used in all the dehydrobromination reactions employing the aqueous work-up procedure. The products were identified by either comparing the retention times of an authentic sample with the peaks in the analysis of the crude residue or by isolation of the unknown substance and its characterization by means of its n.m.r. and i.r. spectra as well as its elemental analysis. The physical constants of the products isolated from these reactions are given in Table 9.

c. Dehydrobromination in dimethylsulfoxide as solvent with non-aqueous work-up procedure.

This procedure was similar to the procedure described by McElvain et. al. (28) except that in this case the boiling point of the solvent is higher than that of the products expected. The dehydrobromination of α-bromo-n-valeraldehyde ethyleneacetal is described here as an example of the procedure.

To a stirred solution of sodium methoxide (5.16 g, 0.096 mole) in 100 ml of dry dimethylsulfoxide was added dropwise 20 g (0.096 mole) of α-bromo-n-valeraldehyde ethyleneacetal over a period of 15 min. In this time the temperature rose to 65°C and the solution turned dark brown. This mixture was stirred a further 30 min at room temperature and then the reaction flask was fitted for downward distillation. The distillation was carried out at reduced pressure and the distillate was collected in a dry ice-acetone

cooled receiver. When the temperature of the distillation reached that determined for dimethylsulfoxide at the pressure used, the distillation was terminated. The distillate was then allowed to warm to room temperature and then was subjected to g.l.c. analysis. This analysis showed the distillate to be comprised of two other substances than the contaminant dimethylsulfoxide. Distillation on a spinning band column removed the dimethylsulfoxide but did not separate the other two substances. These materials were separated by preparative g.l.c. and were characterized by their respective n.m.r. and i.r. spectra as well as their elemental analyses. Upon repetition of this dehydrobromination it was found that the proportion of these two substances was different. Further investigation showed the relative amount of these two substances depended on the time and temperature required to complete the initial distillation and thus figures as to the relative amounts are meaningless. The physical constants of these two substances are given in Table 9 as well as the physical constants of other products obtained by this method.

d. Dehydrobromination in dimethylsulfoxide as solvent using the modified aqueous work-up procedure.

The procedure used in these elimination reactions was the same as that for dehydrobromination in t-butyl alcohol with the modified aqueous work-up except for two modifications. First, with the reaction in dimethylsulfoxide, the bromoacetal was added slowly and the temperature was not allowed to go over 40°C. The reaction mixture was then stirred at room temperature. Second, the reaction

mixture was mixed with a saturated aqueous sodium chloride solution, rather than water, in order to decrease the solubility of the products in the dimethylsulfoxide water mixture. The products were identified by comparison of their g.l.c. retention times with those of authentic materials.

e. Dehydrobromination of α-bromo-n-valeraldehyde ethyleneacetal using the sodium salt of dimethylsulfoxide as base.

Sodium hydride (1.15 g, 0.048 mole), that had been washed free of the stabilizing mineral oil with hexane, was added with stirring to 50 ml of dry dimethylsulfoxide. This mixture was heated to 80°C for 5 hours and was then allowed to cool to room temperature. α-Bromo-n-valeraldehyde ethyleneacetal (10 g, 0.048 mole) was then added dropwise at such a rate as to maintain the reaction temperature below 40°C. After complete addition of the acetal, the mixture was stirred for 1 hour at room temperature and was then mixed with 50 ml of a saturated aqueous sodium chloride solution. The resulting mixture was extracted continuously overnight with ether. The ether layer was dried, filtered free of drying agent and the filtrate freed from ether by fractional distillation at atmospheric pressure. The residue was analyzed by g.l.c. and the products identified by comparison of their g.l.c. retention times with those of authentic samples.

3. Attempted Isomerization of Olefinic Products.

The stability of many of the olefinic products obtained

from the dehydrobromination reactions was investigated by subjecting an authentic sample of the olefin to the dehydrobromination conditions used in its formation. The attempted isomerization of 2-pentenal ethyleneacetal with potassium t-butoxide in t-butyl alcohol is described here as an example of the procedure.

To a stirred solution of potassium t-butoxide (1.93 g, 0.017 mole) in 20 ml of dry t-butyl alcohol was added 2 g (0.017 mole) of 2-pentenal ethyleneacetal. This mixture was heated at 80°C for 23 hours and then was cooled to 50°C and mixed with approximately 40 ml of water. The resulting mixture was extracted continuously with ether for 12 hours. The ether layer was then dried, filtered free of drying agent, and the filtrate freed from ether and t-butyl alcohol by fractional distillation through a four-inch Vigreaux column at atmospheric pressure. The residue (1.7 g) was analyzed by g.l.c. and the products were identified by comparison of the retention times with those of authentic materials.

This general procedure was also used for the attempted isomerization reactions carried out in dimethylsulfoxide except the reaction mixture was mixed with saturated aqueous sodium chloride solution before extraction.

4. Conversion of n-Propylketene ethyleneacetal into Some Derivatives.

2-Hydroxyethyl n-valerate was formed from the hydrolysis of n-propylketene ethyleneacetal by the following procedure.

To a solution of 1 g (0.0078 mole) of n-propylketene ethyleneacetal in 20 ml of water was added one drop of concentrated

hydrochloric acid. This mixture was stirred overnight and then was neutralized to pH = 7 by the addition of a 15% aqueous sodium hydroxide solution. The resulting water solution was extracted with four 20 ml portions of ether. The combined ether extracts were dried, filtered free of drying agent, and the filtrate freed from ether. The residue (0.7 g, 0.0048 mole) was analyzed by g.l.c. and was found to be one pure substance. The n.m.r. and i.r. spectra of this compound were identical to those obtained for 2-hydroxyethyl n-valerate that was isolated and characterized from the aqueous work-up of the dehydrobromination of α-bromo-n-valeraldehyde ethyleneacetal.

Ethylene methyl ortho-n-valerate was formed by the following procedure.

A mixture of n-propylketene ethyleneacetal (2 g, 0.0156 mole) in 20 ml of anhydrous methanol was stirred at room temperature for 15 hours. The excess methanol was then removed on a rotatory evaporator under reduced pressure and the residue was distilled. Yield, 1.5 g (60%). B.p. 66°C at 7 mm; n_D^{24} 1.4316.

Anal. Calcd. for $C_8H_{16}O_3$: C, 59.98; H, 10.07.

Found: C, 60.24; H, 10.21.

The 60 MHz n.m.r. spectrum in CCl_4 was consistent with the proposed structure, showing a multiplet centered at τ 6.05 (4H), a singlet at τ 6.83 (3H) and a multiplet between τ 8.27 and 9.25 (9H).

5. Preparation of Some Authentic Dehydrobromination Products.

Methyl n-valerate was prepared by a Fischer esterification of n-valeric

acid.

To a stirred solution of n-valeric acid (25 g, 0.245 mole) in 100 ml of anhydrous methanol was added 1 ml of concentrated sulfuric acid. This mixture was heated under reflux for 2 hours and was then left overnight. The reaction mixture was then poured into 200 ml of a saturated aqueous sodium chloride solution and the resulting solution was extracted with two 100 ml portions of ether. The combined ether layers were then washed first with three 50 ml portions of saturated aqueous sodium carbonate solution and then with 100 ml of saturated aqueous sodium chloride solution. The ether layer was then dried, filtered free of drying agent, and the filtrate freed from ether by distillation at atmospheric pressure. The residue was also distilled at atmospheric pressure. Yield, 20 g (70%) of a colorless liquid. B.p. 122-123°C at 705 mm; n_D^{24} 1.3952. Lit. b.p. 130°C at 760 mm, n_D^{20} 1.4003 (52).

Ethyl isovalerate was prepared from isovaleric acid and ethanol according to the procedure previously described for the preparation of methyl n-valerate.

A colorless liquid was obtained in 50% yield. B.p. 120-121°C at 700 mm; n_D^{25} 1.3939. Lit. b.p. 134.7°C at 760 mm; $n_D^{18.35}$ 1.39738 (52).

Isopropyl n-valerate was prepared from isopropyl alcohol and n-valeric acid according to the procedure previously described for the preparation of methyl n-valerate.

A colorless liquid was obtained in 57% yield. B.p. 60°C at 20 mm; n_D^{24} 1.3988. Lit. b.p. 153.5°C at 760 mm; n_D^{20} 1.4009 (53).

2-Vinyl-1,3-dioxolane was prepared in Part I of this thesis and the preparation is described on Page 68.

Methacraldehyde ethyleneacetal was prepared in Part I of this thesis and the preparation is described on Page 69.

Cinnamaldehyde ethyleneacetal was prepared in Part I of this thesis and the preparation is described on Page 70.

β-Phenylpropionoyl chloride was prepared by the procedure of Shriner and Damshroder (54).

A stirred mixture of hydrocinnamic acid (100 g, 0.667 mole) and thionyl chloride (100 g, 0.85 mole) was heated at 60°C for 10 hours. At the end of this time, the mixture was subjected to fractional distillation through a four-inch Vigreaux column under reduced pressure. A colorless liquid was obtained in 94% yield. B.p. 102°C at 7mm. Lit. b.p. 110-115 at 17 mm (54).

Hydrocinnamide was prepared by the following procedure.

An excess of ammonia gas was passed through a solution of β-phenylpropionoyl chloride (104 g, 0.62 mole) in 500 ml.of anhydrous ether. A white precipitate resulted. The addition of ammonia was

terminated when an aliquot of the reaction mixture shaken with water proved to be basic to litmus paper. The solid was removed by suction filtration. The filter cake was treated with 200 ml of hot dichloromethane and then filtered again. The two filtrates were combined and the solvents removed. The solid product was then dried in vacuo in a dessicator. Yield 84 g (85%). M.p. 105-107°C. Lit m.p. 106-108°C (53).

β-Phenylpropionitrile was prepared by the procedure of McElvain, Clarke and Jones (2).

An intimate mixture of hydrocinnamide (84 g, 0.56 mole) and phosphorous pentoxide (70 g, 0.49 mole) was heated at 90°C overnight under a nitrogen atmosphere. The temperature was then raised to 130°C for 2 hours and then the crude product was removed by vacuum distillation into a dry ice-acetone cooled receiver. This distillation was terminated when no more volatile products remained. The crude distillate was then distilled from 5 g of phosphorous pentoxide under reduced pressure and gave a colorless liquid (48 g, 65%). B.p. 82°C at 1 mm; n_D^{26} 1.5201. Lit. b.p. 142°C at 25 mm (55).

Methyl ethylene orthohydrocinnamate was prepared by the following combination of the procedures of McElvain and Aldridge (56) and McElvain and Venerable (57).

To a solution of β-phenylpropionitrile (20 g, 0.153 mole)

and methanol (5.4 g, 0.168 mole) in 200 ml of anhydrous ether cooled to 0°C by means of an ice bath was added dry hydrogen chloride gas until 7.25 g (0.0199 mole) had been collected. The flask was then stoppered and stored in the refrigerator for one day. The solid methyl iminohydrocinnamate hydrochloride was collected by suction filtration under nitrogen and was washed with 200 ml of anhydrous ether. Since this material was extremely sensitive to the moisture of the air it was subjected to the next step of the reaction immediately.

A mixture of methyl iminohydrocinnamate hydrochloride (15 g, 0.075 mole) and ethylene glycol (4.7 g, 0.075 mole) in 500 ml of anhydrous ether under nitrogen was shaken for 55 hours. At the end of this time the solid material was removed by suction filtration and the filtrate was made basic (pH = 8) by the addition of solid sodium methoxide. This mixture was again freed of solid material by suction filtration and the filtrate was freed from ether. The residue was distilled and gave 6 g (42%) of a colorless liquid. B.p. 78°C at 0.2 mm; n_D^{26} 1.5350.

Anal. Calcd. for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74.

Found: C, 69.51; H, 7.68.

The 60 MHz n.m.r. spectrum in $CDCl_3$ was consistent with the proposed structure, showing a singlet at τ 2.76 (5H), a multiplet centered at τ 5.93 (4H), a singlet at τ 6.71 (3H), a multiplet between τ 7.00 and 7.48 (2H) and a multiplet between τ 7.73 and 8.08 (2H).

Benzylketene ethyleneacetal The attempted synthesis of this compound according to the procedure of McElvain and Aldridge (56) failed to give the desired product.

A mixture of methyl ethylene orthohydrocinnamate (18 g, 0.094 mole) and aluminum tertiary butoxide (24.6 g, 0.1 mole) was placed in a round bottom flask and was heated to 200°C and maintained there for 30 minutes whereupon the distillation of t-butyl alcohol had ceased. The pressure was then lowered gradually and all volatile products were collected in a dry ice-acetone cooled receiver. Less than one ml of distillate was collected and g.l.c. analysis of this liquid showed it to be a complicated mixture. None of the desired product could be isolated.

Table 9

Physical constants of products isolated from dehydrobromination of some α-bromo acetals

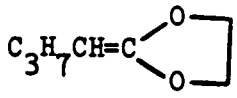
Products	Boiling point °C	n_D(T°C)	Analysis	
			Calcd.	Found
$CH_3CH{=}CHCH(OC_2H_5)_2$	54-56 at 22 mm	1.4133 (24)	C, 66.63 H, 11.18	C, 66.33 H, 11.15
$(CH_3)_2C{=}CHCH(OC_2H_5)_2$	65 at 14 mm	1.4196 (22)	C, 68.31 H, 11.47	C, 68.50 H, 11.02
$C_2H_5CH{=}CHCH(OC_2H_5)_2$	54 at 13 mm	1.4175 (22)	C, 68.31 H, 11.47	C, 68.05 H, 11.67
$C_2H_5CH{=}CHCH(OCH_3)_2$	67 at 55 mm	1.4156 (22)	C, 64.58 H, 10.84	C, 64.58 H, 11.11
$C_2H_5CH{=}CHCH[OCH(CH_3)_2]_2$	74 at 10 mm	1.4172 (26)	C, 70.92 H, 11.90	C, 70.98 H, 11.90
$CH_2{=}CHCH(OC_2H_5)_2$	120 at 720 mm	1.4002 (24)	C, 64.58 H, 10.84	C, 64.44 H, 10.67
	66 at 16 mm	1.4850 (23)	C, 65.60 H, 9.44	C, 65.61 H, 9.23
$C_4H_9COOC_2H_4OH$	92 at 4 mm	1.4315 (25)	C, 57.51 H, 9.65	C, 57.78 H, 9.80
$(CH_3)_2CHCH_2COOC_2H_4OH$	75 at 2 mm	1.4298 (25)	C, 57.51 H, 9.65	C, 57.41 H, 9.41

Table 9-Continued

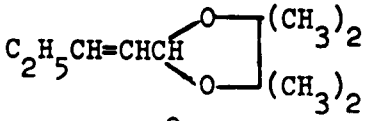
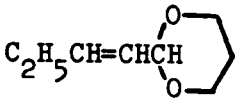
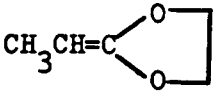
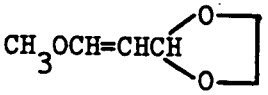
Products	Boiling Point °C	$n_D(T^oC)$	Analysis Calcd.	Found
	64-66 at 5.5 mm	1.4422 (22)	C, 71.70 H, 10.94	C, 71.46 H, 10.82
	78-80 at 12 mm	1.4503 (24)	C, 67.57 H, 9.92	C, 67.33 H, 9.74
$C_4H_9COO(CH_2)_3OH$	88-90 at 2 mm	1.4324 (25)	C, 59.98 H, 10.07	C, 60.27 H, 10.07
$C_2H_5COOC_2H_4OH$	87 at 10 mm	1.4328 (27)	C, 50.84 H, 8.53	C, 51.05 H, 8.78
$(CH_3)_2CHCOOC_2H_4OH$	78-79 at 8 mm	1.4224 (25)	C, 54.53 H, 9.15	C, 54.13 H, 9.17
$C_6H_5CH=CHCH(OC_2H_5)_2$	102 at 1 mm	1.5124 (24)	C, 75.69 H, 8.80	C, 75.99 H, 8.81
	76 at 90 mm	1.4459 (24)	C, 59.98 H, 8.05	C, 60.07 H, 7.70
	55-57 at 5 mm	1.4573 (24)	C, 55.37 H, 7.74	C, 55.08 H, 7.55
$CH_3OC_2H_4COOC_2H_4OH$	91 at 1.5 mm	1.4364 (24)	C, 48.64 H, 8.16	C, 48.49 H, 8.57

Table 9-Continued

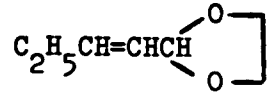
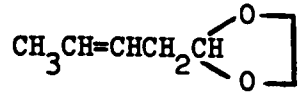
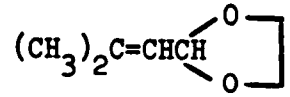
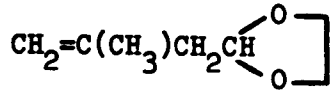
Products	Boiling Point °C	$n_D(T^\circ C)$	Analysis Calcd.	Analysis Found
	64-67 at 14 mm	1.4442 (22)	C, 65.60 H, 9.44	C, 65.82 H, 9.33
	57 at 14 mm	1.4434 (24)	C, 65.60 H, 9.44	C, 65.77 H, 9.57
	63 at 10 mm	1.4494 (23)	C, 65.60 H, 9.44	C, 65.42 H. 9.27
	50 at 10 mm	1.4415 (23)	C, 65.60 H, 9.44	C, 65.42 H, 9.64

Table 10

Pertinent spectral data for compounds reported in Table 9

Compound	N. M. R.				I. R.	
	Proton	Multiplicity	Chemical Shift τ	Coupling(Hz)	Absorption cm^{-1}	Assignment
$CH_3CH=CHCH(OR)_2$ (4 3 2 1)	H-1	doublet	5.27	$J_{1,2}=4$		
	H-2,H-3	multiplet	4.27-4.58			
	H-4	doublet	8.30	$J_{3,4}=4$		
$(CH_3)_2C=CHCH(OR)_2$ (3 2 1)	H-1,H-2	multiplet	4.68-5.08		1680(w)	C=C
	H-3	broad singlet	8.28	W/2=5		
$CH_3CH_2CH=CHCH(OR)_2$ (4 3 2 1)	H-1	doublet	5.29	$J_{1,2}=4$	1685(w)	C=C
	H-2,H-3	multiplet	4.12-4.57			
	H-4	multiplet	7.96			
$CH_3CH_2CH=CHCH(OCH_3)_2$ (4 3 2 1 5)	H-1,2,3 and 4. Same as above				1680(w)	C=C
	H-5	singlet	6.82			
$CH_3CH_2CH=CHCH[OCH(CH_3)_2]_2$ (4 3 2 1 5 6)	H-1,2,3 and 4. Same as above				1680(w)	C=C
	H-5	multiplet	6.18			
	H-6	two doublets	8.89	$J_{5,6}=6.5$		

Table 10-Continued

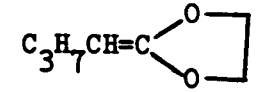
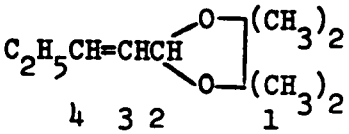
Compound	N. M. R.				I. R.	
	Proton	Multiplicity	Chemical Shift τ	Coupling(Hz)	Absorption cm^{-1}	Assignment
$CH_2{=}CHCH(OR)_2$ (3 2 1)	H-1	doublet	5.20	$J_{1,2}=3.5$		
	H-2,H-3	multiplet	4.0-4.95			
	n.m.r. is discussed on page 134.				1720(s)	C=C
$C_3H_7CH_2COOCH_2CH_2OH$ (4 3 2 1)	H-1,H-2	multiplet	6.12-6.52		3650-3100	O-H
	H-3	triplet	5.84	$J_{3,2}=5.5$	1740	C=O
	H-4	multiplet	7.50-7.84			
$(CH_3)_2CHCH_2\overset{O}{\overset{\|}{C}}OCH_2CH_2OH$ (5 4 3 2 1)	H-1	multiplet	6.26		3650-3150	O-H
	H-2	multiplet	5.87		1750	C=O
	H-3,H-4	multiplet	7.80			
	H-5	doublet	9.00	$J_{5,4}=6.5$		
 (4 3 2 1)	H-1	singlet	8.85		1680(w)	C=C
	H-2	multiplet	4.82			
	H-3,H-4	multiplet	4.20-4.63			

Table 10-Continued

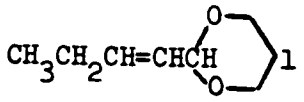
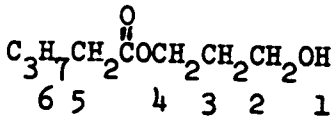
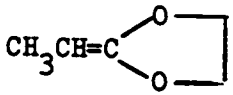
Compound	N. M. R.				I. R.	
	Proton	Multiplicity	Chemical Shift τ	Coupling(Hz)	Absorption cm^{-1}	Assignment
	H-1,H-6	multiplet	7.58-8.52		1680(w)	C=C
6 5 4 3 2	H-2	multiplet	5.78-6.18			
	H-3	doublet	5.25	$J_{3,4}=4.5$		
	H-4,H-5	multiplet	3.97-4.97			
	H-1	singlet	7.05		3650-3150	O-H
6 5 4 3 2 1	H-2	triplet	6.44	$J_{2,3}=6$	1730	C=O
	H-4	triplet	5.85	$J_{4,3}=6.5$		
	H-3,5 and 6	multiplet	7.60-9.28			
	H-1	singlet	5.88		3060(w)	vinyl C-H
3 2 1	H-2	quartet	6.53	$J_{2,3}=6.5$	1730(s)	C=C
	H-3	doublet	8.55	$J_{3,2}=6.5$		

Table 10-Continued

Compound	N. M. R.				I. R.	
	Proton	Multiplicity	Chemical Shift τ	Coupling(Hz)	Absorption cm^{-1}	Assignment
$CH_3CH_2\overset{O}{\overset{\|}{C}}OCH_2CH_2OH$ (5 4 3,3' 2 1)	H-1	singlet	6.67		3650-3100	O-H
	H-2	two doublets	6.32	$J_{2,3}=5;J_{2,3'}=7$	1740(s)	C=O
	H-3,H-3'	two doublets	5.87, 5.94	$J_{3,2}=5;J_{3',2}=7$		
	H-4	quartet	7.67	$J_{4,5}=7.5$		
	H-5	triplet	8.90	$J_{5,4}=7.5$		
$(CH_3)_2CH\overset{O}{\overset{\|}{C}}OCH_2CH_2OH$ (5 4 3,3' 2 1)	H-1	singlet	7.10		3650-3100	O-H
	H-2	two doublets	6.31	$J_{2,3}=5.5;J_{2,3'}=6.5$	1735(s)	C=O
	H-3,H-3'	two doublets	5.85, 5.90	$J_{3,2}=5.5;J_{3',2}=6.5$		
	H-4	multiplet	7.46	$J_{4,5}=7$		
	H-5	doublet	8.85	$J_{5,4}=7$		
$C_6H_5CH=CHCH(OR)_2$ (4 3 2 1)	H-1	doublet	5.00	$J_{1,2}=4.5$		
	H-2	doublet of doublets	3.94	$J_{2,1}=4.5;J_{2,3}=17$		
	H-3	doublet	3.34	$J_{3,2}=17$		
	H-4	multiplet	2.70			

Table 10-Continued

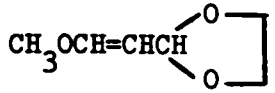
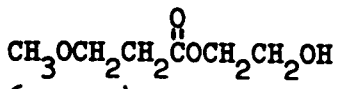
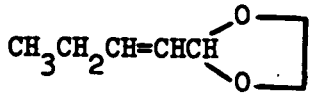
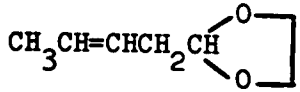
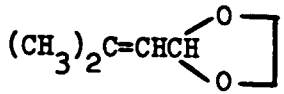
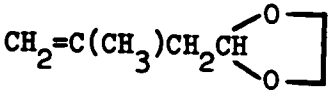
Compound	N. M. R.				I. R.	
	Proton	Multiplicity	Chemical Shift τ	Coupling(Hz)	Absorption cm^{-1}	Assignment
 5 4 3 2 1	H-1	multiplet	6.15		1670(s)	vinyl ether
	H-2	doublet	4.98	$J_{2,3}=6.5$		
	H-3	doublet of doublets	5.37	$J_{3,2}=6.5; J_{3,4}=13$		
	H-4	doublet	3.38	$J_{4,3}=13$		
	H-5	singlet	6.43			
 6 5 4 3 2 1	H-1,2,4	multiplet	6.07-6.48		3650-3100	O-H
	H-3	multiplet	5.54-5.84		1725(s)	C=O
	H-5	triplet	7.35	$J_{5,4}=6$		
	H-6	singlet	6.58			
 6 5 4 3 2 1	H-1	multiplet	6.20		1685(w)	C=C
	H-2	doublet	4.95	$J_{2,3}=5.5$		
	H-3,H-4	multiplet	3.90-4.65			
	H-5	multiplet	7.92	$J_{5,4}=J_{5,6}=7$		
	H-6	triplet	8.97	$J_{6,5}=7$		

Table 10-Continued

Compound	N. M. R.				I. R.	
	Proton	Multiplicity	Chemical Shift τ	Coupling(Hz)	Absorption cm^{-1}	Assignment
	H-1	multiplet	6.20		1665(w)	C=C
6 5 4 3 2 1	H-2	triplet	5.25	$J_{2,3}=4.5$		
	H-3	multiplet	7.70			
	H-4,H-5	multiplet	4.57			
	H-6	doublet	8.40	$J_{6,5}=5.5$		
	H-1	multiplet	6.18		1680(w)	C=C
4 3 2 1	H-2,H-3	multiplet	4.54-4.85			
	H-4	singlet	8.27			
	H-1	multiplet	6.16		1670(w)	C=C
5 4 3 2 1	H-2,H-5	multiplet	5.04-5.28			
	H-3	doublet	7.73	$J_{3,2}=5.5$		
	H-4	singlet	8.24			

R = C_2H_5

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