1,3-DIOXOLAN-2-YLIUM AND RELATED HETEROCYCLIC CATIONS

CHARLES U. PITTMAN, JR.,* SAMUEL P. McMANUS, AND JOHN W. LARSEN

Departments of Chemistry, University of Alabama, University, Alabama 35486, University of Alabama in Huntsville, Huntsville, Alabama 35807, and University of Tennessee, Knoxville, Tennessee 37916

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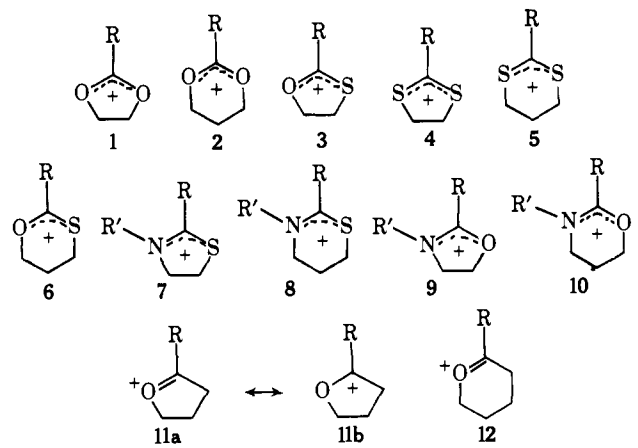
I. Introduction

This manuscript is dedicated to the memory of both Saul Winstein and Hans Meerwein. These two great chemists provided the basis upon which rest all current investigations of heterocyclic carbonium ions. Their accomplishments, which permeate this review, provided the inspiration for much of the work discussed here and led directly to this review. This review covers the chemistry of 1,3-dioxolan-2-ylium cations (**1**) and related cations such as 1,3-dioxan-2-ylium (**2**), 1,3-oxathiolan-2-ylium (**3**), 1,3-dithiolan-2-ylium (**4**), 1,3-dithian-2-ylium (**5**), and 1,3-oxathian-2-ylium (**6**) cations. In addition, related nitrogen-containing cations such as 1,3-thiazolinium (**7**), 5,6-dihydro-4*H*-1,3-thiazinium (**8**), 1,3-oxazolinium (**9**), and 5,6-dihydro-4*H*-1,3-oxazinium (**10**) ions are briefly discussed for appropriate comparisons. Ions with one oxygen atom such as **11** and **12** are also covered.

Since a comprehensive coverage of these classes of cations could not be compressed into an article of reasonable length, this paper selectively reviews work which generally reflects the current state of knowledge while emphasizing important historical developments and key principles. After a discussion of the origin of key developments and an introduction to the nomenclature, the synthesis and occurrence of these cations are reviewed; their role in reaction mechanisms and syntheses, their ambident nature in reactions with nucleophiles, their kinetics and thermodynamics of formation, and aspects of their structural identification by spectroscopic methods are discussed.



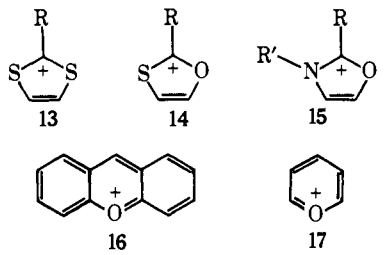
Several important reviews covering topics dealt with in this manuscript have appeared. The reactions of carbohydrates and related substances in liquid hydrogen fluoride which proceed through 1,3-dioxolan-2-ylium and related cations have been compiled by Lenard[1] through 1967. Olah, *et al.*,[2] have reviewed protonated heteroaliphatic compounds including several systems such as protonated amides, thioamides, carboxylic acids, carbonic acid derivatives, and carbamic acid derivatives which are related to ions discussed here. The chemistry of oxazolines has been reviewed[3] as has heterocyclic synthesis involving nitriles under acidic conditions.[4,5] The modes of reactions of ambident cations was the subject of a review by Hünig,[6] and a book by Perst[7] on oxonium ions has now appeared. The chemistry of salts of Δ^2-oxazolines and 4*H*-5,6-dihydrooxazines is discussed by Hellmann.[8] Neighboring group participation by all types of functions, including acetoxy and ester groups, have been treated by Capon,[9] and Goodman[10] has reviewed neighboring groups in carbohydrate

* Author to whom correspondence should be addressed at the University of Alabama. University, Ala.

(1) J. Lenard, *Chem. Rev.*, 69, 625 (1969).
(2) G. A. Olah, A. M. White, and D. H. O'Brien, *ibid.*, 70, 561 (1970).
(3) R. H. Wiley and L. L. Bennett, Jr., *ibid.*, 44, 447 (1949).
(4) F. Johnson, Dow Chemical Co., Report No. FL-163, April 1964.
(5) L. I. Krimen and D. J. Cota, *Org. React.*, 17, 213 (1969).
(6) S. Hünig, *Angew. Chem., Int. Ed. Engl.*, 3, 548 (1964).
(7) H. Perst, "Oxonium Ions," Academic Press, New York, N. Y., 1971.
(8) W. Seelinger, E. Aufderhaar, W. Diepers, R. Feinauer, R. Nehring, W. Thier, and H. Hellmann, *Angew. Chem., Int. Ed. Engl.*, 5, 875 (1966).
(9) B. Capon, *Quart. Rev., Chem. Soc.*, 18, 45 (1964).
(10) L. Goodman, *Advan. Carbohyd. Chem.*, 22, 109 (1967).

chemistry where the neighboring acetoxy group participates in scores of reactions of acetylated carbohydrate derivatives. Neighboring amide group participation, previously observed in the hydrolysis of esters, amides, and alkyl halides, has been discussed by Bruice and Benkovic.[11] These reviews provide valuable supplemental coverage of the topics discussed in this manuscript.

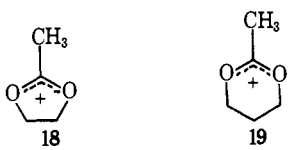
Unsaturated analogs of the cations **1–12** are now well known. They frequently exhibit aromaticity. Examples include 1,3-dithiolium (**13**), 1,3-oxathiolium (**14**), 1,3-oxazolium (**15**), and xanthylium and pyrrilium (**16** and **17**, respectively) cations.[12–15] They will not be discussed.



13 14 15 16 17

II. Nomenclature

Throughout this review we have chosen to use current *Chemical Abstracts* nomenclature, and we strongly recommend its adoption for heterocyclic carbonium ions. The rather confused state of nomenclature at present may be illustrated by the 2-methyl-1,2-dioxolan-2-ylium cation (**18**). By far, the most common root name applied in the literature has been dioxolenium. Thus, **18** would be 2-methyldioxolenium tetrafluoroborate, and for a short time this name was used in *Chemical Abstracts*. Another name which was applied for several years was 2-methyl-1,3-dioxolano-2-carbonium tetrafluoroborate (see, for example, *Chemical Abstract* indexes, Vol 53–55). However, the root 1,3-dioxolan-2-ylium is clearly preferred because it follows directly from its parent heterocyclic name, 1,3-dioxolane. Thus, it follows that ion **19** (R = CH_3), which



18 19

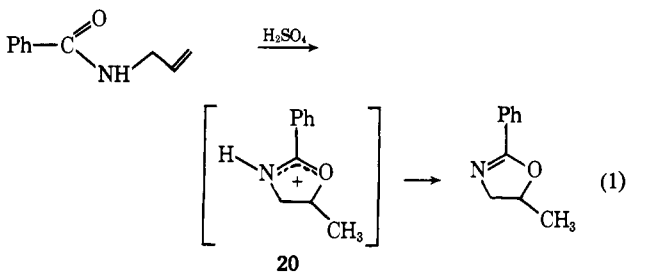
is a 1,3-dioxane derivative, would be named 2-methyl-1,3 dioxan-2-ylium tetrafluoroborate instead of the more com monly used 2-methyldioxenium tetrafluoroborate. The parent heterocycle of ion **4** is 1,3-diothiolane. Thus, ion **4** would be a (2*R*)-1,3-dithiolan-2-ylium cation. Similarly, ions **5** and **6**, derived respectively from (2*R*)-1,3-dithiane and (2*R*)-1,3-oxathiane, would be named (2*R*)-1,3-dithian-2-ylium and (2*R*)-1,3-oxathian-2-ylium cations, respectively.

The root name for ions **11** and **12** would be oxolan-2-ylium and oxan-2-ylium, respectively, in analogy with the 1,3-dioxolan-2-ylium cations. Several other names have also been used for **11** including (when R = CH_3) 2-methyl-1,3-oxoniacyclopent-1-enyl cation and 2-methyl-1-oxacyclopent-1-enyl cation. These emphasize the preeminence of resonance structure **11a**.

Ion **7** would be named as 1,3-thiazolin-2-ylium, but we will apply the term thiazolinium to this type of ion throughout the review. Similarly, ion **9**, the 2-oxazolin-2-ylium ion, will be given the name oxazolinium ion. We do this because *Chemical Abstracts* does not yet appear to be completely consistent on the names of these species.

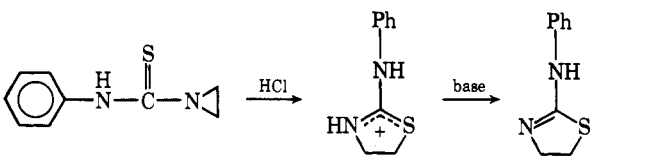
III. Background

The first heterocyclic carbonium ions (of interest in this review) to be prepared were oxazolinium and thiazolinium ions. Gabriel[16] first identified the oxazoline ring system in 1889. Shortly thereafter, in 1893, Kay[17] described the first acid-catalyzed formation of 5-methyl-2-phenyl-2-oxazoline from *N*-allylbenzamide on heating with concentrated sulfuric or hydrochloric acid. This reaction generated oxazolinium ion (**20**) in solution before neutralization, although this ion was



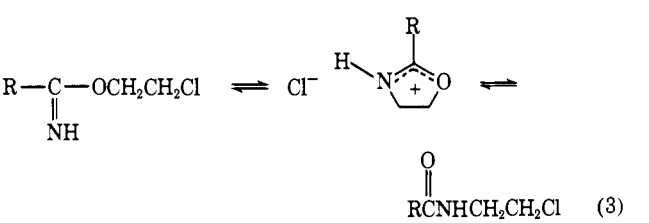
20 (1)

not specifically recognized at that time. The same results were reported by Diels and Beccard in 1906.[18] In 1895 Gabriel and Stelzner[19] reported the earliest example of an acid-catalyzed isomerization of an aziridine. In this study 1-(*N*-phenylthiocarbamoyl)aziridine was converted to 2-anilino-2-thiazoline in hydrochloric acid, and it is clear today that a thiazolinium ion is formed in the acid solution before neutralization (see eq 2).



(2)

Wislicenus and Körber[20] provided one of the earliest examples of the intervention of an oxazolinium salt in a molecular rearrangement when he demonstrated that the migration of an alkyl group from the oxygen of an imino ester to the nitrogen in an amide (eq 3) occurs through an oxazolinium ion. Söderbaum found that heating β-hydroxyalkylureas with



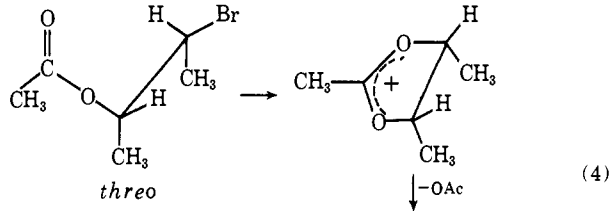
(3)

(11) T. C. Bruice and S. J. Benkovic, "Bioorganic Mechanisms," Vol. I, W. A. Benjamin, New York, N. Y., 1966. p 187.
(12) W. R. Hurtley and S. Smiles, *J. Chem. Soc.*, 1821 (1926); 534 (1927).
(13) E. Klingsberg, *J. Amer. Chem. Soc.*, 86, 5290 (1964).
(14) Y. Hiroyoshi, *Chem. Pharm. Bull.*, 16, 1451 (1968).
(15) K. M. Pazdro, *Rocz. Chem.*, 43, 1089 (1969).
(16) S. Gabriel, *Ber.*, 22, 1139 (1889).
(17) P. Kay, *ibid.*, 26, 2848 (1893).
(18) O. Diels and E. Beccard, *ibid.*, 39, 4125 (1906).
(19) S. Gabriel and R. Stelzner, *ibid.*, 28, 2929 (1895).
(20) W. Wislicenus and H. Körber, *ibid.*, 35, 164 (1902).

hydrochloric acid gave 2-amino-2-oxazolines, presumably *via* oxazolinium ions.[21] Menne[22] demonstrated that 2-amino-2-oxazolines were strongly basic and formed well-characterized salts. The dehydration of β-hydroxyalkylamides in sulfuric acid has become a standard oxazoline synthesis, and oxazolinium ions are the end product in these acid solutions before neutralization.[23-25] Thus, oxazolinium and thiazolinium salts were well known far earlier than their 1,3-dioxolan-2-ylium counterparts. To date, a prodigious number of these salts have been isolated and characterized, most commonly as their iodide, chloride, and picrate salts.

The dogma of "consistency of valency" made it difficult to envision oxonium ions in the late 1800's and early 1900's. Brilliant early work by Von Baeyer, Hantzch, and Werner paved the way for an understanding of oxonium ion structure, and this early work has been reviewed by Nenitzescu.[26] Xanthylium salts, discovered by Werner[27] in 1901, were characterized as oxonium ion salts. Their great similarity to triaryl carbonium ion salts was emphasized by Von Baeyer.[28] Conant and his coworkers[29-31] were the first to notice a difference in the solvolytic reactivity of various aliphatic halo ketones. For example, they found that ω-chloroacetophenone reacts extremely rapidly with KI in absolute acetone while β-chloropropiophenone reacts rather slowly. Conant ascribed the relative rates to a phenomenon called "alternating polarity," and he also found the phenomenon applicable to halo esters. The participation of the neighboring oxygen was not recognized in this early work. However, it was in the pioneering work of Winstein and of Meerwein that the existence 1,3-dioxolan-2-ylium and related oxonium ions was demonstrated.

In 1942 Winstein and Buckles[32] reported the solvolyses of both *threo*- and *erythro*-2-acetoxy-3-bromobutane, and *trans*-1-acetoxy-2-bromocyclohexane with silver acetate in dry acetic acid. Surprisingly, *threo*-2-acetoxy-3-bromobutane gave only *dl*-2,3-diacetoxybutane (**21**) which corresponded to a minimum of 98% retention of configuration (eq 4). The erythro isomer gave *meso*-2,3-diacetoxybutane (**22**), the product with retained configuration. Finally, *trans*-1-acetoxy-2-bromocyclohexane gave *trans*-1,2-diacetoxycyclohexane (**23**) corresponding to 97% retention. Similar results were obtained in acetic anhydride solution. Furthermore, starting with optically active *trans*-1-acetoxy-2-bromocyclohexane, Winstein and Buckles found the resulting trans diacetate was racemic.[33] In order to logically account for these stereochemical observations, Winstein proposed the neighboring acetoxy function was participating in the solvation of the developing carbonium ion as the C–Br bond was breaking. In his view, the carbonyl oxygen became increasingly bonded to the back-side of the adjacent charged carbon until



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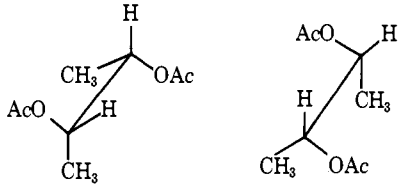
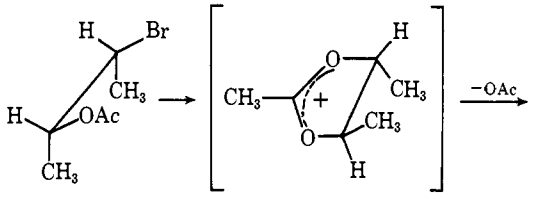
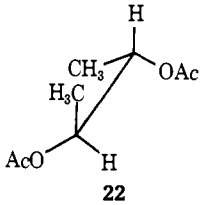


21 (*dl*)





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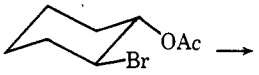
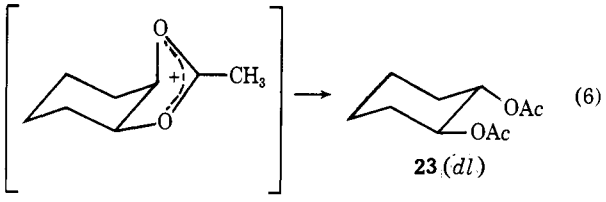


dl or optically active



(6)

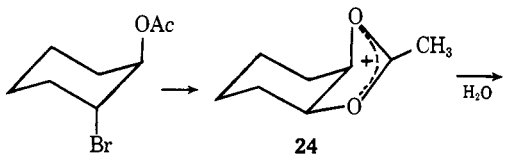
23 (*dl*)

a symmetrical intermediate was formed in which a fully developed C–O bond had been formed with inversion of configuration. The intermediate 1,3-dioxolan-2-ylium ion (called an "acetoxonium ion") could then react with acetate anion with inversion, at either carbon, to give the observed products with net retention of configuration. The term "neighboring group participation" was given to this involvement of the acetoxy group in the reaction. Winstein further reasoned that internal participation must increase the rate of solvolysis, compared to a suitable model compound without the participating neighboring group, or such participation would not occur to the exclusion of ionization without participation. In accord with this view, a large difference in rate was observed for *cis*- and *trans*-1-acetoxy-2-chlorocyclohexane toward silver acetate. The trans compound was far more reactive in accord with its ability to bring to bear a special driving force (the neighboring acetoxy participation) which the cis isomer could not do.

When small amounts of water were added to acetic acid in

(21) H. G. Söderbaum, *Ber.*, 28, 1897 (1895).
(22) E. Menne, *ibid.*, 33, 657 (1900).
(23) W. Krabbe, W. Eisenlohr, and H. Schöne, *ibid.*, 73, 656 (1940).
(24) W. N. Nagar and S. Kanao, *Justus Liebigs Ann. Chem.*, 470, 157 (1939).
(25) M. T. Leffler and R. Adams, *J. Amer. Chem. Soc.*, 59, 2252 (1937).
(26) C. D. Nenitzescu in "Carbonium Ions," Vol. I, G. A. Olah and P. v. R. Schleyer, Ed., Interscience, New York, N. Y., 1968, pp 1–77.
(27) A. Werner, *Ber.*, 34, 3300 (1901).
(28) A. Von Baeyer, *ibid.*, 38, 569 (1905).
(29) J. B. Conant, W. R. Kirner, and R. E. Hussey, *J. Amer. Chem. Soc.*, 47, 478 (1925).
(30) J. B. Conant, W. R. Kirner, and R. E. Hussey, *ibid.*, 47, 488 (1925).
(31) J. B. Conant and W. R. Kirner, *ibid.*, 46, 232 (1924).
(32) S. Winstein and R. E. Buckles, *ibid.*, 64, 2780 (1942).
(33) S. Winstein and R. E. Buckles, *ibid.*, 64, 2787 (1942).

these solvolyses, the stereochemistry of the products shifted steadily toward inversion and a predominance of monoacetate product.[33] This result was easily accounted for by invoking water attack at the 1,3-dioxolan-2-ylium ion intermediate (**24**) to give an ortho ester (**25**) which subsequently ring opens to the cis monoacetate (**26**). Since a second inversion step never



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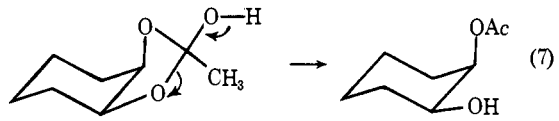
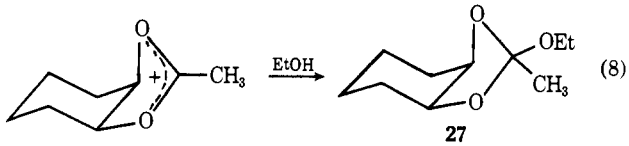


25 **26** (7)

occurs, net inversion is observed. When heated with potassium acetate in dry acetic acid, *trans*-2-acetoxy-cyclohexyl *p*-toluenesulfonate is converted to the 1,2-diacetate with retention of configuration, and the optically active starting tosylate gives racemic product.[34] As with the bromide solvolyses, neighboring group participation giving an intermediate 1,3-dioxolan-2-ylium ion was invoked. Adding ethanol to the reaction medium allowed the formation and isolation of the ortho ester (**27**). This strengthened the argument for an intermediate 1,3-dioxolan-2-ylium ion.[35,36]

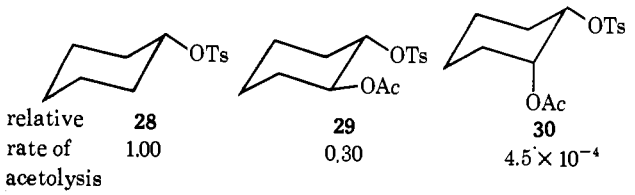


27 (8)

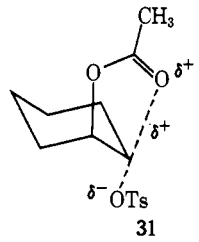
The rate enhancement, required for neighboring group participation, was termed "anchimeric acceleration,"[37,38] and the term L expressed the driving force due to participation (eq **9**), where k_Δ is the rate constant of the assisted reaction

$$L = RT \ln (k_\Delta/k_c) \qquad (9)$$

and k_c the rate constant of the reaction where assistance is not occurring. Winstein[39] then provided the detailed kinetic evidence necessary to support the view that neighboring acetoxy participation was indeed occurring. The solvolysis of *trans*-2-acetoxycyclohexyl *p*-toluenesulfonate in acetic acid was first order in the presence of either water or added acetate, and small changes in concentration did not appreciably affect the rates. This was in accord with rate-determining intermediate dioxolan-2-ylium ion formation. The water and acetate anion, which do control the nature of the product, do not exercise this control in the rate-determining step. This was followed by the observation[40] that the rate of acetolysis of *cis*-2-acetoxycyclohexyl *p*-toluenesulfonate (**30**) was 4.5 × 10^4 times slower than cyclohexyl *p*-toluenesulfonate (**28**), whereas the trans isomer (**29**) solvolyzed with about the same rate. The trans isomer solvolyzed 670 times faster than the cis compound. The rates of the corresponding chlorides with AgOAc were qualitatively similar. In the cis compounds the negative inductive effect slowed down solvolyses, while in the trans compounds the negative inductive effect is counterbalanced by the rate-enhancing anchimeric assistance. Thus, neighboring group participation effectively lowers the energy of the solvolysis transition state **31**.



	28	**29**	**30**
relative rate of acetolysis	1.00	0.30	4.5×10^{-4}



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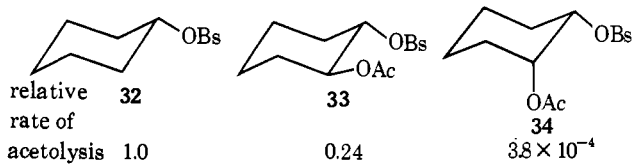
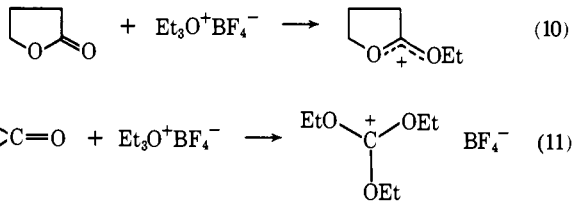
Next, the rates of solvolyses of a series of 2-substituted cyclohexyl *p*-bromobenzenesulfonates were reported.[37] For *trans*-2-acetoxycyclohexyl *p*-bromobenzenesulfonates these studies indicated $k_\Delta/k_c = 2.33 \times 10^3$. Thus, it was Winstein's studies which provided the fundamental stereochemical and kinetic evidence for the existence of 1,3-dioxolan-2-ylium ions. It remained for Meerwein to prepare, isolate, and identify these species.



	32	**33**	**34**
relative rate of acetolysis	1.0	0.24	3.8×10^{-4}

Meerwein reported the first stable oxonium salts in 1937.[41] In a series of now classic papers, Meerwein broke open the area of oxonium ions.[41-48] Even into his 80's, he made important contributions to this field. Trialkyloxonium ion salts were prepared and developed as reagents which could alkylate lactones and esters (eq 10 and 11) to give a series of new oxonium ion salts.[42,43] Direct alkylations of O- and N-containing compounds with alkyl halides and $AgBF_4$ were developed

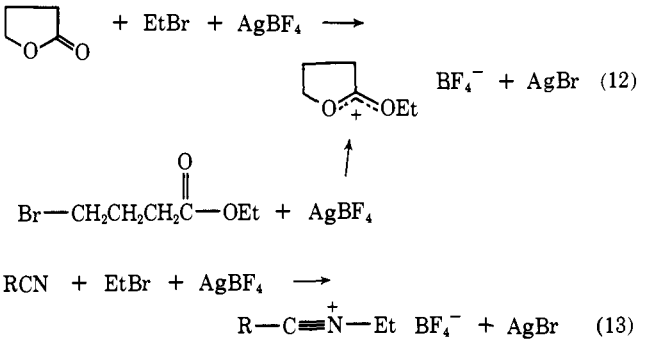
(34) S. Winstein, H. V. Hess, and R. E. Buckles, *J. Amer. Chem. Soc.*, 64, 2796 (1942).
(35) S. Winstein and R. E. Buckles, *ibid.*, **65**, 613 (1943).
(36) S. Winstein and D. Seymour, *ibid.*, **68**, 119 (1946).
(37) S. Winstein, E. Grunwald, and L. L. Ingraham, *ibid.*, 70, 821 (1948).
(38) S. Winstein, C. B. Lindgren, H. Marshall, and L. L. Ingraham, *ibid.*, **75**, 147 (1953).
(39) S. Winstein, C. Hanson, and E. Grunwald, *ibid.*, 70, 812 (1948).
(40) S. Winstein, E. Grunwald, R. E. Buckles, and C. Hanson, *ibid.*, 70, 816 (1948).
(41) H. Meerwein, G. Hinz, D. Hoffman, E. Konig, and E. Pfeil, *J. Prakt. Chem.*, **147**, 257 (1937); **154**, 83 (1939).
(42) H. Meerwein, *Angew. Chem.*, 67, 374 (1955).
(43) H. Meerwein, P. Borner, O. Fuchs, H. J. Sasse, H. Schrodt, and J. Spille, *Chem. Ber.*, 89, 2060 (1956).
(44) H. Meerwein and K. Wunderlich, *Angew. Chem.*, 69, 481 (1957).
(45) H. Meerwein, H. Allendoerfer, P. Beekmann, F. Kunert, H. Morschel, F. Pawellek, and K. Wunderlich, *ibid.*, 70, 211, 630 (1958).
(46) H. Meerwein, V. Hederich, and K. Wunderlich, *Arch. Pharm.*, **291**, 541 (1958).
(47) H. Meerwein, V. Hederich, H. Morschel, and K. Wunderlich, *Justus Liebigs Ann. Chem.*, **635**, 1 (1960).
(48) H. Meerwein, K. Bodenbrenner, P. Borner, F. Kunert, and K. Wunderlich, *ibid.*, **632**, 38 (1968).



(10)

(11)

as illustrated by the synthesis of *O*-ethyl butyrolactonium fluoroborate in eq 12 and by the alkylation of nitriles to give *N*-alkylnitrilium salts[44,46] in eq 13. The reaction of 2-bromo-



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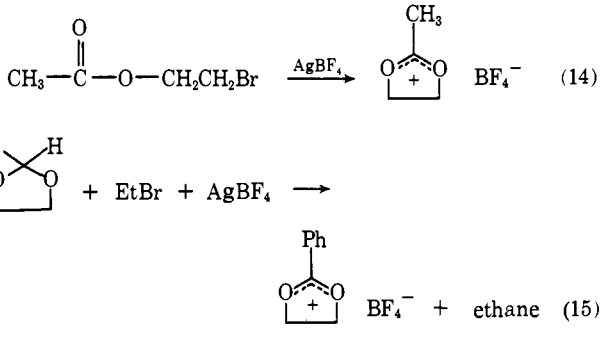
(13)

ethyl acetate with $AgBF_4$ resulted in an 84.5% (isolated) yield of 2-methyl-1,3-dioxolan-2-ylium tetrafluoroborate.[44] This, along with the reaction of 2-phenyldioxolane with ethyl bromide and $AgBF_4$ to give the 2-phenyl salt, was the first direct proof of the existence of these ions[42,45] and further confirmed Winstein's earlier postulates (eq 14 and 15).



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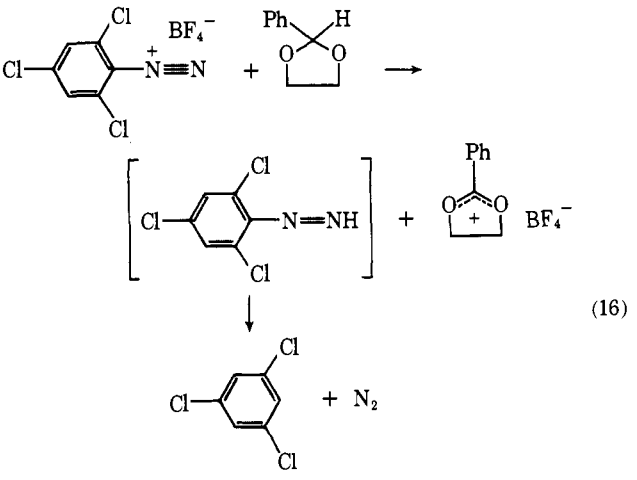
(15)

Evidence for hydride transfer in the reaction of arenediazonium salts with ethers such as dioxane, THF, glycol dimethyl ether, and 1,3-dioxolane was obtained.[45] For example, the diazonium salts obtained from anilines, substituted with strongly electron-attracting groups, were reduced to the corresponding ArH derivatives in yields greater than 80%[45] (eq 16). Cyclic ketals were particularly efficient hydride donors, especially 2-methyl- and 2-phenyl-1,3-dioxolanes which were readily converted to their corresponding 1,3-dioxolan-2-ylium salts by triphenyl carbonium ion salts[47] (eq 17). The triphenyl carbonium ion also abstracts cyanide ion from 2-cyano-2-methyl-1,3-dioxolane in acetonitrile (eq 18). Meerwein explored other routes to cyclic oxonium ions including the reaction of 2-ethoxy-1,3-dioxolane and its substituted derivatives with boron trifluoride etherate in CH_3Cl_2 to give salts **35a–i** as shown in eq 19.[48]

Other Lewis acids such as $SbCl_5$ in CH_2Cl_2 gave similar results. The preparation of 4-methyl-1,3-dioxan-2-ylium tetrafluoroborate was accomplished by treating 4-methyl-2-ethoxy-1,3-dioxane with $BF_3 \cdot O(Et)_2$ (eq 20). However, with



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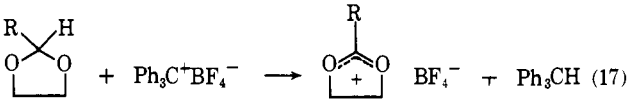
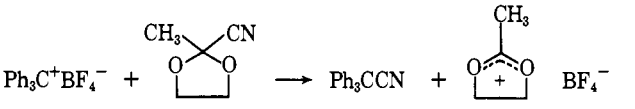


(17)

yields >80%

R = Ph, CH_3, H



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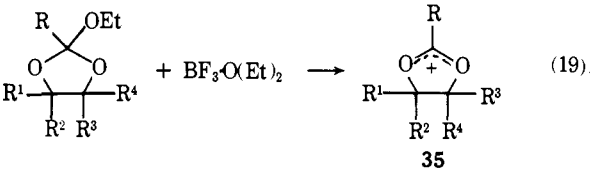
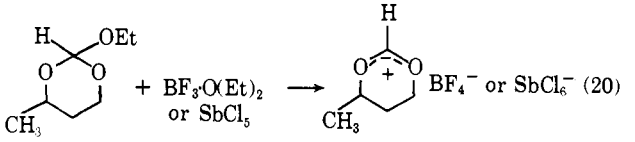


(19)

35

	R	R^1	R^2	R^3	R^4	Yield, %	Mp, °C
35a	H	H	H	H	H	81	94–96
b	Me	H	H	H	H	66	164–166
c	Et	H	H	H	H	96	54–55
d	Ph	H	H	H	H	89	166
e	Me	Me	H	H	H	97	53–55
f	H	Me	H	Me	H	87	61
g	H	Me	Me	H	H	64	73–74
h	H	Me	Me	Me	H	66.5	77–78
i	H	Me	Me	Me	Me	95	112

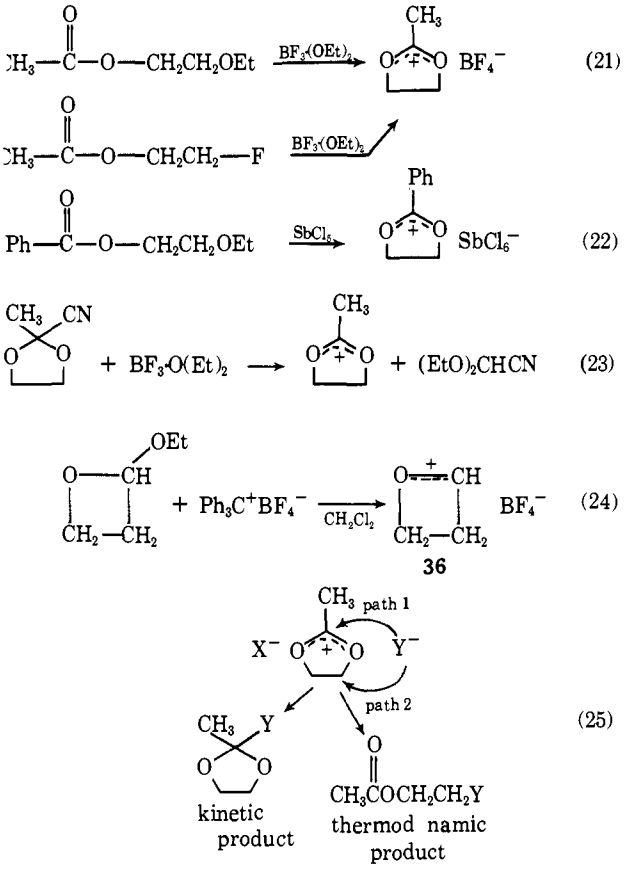


(20)

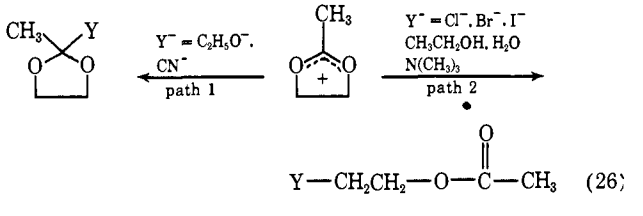
2-ethoxy-1,3-dioxacycloheptane, no carbonium ion salt was isolated.[48] Other reactions pioneered by Meerwein include eq 21–23 shown below. Throughout these reactions the need for a strong Lewis acid which forms a very stable anion in a medium of low nucleophilicity is emphasized.

In one interesting example, 2-ethoxyoxetane reacted with triphenylmethyl tetrafluoroborate to generate the oxetan-2-ylium tetrafluoroborate (**36**).

Meerwein also first pointed out the ambident nature of these cyclic oxonium ions in their reaction with nucleophiles (see eq 25). A nucleophile such as Y^- can rapidly add to the position

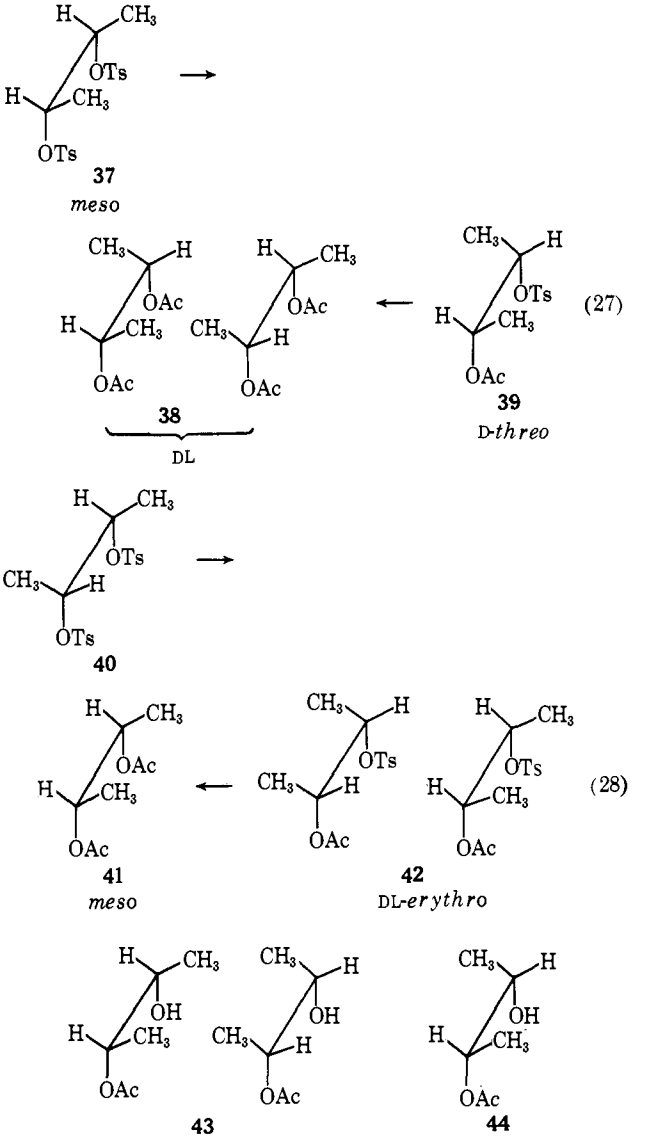


of lowest electron density (path 1), or it can attack at the backside of C-4 dealkylating the ion. Path 1 gives the kinetic product because the activation energy for the combination of the cation and nucleophile Y^- is small. If enough energy is released in this process (*i.e.*, if the kinetic product is stable enough), dissociation back to the cation may be avoided and the kinetic product may be isolated. If, however, an equilibrium is set up between the kinetic product and the cation, then a steady increase in the thermodynamic product will result. Nucleophile Y^- can, in this case, attack by path 2 which has a higher activation energy than path 1 (since major bond reorganization must take place in path 2). The relative importance of paths 1 and 2 depend on the nature of the nucleophile, the stability of the ambident cation, and the temperature, reaction time, and solvent. Meerwein demonstrated each of these principles in his early studies. He showed that 2-methyl-1,3-dioxolan-2-ylium ion gives the products of path 2 with weakly nucleophilic agents such as Cl^-, Br^-, I^-, ethanol, water, and trimethylamine.[48] However, products from path 1 were isolated when the nucleophile was ethoxide or cyanide.[48] Similar results were obtained for many other ambident cations



in the early work of Meerwein, Winstein, and others, and these are summarized in Table IV in section V.A.

Several other early papers are of note. Lucas, Mitchell, and Garner[49] reported that treatment of *meso*- (**37**) and D-2,3-bis-(*p*-tolylsulfonyloxy)butane (**40**) with potassium acetate and acetic acid gave DL- (**38**) and *meso*-2,3-diacetoxybutane (**41**), respectively. Similarly, D-*threo*- (**39**) and DL-*erythro*-2-(*p*-tolysulfonoxy)-3-acetoxybutane (**42**) also gave **38** and **41**, respectively. Both **37** and **39** reacted with potassium acetate and acetic acid to give DL-*erythro*-2-acetoxy-3-hydroxybutane (**43**). When subjected to the same conditions, **40** gave the L-(+)-threo form **44** and **42** formed the DL-threo form of **43**. The interpretation, following lines similar to those postulated



by Winstein, concluded that there were three Walden inversions each for **37** and **40** during anhydrous acetolysis while **39** and **42** exhibited two such inversions. The hydrous acetolysis of **37** and **40** also exhibited two inversions. This interpretation can be completely fitted by invoking the intermediacy of the 2,4,5-trimethyl-1,3-dioxolan-2-ylium cation as a reaction intermediate.

The involvement of 1,3-dioxolan-2-ylium ions in reactions of carbohydrates was indicated in early studies and a systematic interpretation was provided by Lemieux.[53-57] The fact that tetra-*O*-acetyl-α-D-mannopyranosyl halides, which have a

(49) H. J. Lucas, F. W. Mitchell, Jr., and H. K. Garner, *J. Amer. Chem. Soc.*, 72, 2138 (1950).

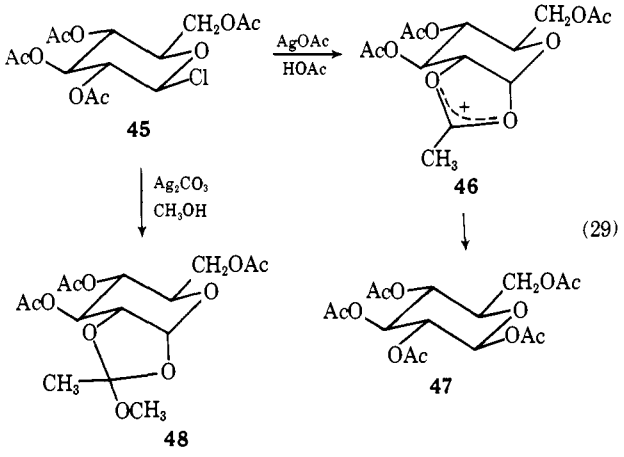
1,2-trans arrangement, yield 1,2-ortho acetates under conditions of the Koenigs–Knorr reaction was noted by both Dale[50] and Pacsu.[51] Isbell[52] observed that the rate of C-1 acetoxy group dissociation of sugar acetates is strongly dependent on the configurations of other asymmetric centers in the molecule, particularly the stereochemistry of a neighboring acetate function. Lemieux demonstrated that β-D-glucose pentaacetate undergoes mercaptolysis much more rapidly than does the α-D anomer.[53,54] Furthermore, the high reactivity of β-D-glucose pentaacetate, compared to its α anomer, in undergoing dissociation of the C-1 acetoxy group under conditions of acid catalysis was attributed to participation of the C-2 acetoxy group in the 1,2-trans-β-D anomer.[53–56] Table I summarizes

Table I

Relative Rates of C-1 Acetoxy Group Exchange of Sugar Acetates (0.05 *M*) with $SnCl_3OAc$* (0.05 *M*) in the Presence of $SnCl_4$ (0.05 *M*) at 40° in $CHCl_3$

Pentaacetate used	*Rel exchange rate*
1,2-*cis*-α-D-Glucose	1
1,2-*trans*-β-D-Glucose	450
1,2-*cis*-β-D-Mannose	8
1,2-*trans*-α-D-Mannose	56

the rates of exchange of the C-1 acetoxy group of a few sugar acetates from Lemieux's work[56] and illustrates that the exchange reaction of the C-1 acetoxy group is markedly accelerated by a trans C-2 acetate function. Further evidence for acetoxy participation, *via* a 1,3-dioxolan-2-ylium cation intermediate (**46**), was found in the solvolysis of tetra-*O*-acetyl-β-D-glucopyranosyl chloride (**45**) in silver acetate–dry acetic acid to produce β-D-glucose pentaacetate (**47**). When **45** was treated with silver carbonate in dry methanol, methyl 1,2-*O*-*o*-acetyl-α-D-glucopyranose triacetate (**48**) was obtained.

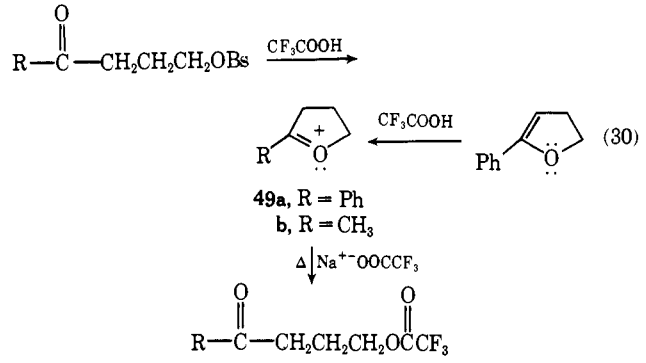


The involvement of 1,3-dioxolan-2-ylium and related cations in carbohydrate reactions are now well known and of increasingly greater synthetic importance. They will be further discussed in section VIII.

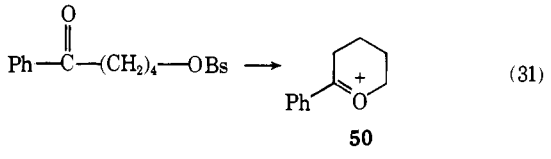
IV. Methods of Formation

A. OXOLAN-2-YLIUM AND OXAN-2-YLIUM IONS

Oxolan-2-ylium ions have not been as extensively studied as their 1,3-dioxolan-2-ylium analogs. Two major methods of preparation have been employed in the recent literature. These are (1) the cyclization of ketones and (2) rearrangement of cyclopropyl carbonyl compounds. Dissolving the γ-brosylate of butyrophenone in trifluoroacetic acid gives a solution of the 2-phenyl-2-oxolan-2-ylium cation (**49a**) which is stable for 30 days at room temperature.[58,59] Similar results were obtained when 5-(*p*-bromobenzenesulfonoxy)-2-pentanone produced the 2-methyl-2-oxolan-2-ylium cation (**49b**). Nmr spectroscopy confirmed the cyclic species is formed quantitatively in the acid solution. Cation **49a** is formed by quantitative protonation of 2-phenyl-4,5-dihydrofuran in the same acid. Upon addition of excess sodium trifluoroacetate and heating, the γ-trifluoroacetate of butyrophenone is formed (eq 30).



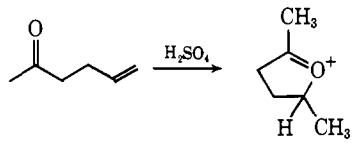
Similarly, **50** is formed by dissolving 5-(*p*-bromobenzenesulfonoxy)valerophenone in the strong acid medium. Ions **49** and **50** are much less stable in trifluoroacetic acid. Ward and



Sherman[58,59] prepared and isolated the hexachloroantimonate salts of **49** and **50** by treating 4-chlorobutyrophenone and 5-chloro-2-valerophenone, respectively, with a mole equivalent of antimony pentachloride. The salt of **49a** decomposed only slowly in air and was very stable, decomposing at 120–123°, while that of **49b** decomposed at 110–120°.

Pittman and McManus[60] demonstrated that γ,δ-unsaturated ketones exist as their corresponding oxolan-2-ylium ions in H_2SO_4. For example, instead of observing the O-protonated ketone, they observed the 2,5-dimethyloxolan-2-ylium ion (**51**) when 5-hexen-2-one was dissolved in 60–98% H_2SO_4 (eq 32). In 96% D_2SO_4 at both 24° and 120°, deuterium is in-

(50) J. K. Dale, *J. Amer. Chem. Soc.*, 46, 1046 (1924).
(51) E. Pacsu, *Advan. Carbohyd. Chem.*, 83 (1945).
(52) H. S. Isbell and H. L. Frush, *J. Res. Nat. Bur. Stand.*, 24, 125 (1940); 43, 161 (1949).
(53) R. U. Lemieux, *Can. J. Chem.*, 29, 1079 (1951).
(54) R. U. Lemieux, *ibid.*, 30, 295 (1952).
(55) R. U. Lemieux and W. P. Shylak, *ibid.*, 31, 528 (1953).
(56) R. U. Lemieux and C. Brice, *ibid.*, 33, 109 (1955).
(57) R. U. Lemieux, *Advan. Carbohyd. Chem.*, 9, 1 (1954).
(58) H. R. Ward and P. D. Sherman, Jr., *J. Amer. Chem. Soc.*, 89, 4222 (1967).
(59) H. R. Ward and P. D. Shermna, Jr., *ibid.*, 90, 3812 (1968).
(60) C. U. Pittman, Jr., and S. P. McManus, *Chem. Commun.*, 1479 (1968).



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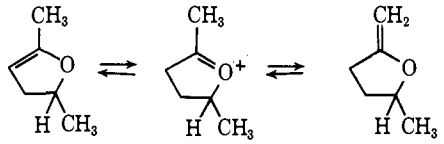
corporated into the C-2 methyl and C-3 methylene positions. The C-2 methyl hydrogens were 34% exchanged while the C-3 methylene hydrogens were 43% exchanged after 68 hr at 24°. At 120° after 7 min, the C-2 methyl was 65% exchanged while the C-3 methylene group was 78% exchanged (eq 33). Lack



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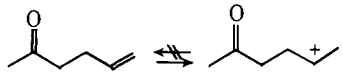

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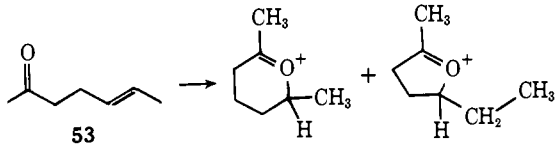
of exchange at C-4 and C-5 demonstrates that if equilibration to secondary ion (**52**) is taking place, **52** does not live long enough to equilibrate back to 5-hexen-2-one. Also, ring closure from the ketone to the 2,5-dimethyl-oxolan-2-ylium ion (**51**) must occur before appreciable enolization of the ketone can occur.

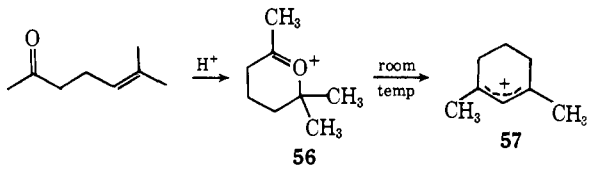
Brouwer[61] reported a similar cyclizations of 5-hexen-2-one, 5-methyl-5-hexen-2-one, 5-hepten-2-one, and 5-methyl-5-hepten-2-one in strong acids such as HF, HF–SbF_5, H_2SO_4, FSO_3H, and FSO_3H–SbF_5. At temperatures below −40° in HF, 5-hepten-2-one (**53**) was simply O-protonated but cyclized to **54** as the temperature was raised. In H_2SO_4 (at 0 and 35°), in FSO_3H (−78 and 20°), and in FSO_3H–SbF_5 (−78 and 20°) mixtures of **54** and 2-methyl-4-ethyloxolan-2-ylium ion (**55**)



(34)

53 54 55

are obtained with 45, 55, and 80% of **54**, respectively. In HF at −50°, **55** predominates. These are kinetically controlled ratios, and **54** and **55** can be equilibrated in H_2SO_4 where the **55**/**54** ratio is 73:27 over the 30 to 90° temperature range. This equilibration presumably occurs through the open-chain secondary cations of the C-protonated ketone. In all acids, 6-methyl-5-hepten-2-one gives the 2,6,6-trimethyloxan-2-ylium ion (**56**). In H_2SO_4 and FSO_3H at room temperature, this cation is rapidly and quantitatively converted to the 1,3-dimethylcyclohexenyl ion (**57**).

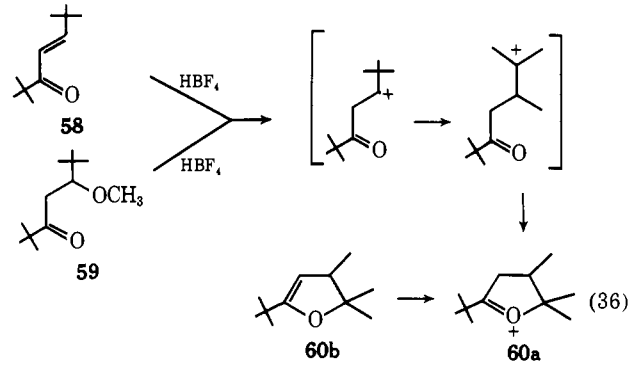


(35)

56 57

(61) D. M. Brouwer, *Recl. Trav. Chim. Pays-Bas*, **88**, 530 (1968).

Dimroth and Mach[62] utilized a similar olefin protonation route to generate 2-*tert*-butyl-4,5,5-trimethyloxolan-2-ylium tetrafluoroborate (**60a**) from 2,2,6,6-tetramethyl-4-hepten-3-one (**58**) on heating with HBF_4. Ion **60a** is also formed under the same conditions from 2,2,6,6-tetramethyl-5-methoxy-3-heptanone (**59**). Furthermore, protonation of 2-*tert*-butyl-

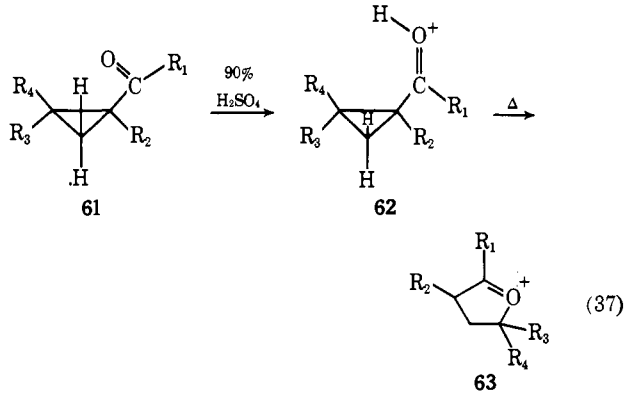


(36)

58 59 60b 60a

4,5,5-trimethyldihydrofuran (**60b**) also generates this ion.

On heating in strong acids, protonated cyclopropyl ketones rearrange to oxolan-2-ylium ions. Pittman and McManus[63] showed that eight representative cyclopropyl ketones (**61a–h**) undergo this rearrangement in 90% H_2SO_4 at rates which depend on the degree of substitution at the β position of the ring. Conversion to ions **63a–h** was quantitative with the exception of **63h** where only a 45% yield could be obtained, owing to a competing cleavage of the 2-cyclopropyl function. Protonated cyclopropyl methyl ketone (**61a**) is completely con-



(37)

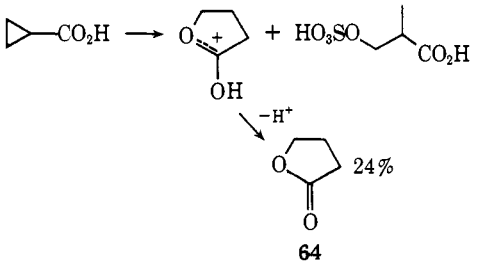
61 62 63

a, $R_1 = CH_3, R_{2,3,4} = H$
b, $R_1, R_2 = CH_3; R_3, R_4 = H$
c, $R_1, R_2R_3 = CH_3; R_4 = H$
d, $R_1, R_3, R_4 = CH_3; R_2 = H$
e $R_1 = CH_3R_2, R_4 = H; R = C_6H_5$
f $R_1 = C_6H_5; R_2, R_3, R_4 = H$
g, $R_1, R_3 = C_6H_5; R_2, R_4 = H$
h, $R_1 = c\text{-}C_3H_5; R_2, R_3, R_4 = H$

verted to the 2-methyloxolan-2-ylium ion (**63a**) after 50 min at 81°. On the other hand, 2,2-dimethyl-1-acetylcyclopropane (**61d**) rearranged quantitatively to ion **63d**, at 10°, faster than could be followed by nmr. Substitution of methyl for hydrogen at the α position does not increase the rearrangement rate. The rearrangements were first order, and the rates increased with a decrease in the acidity of the media. The mechanism of the rearrangement was discussed in terms of (1) ring opening to a classical carbonium ion, (2) formation of a protonated cyclopropane, (3) a concerted C-protonation ring opening with neighboring carbonyl oxygen participation. H–D exchange studies[63] during the rearrangement of **61d** ruled out a pro-

(62) K. Dimroth and W. Mach, *Angew. Chem., Int. Ed. Engl.*, **7**, 461 (1968).
(63) C. U. Pittman, Jr., and S. P. McManus, *J. Amer. Chem. Soc.*, **91**, 5915 (1969).

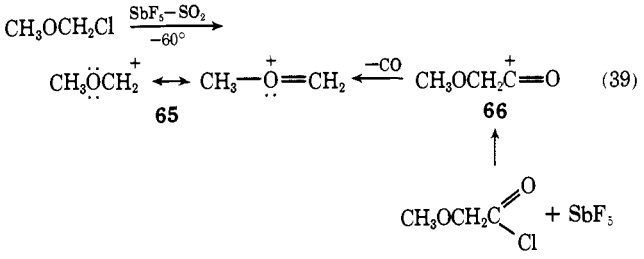
tonated cyclopropane with a sufficient lifetime to give the scrambling characteristic of these intermediates in 57–99% H_2SO_4.[64] Independently, Kushner[65] isolated 5-hydroxy-2-pentanone upon heating and neutralizing concentrated H_2SO_4 solutions of acetylcyclopropane. This transformation, as demonstrated above, occurs through an oxolan-2-ylium intermediate. In a related reaction, Deno and coworkers[66] obtained a 24% yield of lactone **64** upon heating cyclopropane



(38)

carboxylic acid in 98% H_2SO_4. This reaction certainly proceeds through the 2-hydroxyoxolan-2-ylium cation.

Related to oxolan-2-ylium ions are primary alkoxycarbonium ions such as the methoxymethyl cation (**65**). The first observations of this class of ions was reported by Olah and Bollinger.[67] Ion **65** could be prepared by dissolving chloromethyl ether in antimony pentafluoride diluted with SO_2 or by decarbonylation of the methoxyacetyl cation (**66**) which is

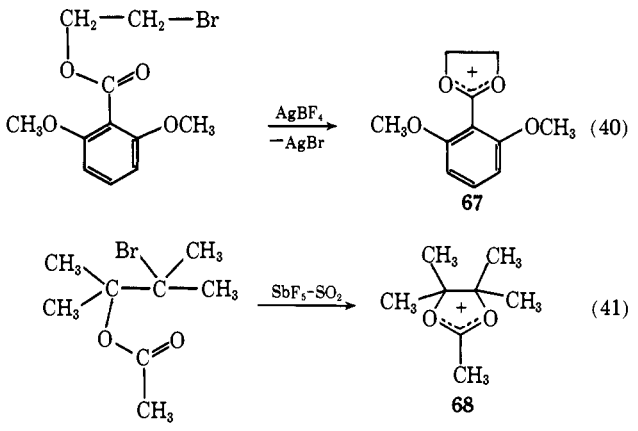


(39)

formed when methoxyacetyl chloride is treated with antimony pentafluoride in SO_2.

B. 1,3-DIOXOLAN-2-YLIUM, 1,3-OXATHIOLAN-2-YLIUM, AND 1,3-DITHIOLAN-2-YLIUM IONS

The basic methods of preparing 1,3-dioxolan-2-ylium ions were developed by Meerwein and were previously covered in section III. These techniques were expanded and modified in subsequent work. The cyclization of β-haloethyl esters has been employed by Beringer[68] to produce 2-(2′,6′-dimethoxyphenyl)-1,3-dioxolan-2-ylium tetrafluoroborate (**67**) (eq 40) and by Olah[69] to generate 2,4,4,5,5-pentamethyl-1,3-dioxolan-2-ylium haloantimonates (**68**). Olofson and coworkers[70] utilized Meerwein's hydride abstraction techniques to prepare dithiomethoxymethyl tetrafluoroborate and the 4,4,5,5-tetra-



(40)

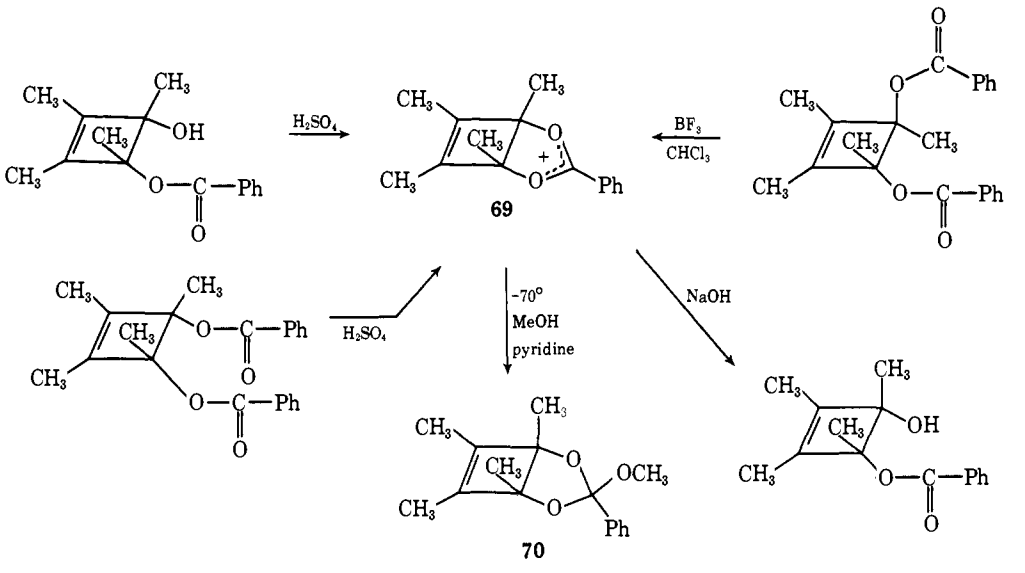
(41)

methyl-1,3-dioxolan-2-ylium tetrafluoroborate. An unusual 2-phenyl-1,3-dioxolan-2-ylium ion fused to a cyclobutene ring (**69**) has been prepared from both *cis*- and *trans*-3,4-dibenzoyl-1,2,3,4-tetramethylcyclobutenes as well as from the *cis*-hydroxy ester in H_2SO_4 or BF_3–$CHCl_3$ media by Wilcox.[71] This ion must be cis fused, and this was confirmed by preparation of the cis ortho ester **70** on treatment of **69** with methanol–pyridine at −70° and by hydrolysis to the *cis*-hydroxybenzoate with NaOH–H_2O (see eq 42).

Wilcox and Nealy[72] studied the position of equilibrium of 2-phenyl-1,3-dioxolan-2-ylium ion (**69**) with a series of para-substituted derivatives (**71**) (eq 43). The equilibrium constant had a very low sensitivity to the electronic nature of the para substituent, indicating such para functions stabilize (or destabilize) the protonated acid to about the same extent they effect the 1,3-dioxolan-2-ylium ion. It was also demonstrated that the methyl groups on the cyclobutene ring are equilibrated at a rate which is far faster than the equilibrium depicted in eq 43 is established.

Bis-2,2′-alkylene-1,3-dioxolan-2-ylium dications (**72**), n = 1–5, were prepared by Hart and Tomalia[73] by treating the appropriate bis(2-bromoethyl) esters with 2 equiv of anhydrous silver tetrafluoroborate in methylene chloride. The reactions (eq 44) went in high yield with the formation of dications complete in 2 hr at 25–30° when n = 3–5. When n = 1 or 2, substantially longer reaction times (8–12 hr) were required. These ions were well characterized by nmr (see section VII). When n = 1 the central methylene protons could not be observed, presumably owing to exchange with the FSO_3H solvent (eq 45). Thus, the two carbonium ion centers cause the methylene protons to be strongly acidic. Attempts to synthesize the bis-1,3-dioxolan-2-ylium ion, where n = 0, were unsuccessful. Hart and Tomalia[74,75] also combined a large series of 2-bromoethyl esters with silver tetrafluoroborate in methylene chloride, and the corresponding 2-alkyl, vinyl, aryl, and amino 1,3-dioxolan-2-ylium salts (**73a–y**) were obtained in yields of 50–87%. In addition, ion **73e** was formed by protonation of ethylene carbonate. Adding 2-hydroxy, 2-acetoxy, or 2-methoxyethyl esters to FSO_3H at room temperature led to the corresponding 2-alkyl- or 2-aryl-1,3-dioxolan-2-ylium ions identical with those obtained on samples formed by dissolving

(64) N. C. Deno, D. LaVietes, J. Mockus, and P. C. Scholl, *J. Amer. Chem. Soc.*, 90, 6457 (1968).
(65) A. S. Kushner, Ph.D. Thesis, Pennsylvania State University, 1966; *cf.* see footnote 15, ref 63.
(66) N. C. Deno, W. E. Billups, D. LaVietes, P. C. Scholl, and S. Schneider, *J. Amer. Chem. Soc.*, 92, 3700 (1970).
(67) G. A. Olah and J. M. Bollinger, *ibid.*, 89, 2993 (1967).
(68) F. M. Beringer and S. A. Galton, *J. Org. Chem.*, 32, 2630 (1967).
(69) G. A. Olah and J. M. Bollinger, *J. Amer. Chem. Soc.*, 89, 4744 (1967).
(70) R. A. Olofson, S. W. Walinsky, J. P. Marino, and J. L. Jernow, *ibid.*, 90, 6554 (1968).
(71) C. F. Wilcox, Jr., and D. L. Nealy, *J. Org. Chem.*, 28, 3446 (1963).
(72) C. F. Wilcox, Jr., and D. L. Nealy, *ibid.*, 29, 3668 (1964).
(73) H. Hart and D. A. Tomalia, *Tetrahedron Lett.*, 1347 (1967).
(74) H. Hart and D. A. Tomalia, *ibid.*, 3383 (1966).
(75) D. A. Tomalia and H. Hart, *ibid.*, 3389 (1966).



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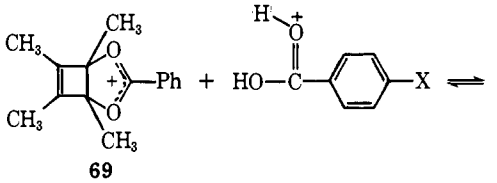

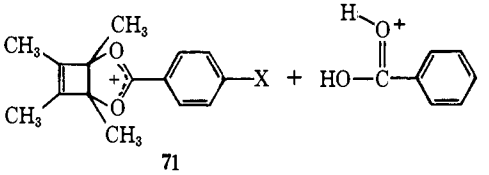

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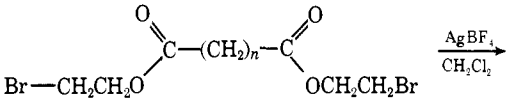

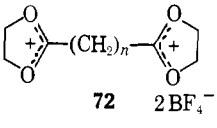

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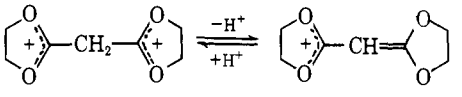

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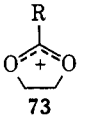
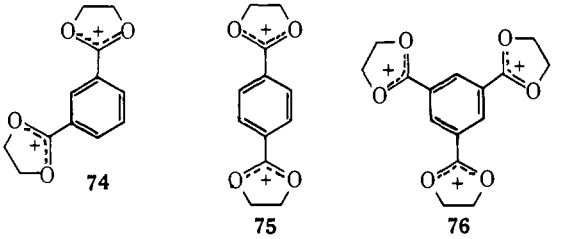
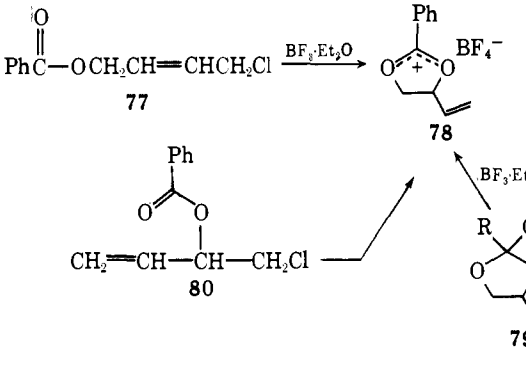


	R
a	$N(Et)_2$
b	c-C_3H_5
c	$CH{=}CHCH_3$
d	$CH{=}CHC_6H_5$
e	OH
f	c-C_4H_7
g	$C(CH_3)_3$
h	CH_3
i	$CH{=}CH_2$
j	$C(CH_3){=}CH_2$
k	$C_6H_4OCH_3(p)$
l	3,4,5-$(CH_3O)_3Ph$
m	$C_6H_4CH_3(p)$
n	$C_6H_4CH_3(m)$
o	C_6H_5
p	$C_6H_4F(p)$
q	$C_6H_4Cl(p)$
r	$C_6H_4Cl(m)$
s	$C_6H_4Br(m)$
t	$C_6H_4F(m)$
u	3,4-Cl_2Ph
v	$C_6H_4CF_3(m)$
w	$C_6H_4CF_3(p)$
x	$C_6H_4NO_2(m)$
y	$C_6H_4NO_2(p)$

authentic cation tetrafluoroborate salts in FSO_3H. The rate of formation of these cations was found to be in the order: OH > $-OOCCH_3$ > OCH_3. Di- and trications **74**, **75**, and **76** were



obtained by treating the appropriate 2-bromoethylphthalate or trimesitate with an equivalent of silver tetrafluoroborate. When treated with $BF_3 \cdot Et_2O$, 4-chloro-2-butenyl benzoate (**77**) underwent an allyl rearrangement[76] to give 4-vinyl-2-



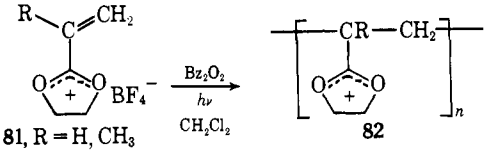
(46)

phenyl-1,3-dioxolan-2-ylium tetrafluoroborate (**78**). Ortho ester **79** also gave ion **78** as did chloro ester **80**.

Tomalia[77,78] has prepared acrylate and methacrylate polymers (**82**) of 1,3-dioxolan-2-ylium and 1,3-dioxan-2-ylium ions. The monomer salts were prepared by the cyclization of the corresponding 2-hydroxyethyl or 2-bromoethyl esters in FSO_3H or with silver tetrafluoroborate in methylene chloride,

(76) S. Kabuss, *Angew. Chem., Int. Ed. Engl.*, **5**, 896 (1965).
(77) D. A. Tomalia, U. S. Patent 3,480,649; *Chem. Abstr.*, **72**, 3180 (1970).
(78) D. A. Tomalia, U. S. Patent 3,417,062; *Chem. Abstr.*, **72**, 38302 (1970).

respectively. For example, 2-isopropenyl-1,3-dioxolan-2-ylium and 2-vinyl-1,3-dioxolan-2-ylium tetrafluoroborate (**81**) prepared in this way were polymerized using benzoyl



(47)

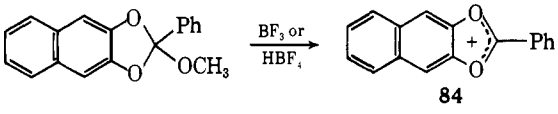
81, R = H, CH_3 **82**

peroxide as the initiator by irradiating solutions of the salts at 18–20° in methylene chloride for 2 days under nitrogen.

Benzo- and 2,3-naphtho-1,3-dioxolan-2-ylium ions (**83** and **84**) were prepared by Dimroth, *et al.*,[79] by treating 2-phenyl-2-

(48)

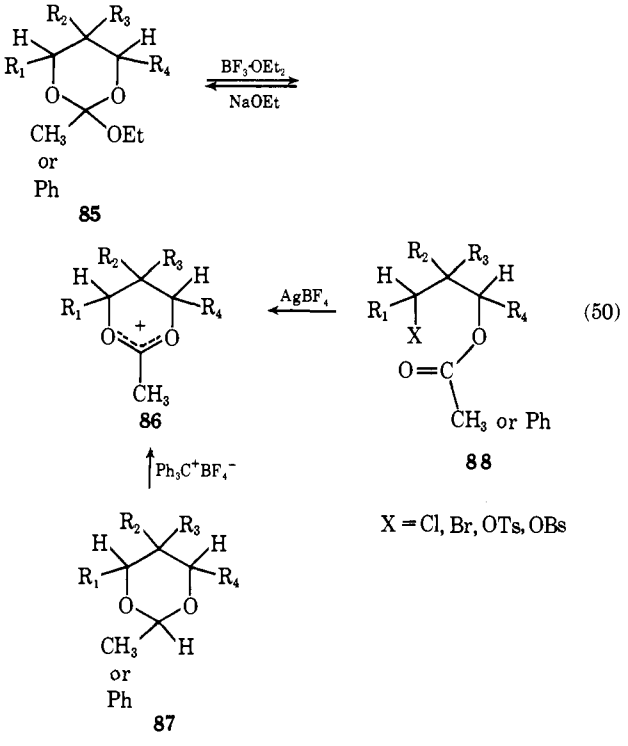
83



(49)

84

methoxybenzodioxolane and the naphtho analog with BF_3 or tetrafluoroboric acid in methylene chloride. This extension of the reactions, originally developed by Meerwein, was employed by Schneider[80] to synthesize a series of substituted 1,3-dioxan-2-ylium salts (**86**). For example, the substituted 2-methyl-2-ethoxy- and 2-phenyl-2-ethoxy-1,3-dioxanes (**85**) gave the corresponding 2-methyl- and 2-phenyldioxan-2-ylium tetrafluoroborates (**86**) on treatment with $BF_3 \cdot Et_2O$.



(50)

85

86

87

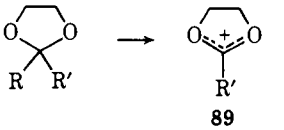
88

R_1, R_2, R_3, R_4 = H, CH_3, Et, C_3H_7, C_4H_9

X = Cl, Br, OTs, OBs

Trityl carbonium ion salts were also effective in abstracting hydride from substituted 2-methyl- and 2-phenyl-1,3-dioxolanes (**87**). The open-chain 1,3-propanediolhaloacetates (**88**) (as well as their tosylates and brosylates) were also converted to the 1,3-dioxan-2-ylium ions by $AgBF_4$. The highest yields of ion **86** obtained from **85** or **87** occurred when $R_1 = R_4 = H$ and $R_2 = R_3$. The cyclizations from **88** to **86** gave best yields when $R_2 = R_3 = H$.

Kabuss[81] reported the formation of 1,3-dioxolan-2-ylium and 1,3-dioxan-2-ylium ions (**89** and **90**) from their ketals by removal of a 2-alkyl group by Lewis acids including oxonium ions (eq 51 and 52).



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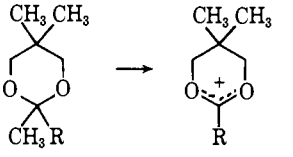

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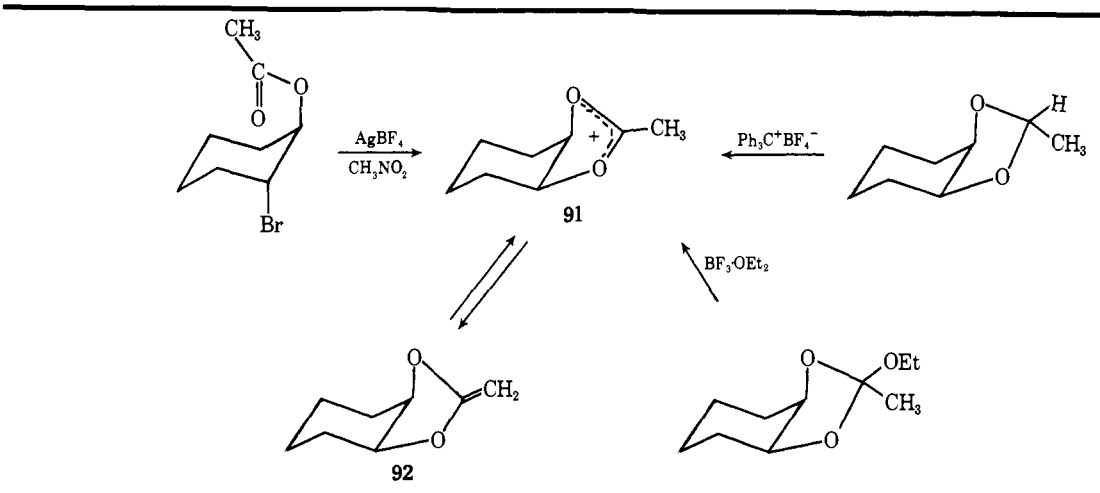
90

One of the most interesting applications of Meerwein's reactions was the preparation of 2-methyl-*cis*-4,5-tetramethylene-1,3-dioxolan-2-ylium tetrafluoroborate (**91**) by Anderson, Friedrich, and Winstein.[82] This work culminated the brilliant early work by Winstein (cited in Introduction) and demonstrated the intermediacy of this ion in the solvolysis reactions reported therein. Ion **91** was prepared in three ways, by treating *trans*-2-acetoxycyclohexyl bromide with silver tetrafluoroborate in nitromethane, from 2-methyl-*cis*-4,5-tetramethylene-1,3-dioxolane and trityl tetrafluoroborate, and from 2-ethoxy-2-methyl-*cis*-4,5-tetramethylene-1,3-dioxolane and boron trifluoride etherate. In deuterioacetic acid the 2-methyl protons of ion **91** were exchanged for deuterium corresponding to a minimum first-order rate constant of about 10^{-3} sec^{-1} at 25°. The observed exchange proceeds *via* the ketene acetal **92**, the equilibrium being rapidly established and lying quite far on the side of the 1,3-dioxolan-2-ylium ion despite the modest acid strength of acetic acid. This demonstrates the relatively high base strength of the double bond and emphasizes the ion's great stability.

Another route to ion **91** was reported by Pedersen.[83] After 8 hr in liquid HF, *cis*-1,2-diacetoxycyclohexane was converted to **91** quantitatively while the trans diacetate remained unchanged for several days. By isolating **91** as its tetrafluoroborate salt and by observing the ion's nmr spectrum, identification was unequivocal. Schneider and Lang[84] isolated both 2-phenyl-*cis*-4,5-tetramethylene-1,3-dioxolan-2-ylium tetrafluoroborate (**93**) and its dioxan-2-ylium analog (**94**). Ion **94** could be prepared from *cis*-2-tosyloxymethylcyclohexyl benzoate (**97**) but not its trans isomer (**98**). It was also prepared from *trans*-2-benzoyloxymethylcyclohexyl tosylate (**96**) but not cis isomer **98**. In addition, Schneider and Kovács[85,86]

(79) K. Dimroth, P. Heinrich, and K. Schromm, *Angew. Chem., Int. Ed. Engl.*, 4, 873 (1965).
(80) G. Schneider, *Tetrahedron Lett.*, 5921 (1966).
(81) S. Kabuss, *Angew. Chem., Int. Ed. Engl.*, 7, 64 (1968).
(82) C. B. Anderson, E. C. Friedrich, and S. Winstein, *Tetrahedron Lett.*, 2037 (1963).
(83) C. Pedersen, *ibid.*, 511 (1967).
(84) G. Schneider and L. K. Lang, *Chem. Commun.*, 13 (1967).
(85) G. Schneider and O. K. J. Kovács, *ibid.*, 202 (1965).
(86) O. K. J. Kovács, G. Schneider, L. K. Lang, and J. Apjok, *Tetrahedron*, 23, 4186 (1967).



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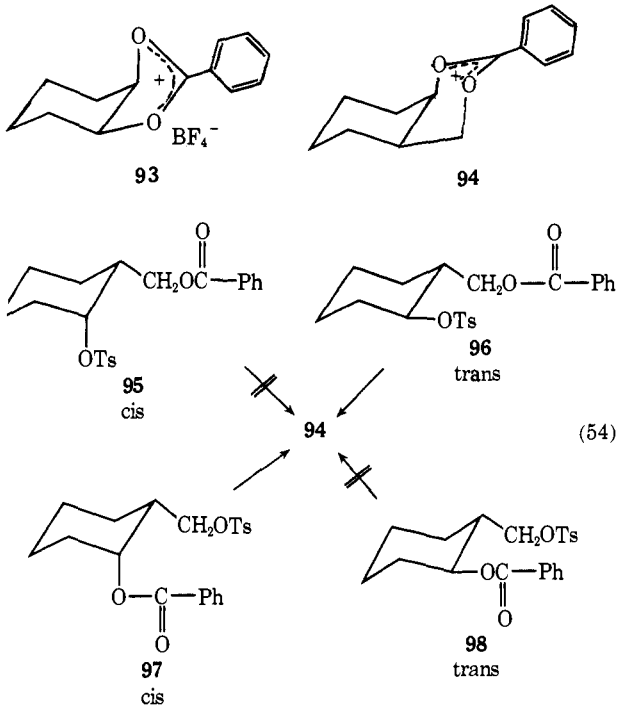


(54)

prepared 2-methyl-*cis*-4,5-tetramethylene-1,3-dioxan-2-ylium tetrafluoroborate (**99**) on (1) treatment of ortho ester **100** with boron trifluoride etherate, (2) treating either **101** or **102** with silver tetrafluoroborate, or (3) treating 2-methyl-*cis*-1,3-dioxadecalin (**103**) with trityl tetrafluoroborate in acetonitrile. However, isomers **104** and **105** did not give salt **99** when treated with silver tetrafluoroborate under conditions identical with those used for **101** and **102**.

Pittman and McManus[87] demonstrated the clean cyclization of methallyl esters and methallylthiol esters to 1,3-dioxolan-2-ylium and 1,3-oxathiolan-2-ylium cations **106, 107,** and **108**. This method appears general for the methallyl derivatives, and it was extended to carbamates. The methallyl derivatives are simply dissolved in 60–96% H_2SO_4 or FSO_3H to generate the corresponding heterocyclic carbonium ions quantitatively. The cyclization of allyl acetate in 96% H_2SO_4 gave only a 30% yield of the 2,4-dimethyl-1,3-dioxolan-2-ylium cation (**109**) and 70% protonated acetic acid. Attempts to cyclize several acetates and benzoates of secondary allylic alcohols (such as 3-acetoxy-1-pentene, 3-benzoyloxy-1-pentene, 3-acetoxy-2-methyl-1-pentene, and 4-acetoxy-2-methyl-2-pentene) resulted in no cyclic ion because rapid, quantitative cleavage (eq 60) by A_{AL}-1 fission occurs instead.[87] Upon heating ions **106** and **107** in H_2SO_4 and D_2SO_4, cleavage to protonated acetic acid occurs and the rate of cleavage is facilitated as acidity decreases. While ions **106–109** were indefinitely stable at 30° and stable for at least 20 min at 70° in 96% H_2SO_4, ion **106** is completely cleaved at 120° in 3 min. Ion **107** requires 5 min for complete cleavage in 96% H_2SO_4, but **108**, which is stabilized by the 2-amino group, is stable for hours at 120°. In 80% H_2SO_4, **106** is 75% cleaved in 29 min at 66° and instantly destroyed at 120°, while **107** is stable at 74° and 20% cleaved after 6 min at 122°. In 60% H_2SO_4 ions **106** (100% cleaved in 5 min) and **107** (47% cleaved in 6 min) are more rapidly degraded.[87]

In 96% D_2SO_4 no deuterium incorporation in ions **106–109** occurs.[87] Thus, the ions are not in equilibrium with either their alicyclic precursors (**110**) or with their 2-methylene derivatives (**111**). As acidity decreases, the water activity sharply increases, and water could function as the base, promoting ring opening by path A (eq 61). In path B, rate constants k_3 and k_4 should be independent of acidity to a first approximation, but the rate of deprotonation of cation **112** will increase as the acidity is lowered. A clear choice between paths A and B is not yet possible. Larsen and Ewing[88,89] have utilized the methallyl ester cyclization route of Pittman and McManus to prepare over 20 1,3-dioxolan-2-ylium and 1,3-dioxan-2-ylium ions. Noting this method gives the ions rapidly and cleanly from readily prepared and purified starting materials, Larsen and Ewing[89] used this reaction to measure the relative heats of formation of these ions in FSO_3H (see section VI.B).

A few other reactions have also been employed. Cyclic siloxane **113** upon treatment with acetyl perchlorate in perchloric acid–ethyl acetate gave[90,91] the 2,4,4,5,5-pentamethyl-1,3-dioxolan-2-ylium ion (**114**). This ion was also prepared from pinacol and acetic anhydride in the same medium. The slow addition of an equimolar amount of 70% perchloric acid to pinacolone in an excess of the anhydride of the appropriate acid was found to be a general route to 1,3-dioxolan-2-ylium ions (eq 63).[92] Stable 1,3-dioxolan-2-ylium and 1,3-dioxan-2-

(87) C. U. Pittman, Jr., and S. P. McManus. *Tetrahedron Lett.*, 339 (1969).

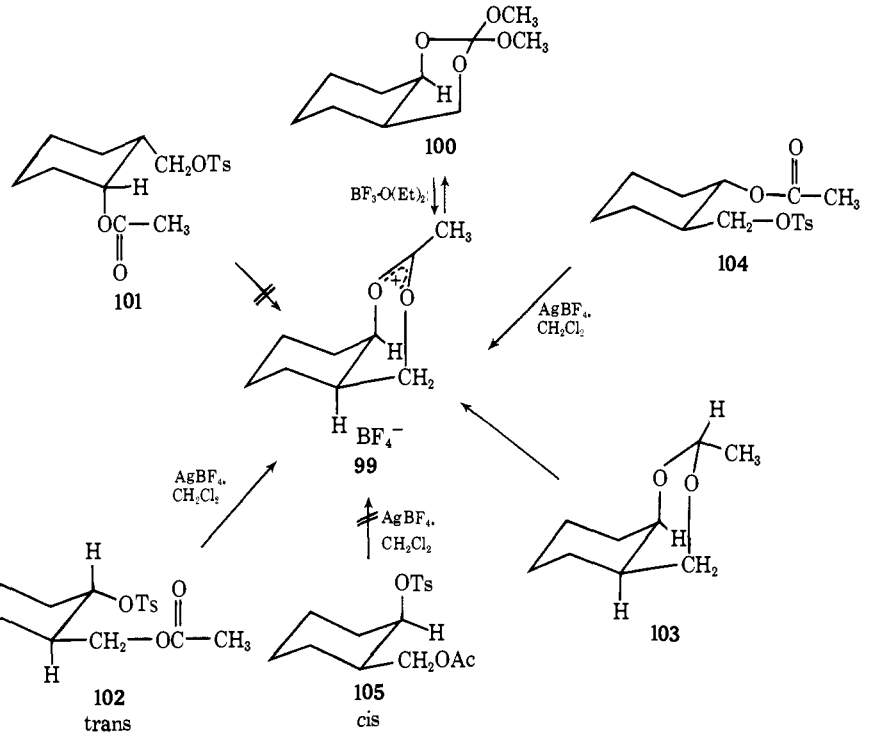
(88) J. W. Larsen, S. Ewing, and M. Wynn, *ibid.*, 539 (1970).

(89) J. W. Larsen and S. Ewing, *J. Amer. Chem. Soc.*, 93, 5107 (1971).

(90) J. A. Magnuson, C. A. Hirt, and P. J. Lauer, *Chem. Ind. (London)*, 691 (1965).

(91) J. A. Magnuson, *Anal. Chem.*, 35, 1487 (1963).

(92) G. N. Dorofeenko and L. V. Mezheritskaya, *Zh. Obshch. Khim.*, 38, 1192 (1968).



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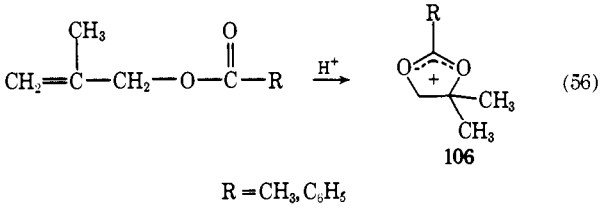

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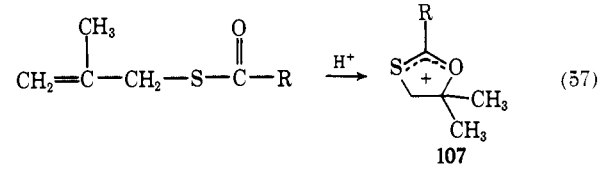

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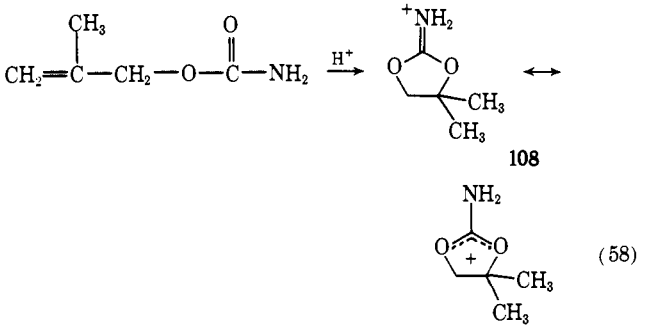

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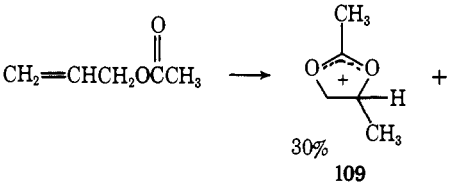

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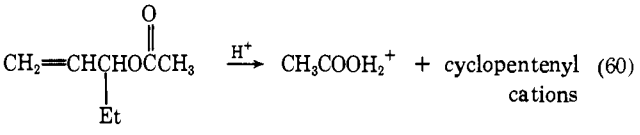

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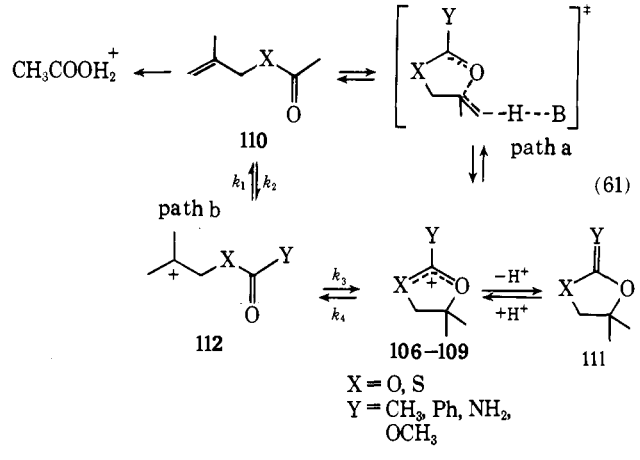


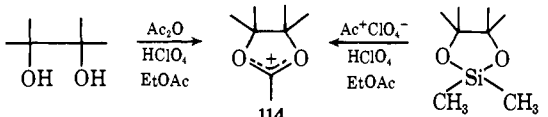
(61)

ylium salts of steroids have been prepared. For example, reaction of 3β,5α-diacetoxy-6β-fluorocholestane (**115**) with perchloric acid in acetic anhydride gives the corresponding 3α,5α-dioxan-2-ylium ion (**116**) as its perchlorate salt.[93,94] Bridged ions **118a–c** were also obtained from 3β-hydroxy-5α-diacetoxy-6β-chlorocholestane (**117**) and its 6-keto and its 6β-acetoxy analogs on treatment with acetic anhydride in sulfuric acid followed by the addition of perchloric acid and ether.[95]

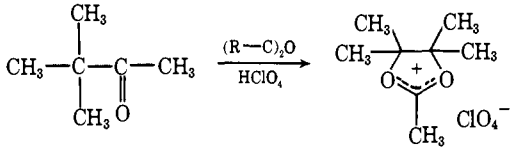
(93) J. W. Blunt, M. P. Hartshorn, F. W. Jones, D. N. Kirk, and S. W. Yoong, *Tetrahedron*, 1567 (1965).

(94) J. W. Blunt, M. P. Hartshorn, and D. N. Kirk, *J. Chem. Soc.*, 1073 (1964).

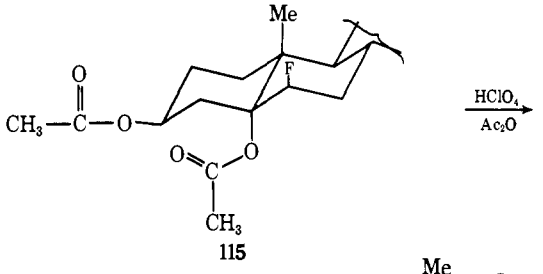
(95) M. J. Coopen, M. P. Hartshorn, and D. N. Kirk, *J. Chem. Soc. C*, 576 (1966).

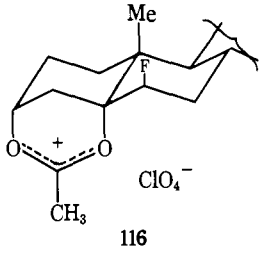


(62)

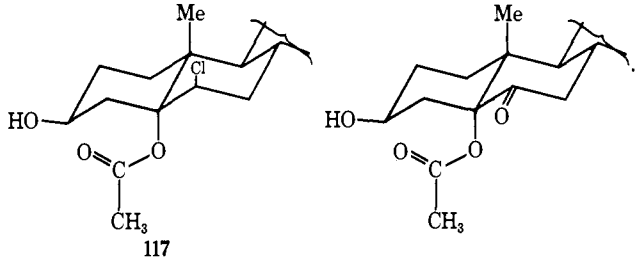


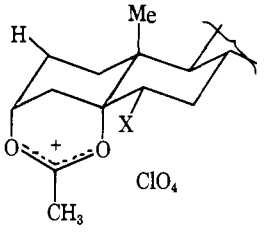
(63)





(64)

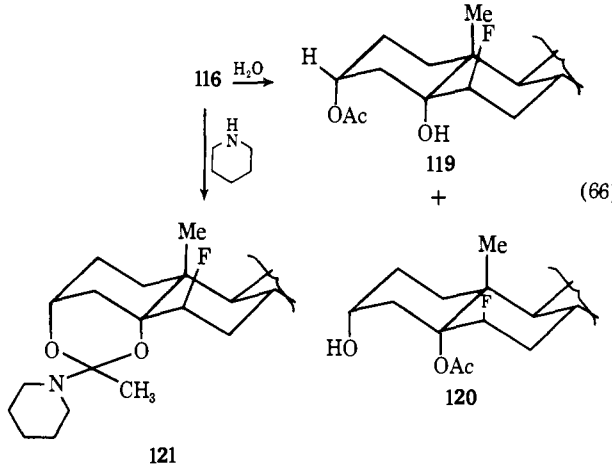




(65)

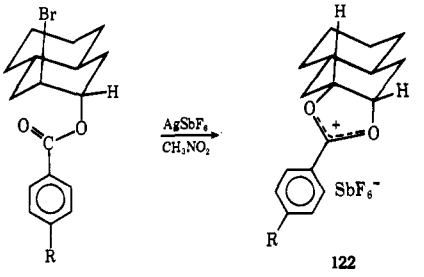
Hydrolysis of the salts **118a–c** with $NaHCO_3$ in aqueous acetone at 20° gave the 3α-hydroxy-5α-acetoxy derivatives. Reaction of **118c** with cold aqueous acetic acid also gave the 3α-hydroxy-5α-acetoxy derivative, but hydrolysis in warm anhydrous acetic acid, buffered with sodium acetate, gave mainly the 3α-acetoxy-5α-hydroxy derivative.

The structure of salt **116** was confirmed from the structures of its hydrolysis products.[94] Both 3α-acetoxy-6β-fluorocholestan-5α-ol (**119**) (thermodynamic product) and 5α-acetoxy-6β-fluorocholestan-3α-ol (**120**, kinetic product) are obtained on water hydrolysis while piperidine gives the cyclic product (**121**). These transformations are summarized in eq 66.

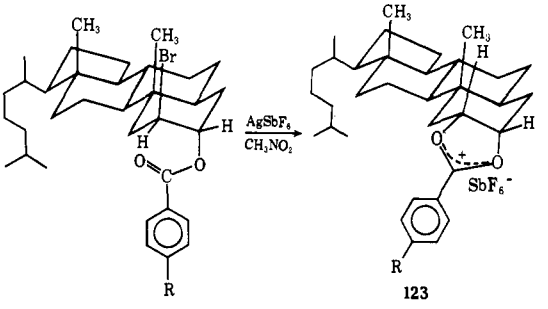


(66)

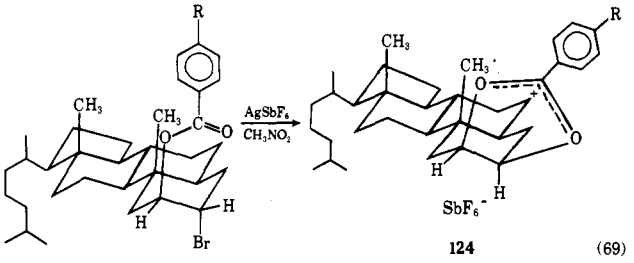
King and Allbutt[96,97] reported the synthesis of 9β,10α-decalin-2β,3β-(2-anisyl-1,3-dioxalan-2-ylium) (**122**), 5α-cholestan-2β,3β-(2′-anisyl-1′,3′-dioxolan-2-ylium) (**123**), and 5α-cholestan-2α,3α-(2′-anisyl-1,3′-dioxolan-2-ylium) (**124**) tetrafluoroborates as well as their 2′-phenyl derivatives by treating the corresponding bromohydrin esters with $AgSbF_6$ in nitromethane (see eq 67–69). From these rigidly anchored



(67)



(68)



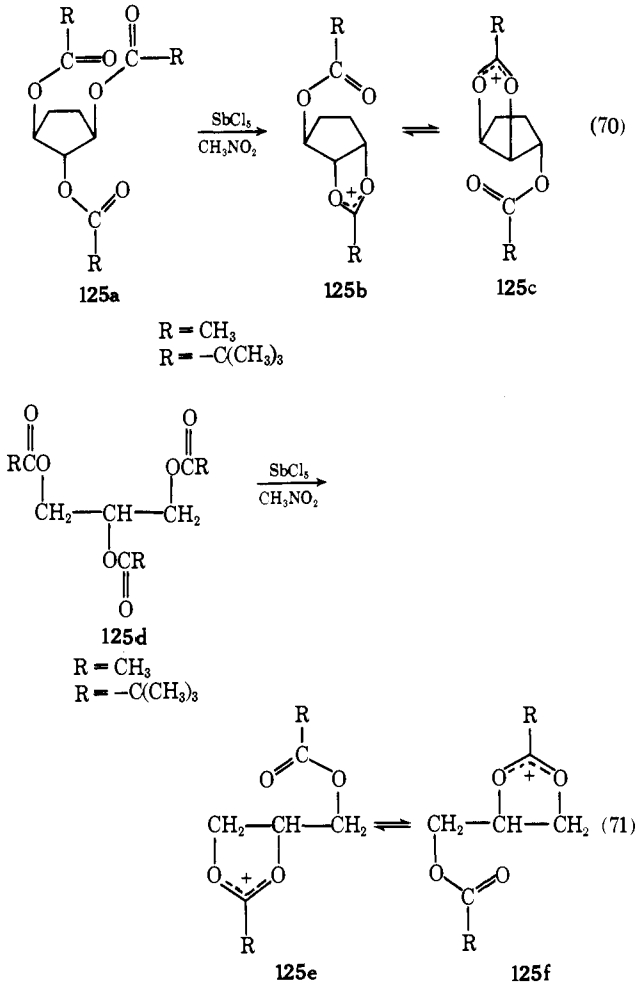
(69)

systems the detailed stereochemistry of the reactions of 1,3-dioxolan-2-ylium ions with various nucleophiles was elucidated (see section V.B).

Paulsen and coworkers have reported several interesting 1,3-dioxolan-2-ylium and 1,3-dioxan-2-ylium ions which are

(96) J. F. King and A. D. Allbutt, *Can. J. Chem.*, **47**, 1445 (1969).
(97) J. F. King and A. D. Allbutt, *ibid.*, **48**, 1754 (1970).

in dynamic degenerate equilibrium.[98-104] For example, trans esters of cyclic triols such as **125a** form equilibrating 1,3-dioxolan-2-ylium ions **125b,c** on treatment with $SbCl_5$ in CH_2Cl_2 or CH_3NO_2. Glycerol triacetate (**125d**, R = CH_3) gives a similar set of equilibrating ions **125e,f** as does glycerol



(70)

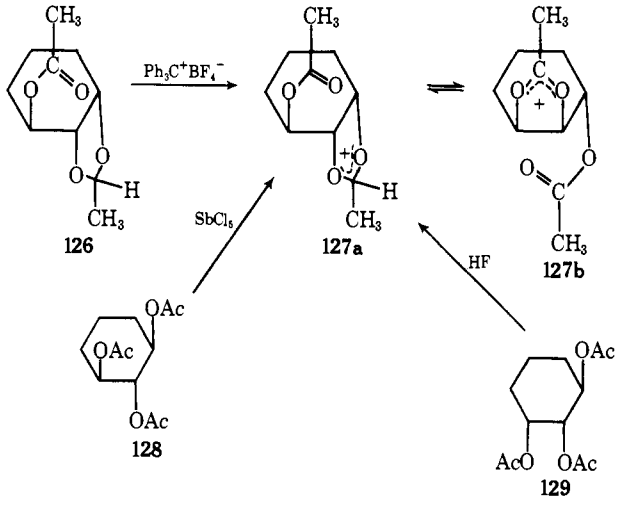
(71)

tripivaloate (**125d**, R = $-C(CH_3)_3$). The equilibria were monitored by nmr in CD_3NO_2 solutions and by varying the temperature; the nmr peaks for the group on the 2 position of the ion coalesce as the rate of equilibration increased. The $\Delta G^{\ddagger}$ values determined from the nmr studies are summarized in Table II. Upon treatment with trityl tetrafluoroborate, 3-*O*-acetyl-1,2-*O*-ethylidene-1,2,3-cyclohexanetriol (**126**) looses a hydride to become equilibrating ion **127**. Ion **127** can also be prepared from the *all-trans*-triacetate **128** with $SbCl_5$ or from the *cis,trans*-triacetate **129** in HF. The $\Delta G^{\ddagger}$ for this equilibration is about the same as that for the open-chain and five-membered ring analogs **125b,c** and **and 125e,f**, respectively. A mixture of *exo*- and *endo*-3,4,5-tri-*O*-acetyl-1,2-*O*-ethylidene-1,2,4/3,5-cyclopentanepentol (**130**) when treated with trityl tetrafluoroborate in CH_3CN gives the

Table II

$\Delta G^{\ddagger}$ for Degenerate Equilibria of Selected Cations

Rearrangement	*R*	T_c, °K	$\Delta G^{\ddagger}$, *kcal/mol*
123a ⇄ 123b	CH_3	365	18.0
	$-C(CH_3)_3$	348	17.8
125a ⇄ 125b	$-CH_3$	378	18.7
	$-C(CH_3)_3$	360	18.4
127a ⇄ 127b	CH_3	368	18.4
134a ⇄ 134b	$-C(CH_3)_3$	383	19.3
131a ⇄ 131b	CH_3	365	18.0



(72)

tetrafluoroborate salt of equilibrating cation **131**. By successive neighboring group reactions cation **131** can regenerate itself after ten conversion steps. Ion **131** is also formed by dissolving **130** in HF.

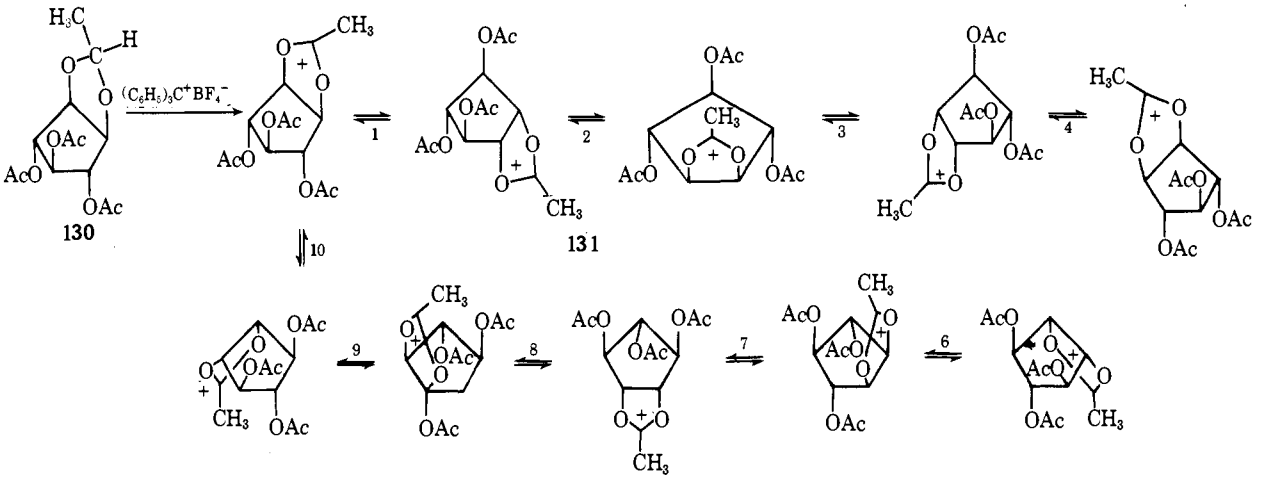
The reaction of 1,2,4-butanetriol esters with $SbCl_5$ permits a direct comparison of the stabilities of 1,3-dioxolan-2-ylium and 1,3-dioxan-2-ylium salts. Paulsen[100] reported that the five-membered ring salt **132** is formed preferentially to **133** in 90% yield at equilibrium. The corresponding 1,3-dioxan-2-ylium salts of 1,3,5-triol esters also undergo degenerate equilibration (eq 75). The tripivalate undergoes ionization to **134** which exhibits a coalescence temperature for the two *tert*-butyl groups of 110° in nitrobenzene. The $\Delta G^{\ddagger}$ of 19.3 kcal/mol for **134** is about 1.0 kcal/mol higher than that found for its glycerol-derived 1,3-dioxolan-2-ylium analog **125e** and **125f** (R = *tert*-butyl).

An interesting spiro-degenerate system is **136** derived from pentaerythritol tetrapivalate (**135**) in $SbCl_5$–CH_2Cl_2.[100] Ion **136** undergoes four rearrangement steps in a spiral manner about the central tetrahedral carbon atom to regenerate itself. In CD_3NO_2 solution the nmr peaks due to the *tert*-butyl groups coalesce at 110°, while those for the methylene protons coalesce at 122°. Taking into account the nmr-derived $\Delta\nu$ values, a value of $\Delta G^{\ddagger}$ = 19.3 kcal/mol was found which was identical with that found for ion **134**.

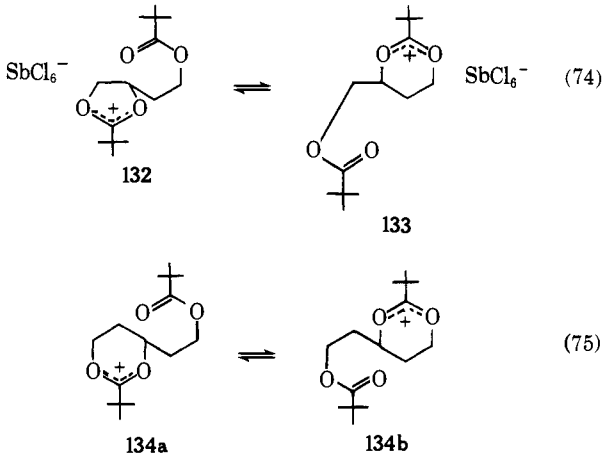
Paulsen and coworkers reported several new stable ions.[101-104] In liquid HF, tetra-*O*-acetyl-1,2,3,4-cyclopentanetetraol (**137**) gives dication **138**. The reaction of diesters **139–144** with $SbCl_5$ in CH_2Cl_2 resulted in the isolation of a series of 1,3-dioxolan-2-ylium and 1,3-dioxan-2-ylium salts **145–150**.

Ions **147–150** are precursors to their respective cis diacetates

(98) H. Paulsen and H. Behre, *Angew. Chem., Int. Ed. Engl.*, 8, 886 (1969).
(99) H. Paulsen and H. Behre, *ibid.*, 8, 887 (1969).
(100) H. Paulsen, H. Meyborg, and H. Behre, *ibid.*, **8**, 888 (1969).
(101) H. Paulsen and H. Behre, *Chem. Ber.*, 104, 1264 (1971).
(102) H. Paulsen and H. Behre, *ibid.*, **104**, 1281 (1971).
(103) H. Paulsen and H. Behre, *ibid.*, **104**, 1299 (1971).
(104) H. Paulsen and C. P. Herold, *ibid.*, **104**, 1311 (1971).



(73)

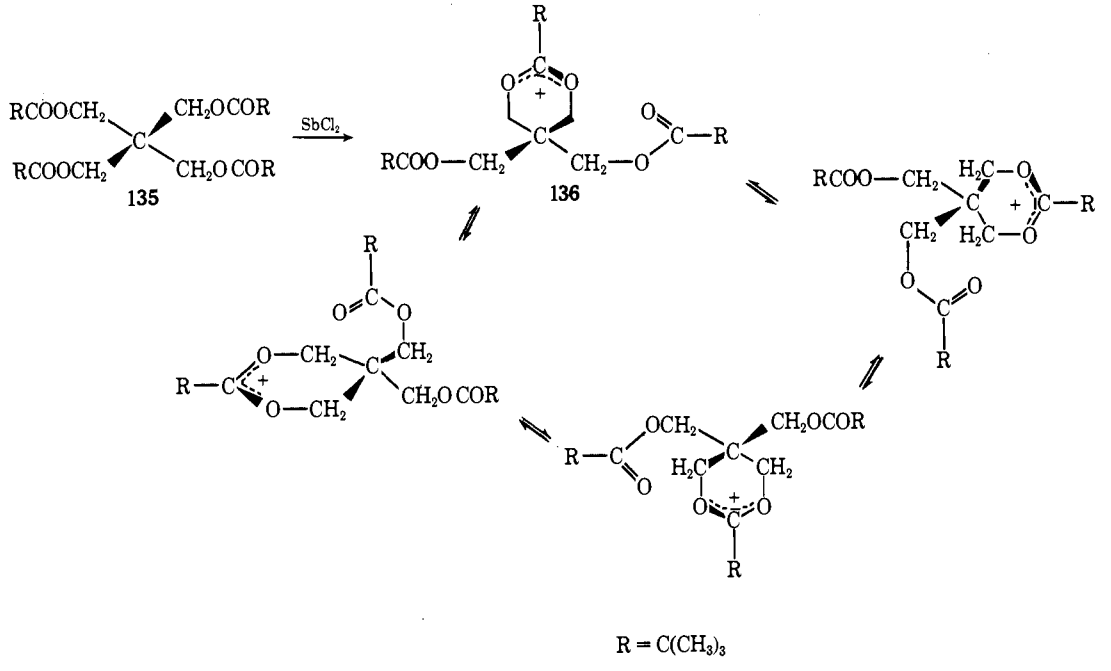


(74)

(75)

pyranodihydrooxazinium ions are more stable than their pyrano-1,3-dioxan-2-ylium counterparts. Illustrating this effect, the 2,3-oxazoline derivative (**156**) of 3-amino-3-deoxy-D-mannose is obtained (see eq 84) starting from the 3-amino-3-deoxy-D-glucose derivative (**155**). Similarly, the 5,6-dihydrooxazine derivative (**158**) of 6-amino-6-deoxy-D-idose is obtained from 6-amino-6-deoxy-D-glucose derivatives such as **157** (see eq 85).

Preparations of 1,3-dithiolan-2-ylium and related ions are not as numerous as their oxygen analogs. Tucker and Roof[105] prepared the accylic trimethylthiomethyl tetrafluoroborate (**159**) by treatment of tetramethyl orthothiocarbonate (eq 86) with trityl cation or by methylation of dimethyl trithiocarbonate (eq 87) with trimethyloxonium tetrafluoroborate. Several trialkylthiomethyl ions including **159** and 1,3-dithio-



(76)

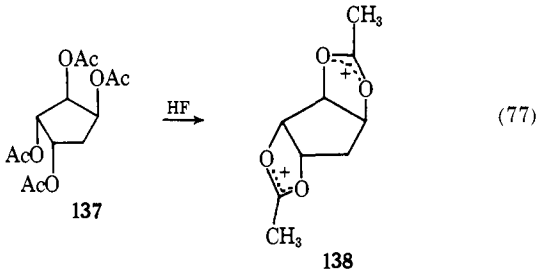
R = $C(CH_3)_3$

(or diols) **151–153**, and this method represents a convenient reaction path to convert from trans to cis substituion.

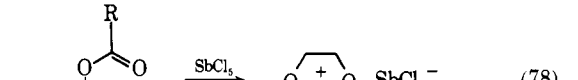
Paulsen and Herold[104] have also compared the stability of 1,3-dioxolan-2-ylium and oxazolinium ions fused to pyranose systems. Where rapid equilibria are permitted which involve both species, the oxazoline derivative is obtained showing that the oxazolinium ion is the more stable system. Similarly,

lan-2-ylium ions (**160**), isolated as their methyl sulfate salts, were prepared by Gompper and Kutter.[106,107] Other such

(105) W. P. Tucker and G. L. Roof, *Tetrahedron Lett.*, 2747 (1967).
(106) R. Gompper and E. Kutter, *Angew. Chem., Int. Ed. Engl.*, 2, 687 (1963).
(107) R. Gompper and E. Kutter, *Chem. Ber.*, 98, 1365 (1965).

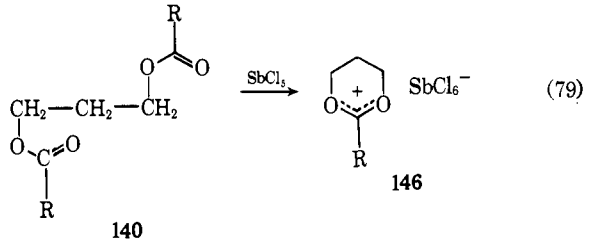


137 138 (77)

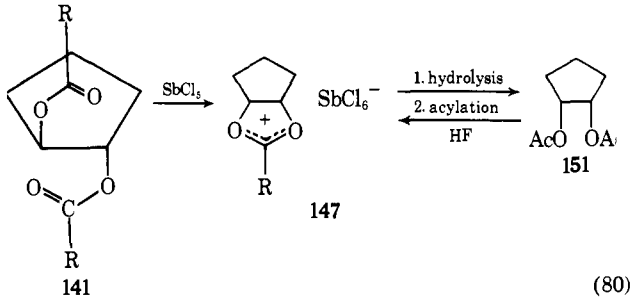


139 145 (78)

R = CH_3, C_2H_5, $C(CH_3)_3$, C_6H_5, $C_6H_4CH_3(p)$, $C_6H_4OCH_3(p)$

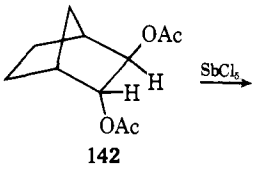


140 146 (79)



141 147 151 (80)

salts have also been reported.[108,109] An interesting zwitterionic 1,3-dithiolan-2-ylium cation (**160a**) has been prepared by Boiko and Petrun'kin.[110] Wizinger and Duerr[111] prepared a series of dithiolan-2-ylium cyanines of the general structure **161** where $n = 0$ or 1. Ion **161** ($n = 0$) was prepared by the condensation of dithioglycol with malonic acid in $POCl_3$. Through the condensation of dithioglycol with dimethylaminobenzaldehyde in the presence of zinc chloride, the 2-[4-dimethylaminophenyl]-1,3-dithiolan-2-ylium ion (**162**) was obtained and isolated as its perchlorate salt. The synthesis of the vinyl homolog (**163**) was also reported. This paper also describes a large series of 2-substituted benz-1,3-dithiolan-2-ylium perchlorates (**164**), benz-1,3-dithiolan-2-ylium cyanines (**165**), as well as their 1,3-oxathiolan-2-ylium analogs (**166** and **167**). Gompper and coworkers prepared a large series of quinonemethides and quinodimethans which exhibit uv spectra very similar to the



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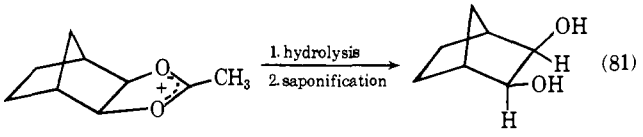
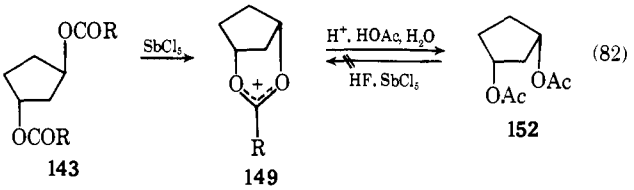
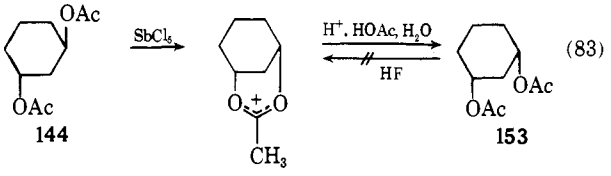


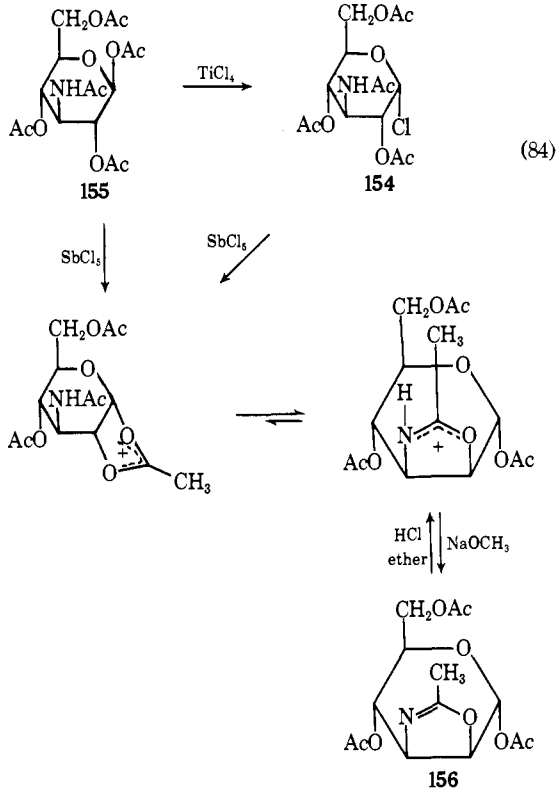
148 151 (81)



143 149 152 (82)



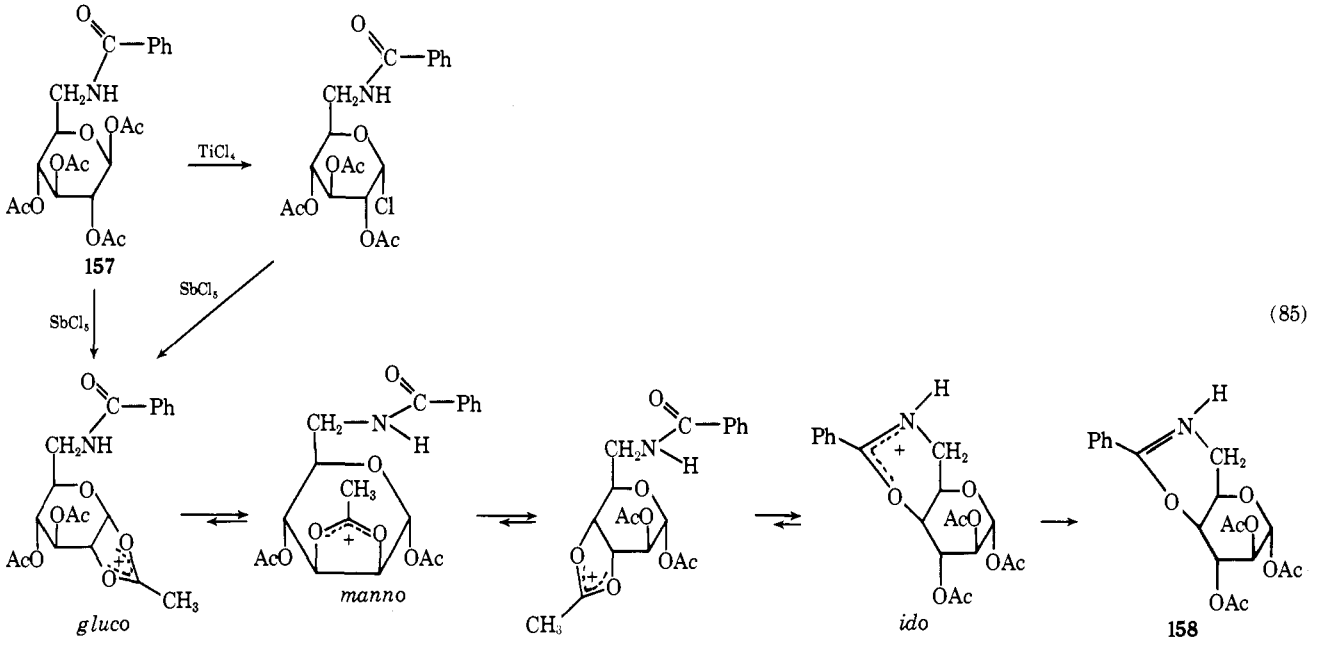
144 150 153 (83)



155 154 156 (84)

corresponding carbonium ions.[106,112–115] In general, these were prepared by treating **170** with compounds possessing an

(108) L. Soder and R. Wizinger, *Helv. Chim. Acta*, 42, 1733 (1959).
(109) E. Campaigne and R. D. Hamilton, *J. Org. Chem.*, 29, 2877 (1964).
(110) V. D. Boiko and V. E. Petrun'kin, *Ukr. Khim. Zh.*, 33, 489 (1967).
(111) R. Wizinger and D. Duerr, *Helv. Chim. Acta*, 46, 2167 (1963).
(112) R. Gompper and H. U. Wagner, *Tetrahedron Lett.*, 165 (1968).
(113) R. Gompper, H. U. Wagner, and E. Kutter, *Chem. Ber.*, 101, 4144 (1968).
(114) R. Gompper and R. Weiss, *Angew. Chem., Int. Ed. Engl.*, 7, 296 (1968).
(115) R. Gompper, E. Kutter, and R. R. Schmidt, *Chem. Ber.*, 98, 1374 (1965).

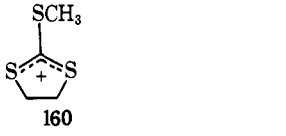


157 158 (85)

$$(CH_3S)_4C + Ph_3C^+BF_4^- \xrightarrow{CH_2Cl_2} (CH_3S)_3C^+BF_4^- \; Ph_3C{-}SMe \quad (86)$$

159

$$(CH_3S)_2C{=}S + (CH_3)_3O^+BF_4^- \longrightarrow \mathbf{159} + CH_3OCH_3 \quad (87)$$



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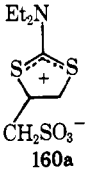
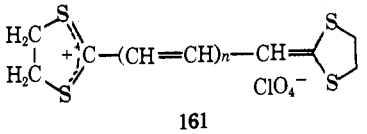


160a



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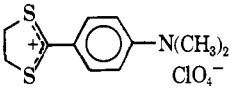

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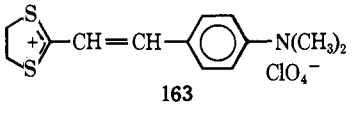

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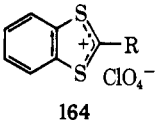

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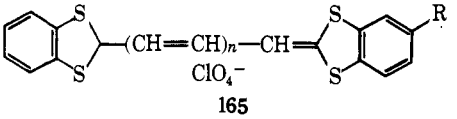

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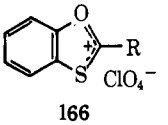

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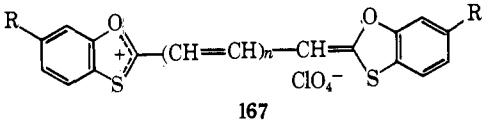
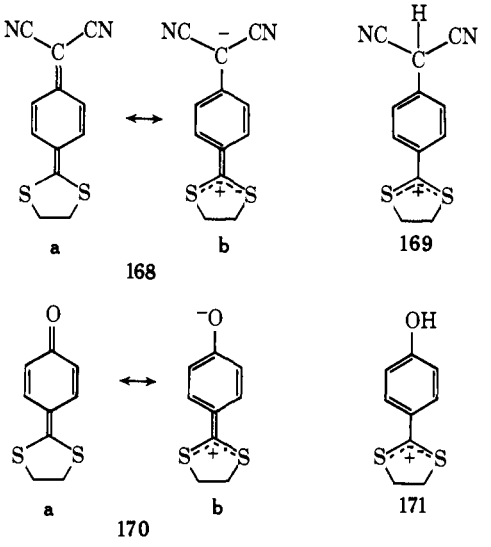


167

active methylene group in pyridine–Et_3N or acetic acid–pyridine. Compound **168**, for example, has a uv spectrum which greatly resembles its protonated form **169**. This is also found for **170** and its protonated form **171**. The resonance



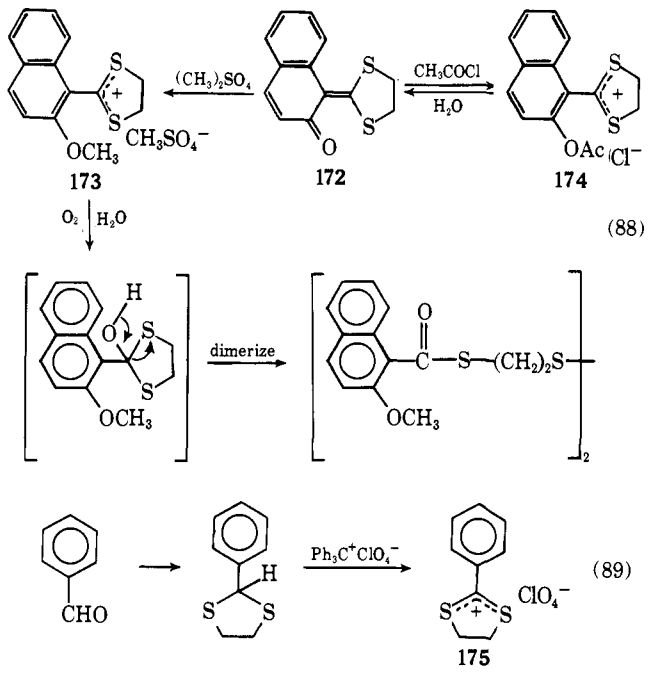
a 168 b 169

a 170 b 171

form **b** and the great stability of the dithiolanyl ion in **168, 170,** and related compounds plays an important role in the reaction of these compounds with acylating agents. For example, **172** reacts readily with acetyl chloride or dimethyl sulfate according to the paths shown in eq 88 which involve the stable 1,3-dithiolan-2-ylium ions **173** and **174**. Gompper also prepared 2-phenyl-1,3-dithiolan-2-ylium perchlorate (**175**) using Meerwein's method of hydride abstraction from a dithioacetal of benzaldehyde (eq 89).

In a series of papers Nakai, Ueno, and Okawara[116,117] have described the syntheses and ambident reactions of 2-dialkylamino-1,3-dithiolan-2-ylium salts. The reaction of 1,2-dichloroethane with sodium *N,N*-dimethyldithiocarbamate gave,

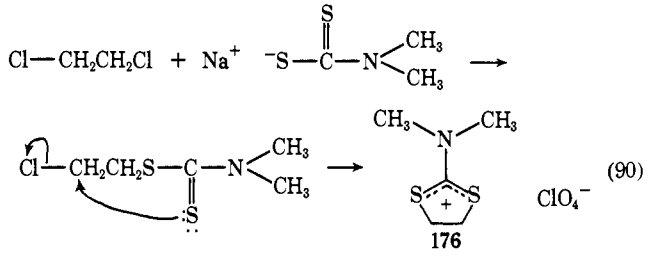
(116) T. Nakai, Y. Ueno, and M. Okawara, *Tetrahedron Lett.*, 3831, 3835 (1967).
(117) T. Nakai, Y. Ueno, and M. Okawara, *Bull. Chem. Soc. Jap.*, **43**, 156 (1970); **43**, 3175 (1970).



173 172 174 (88)

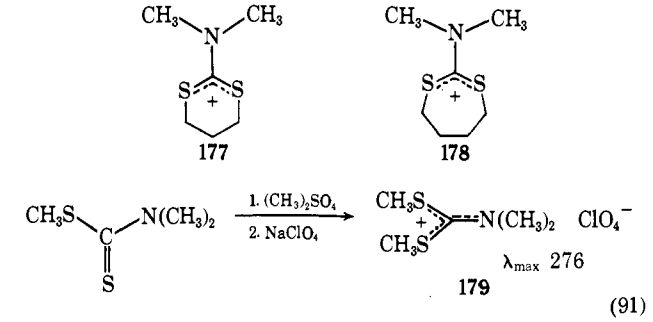
175 (89)

as a major product, 2-dimethylamino-1,3-dithiolan-2-ylium ion (**176**) which was isolated as its chloride, tetraphenylborate,



176 (90)

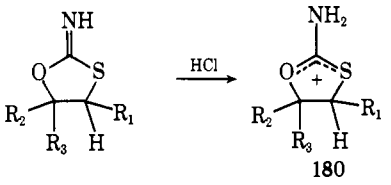
or perchlorate salt. Yields of **176** ranging from 51 to 65% were obtained in ethanol, ethylene glycol, DMF, and DMSO, but in dioxane and THF the yields were below 30%. By using 1,3-dichloropropane and 1,4-dichlorobutane in this reaction, the corresponding 2-dimethylamino-1,3-dithian-2-ylium and 1,3-dithiepan-2-ylium perchlorates (**177** and **178**) were prepared. Treatment of *S*-methyl *N,N*-dimethyldithiocarbamate with dimethyl sulfate followed with sodium perchlorate gave (eq 91)



177 178 179 (91)

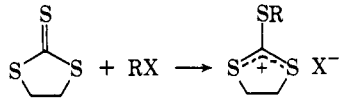
bis(methylthio)dimethylaminocarbonium perchlorate (**179**).

Other examples of sulfur-containing ions have been reported. The protonation of 2-imino-1,3-oxathiolanes gives stable 2-amino-1,3-oxathiolan-2-ylium salts (**180**).[118] Ethylene



180 (92)

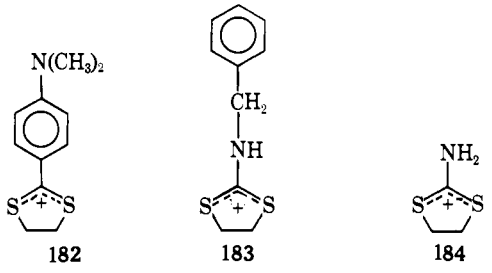
trithiocarbonate has been S-methylated to give the stable 2-thiomethyl-1,3-dithiolan-2-ylium ion and alkylated to give the series of 2-thiosubstituted ions **181**.[119] The condensation of



(93)

181a, R = CH_3, $X^- = I^-, ClO_4^-, CH_3SO_4^-$
b, R = $-CH_2COC_6H_4Br(p)$; $X^- = Br$

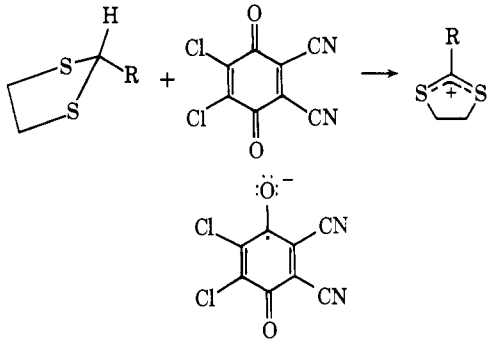
181a (X = I) with *N,N*-dimethylaniline gave 2-(*p*-*N,N*-dimethylanilino)-1,3-dimethylthiolan-2-ylium iodide (**182**), and reaction of **181a** with primary amines, for example, benzylamine, gave 2-(*N*-benzylamino)-1,3-dithiolan-2-ylium salts (**183**). The parent 2-amino-1,3-dithiolan-2-ylium salts **184**



182 183 184

were prepared on treatment of **181** with hydrazine hydrate.

1,3-Dithiolan-2-ylium ions have recently been prepared by dichlorodicyanoquinone (DDQ) oxidation.[120,121] The oxidation of thioacetals leads to stable salts (eq 94). The oxidation

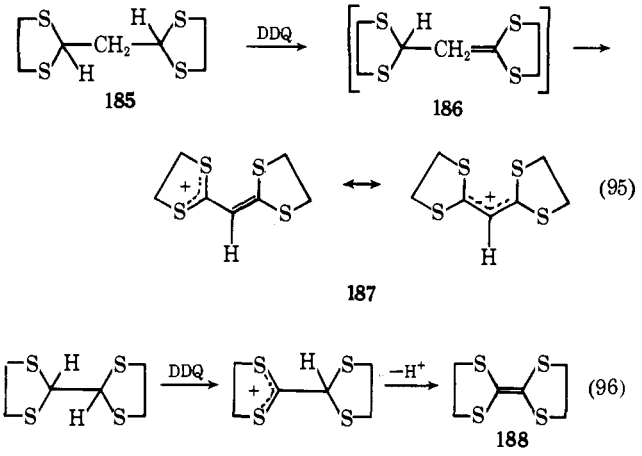


(94)

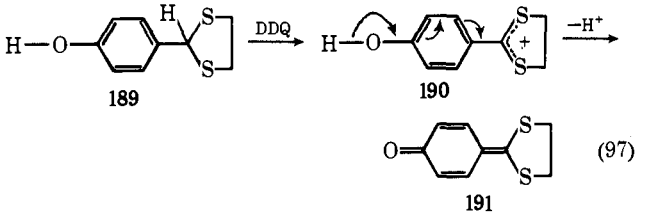
of 2,2′-bis(1,3-dithiolanyl)methane (**185**) proceeds through the ketene thioketal (**186**) to ion **187** which can be viewed as a tetrasubstituted allylic cation or a 1,3-dithiolan-2-ylium ion. When possible, the loss of a proton from the β-carbon occurs leading to ketene thioketals such as **188** (see eq 96).[120-128] In the case of 2-(*p*-hydroxyphenyl)-1,3-dithiolane (**189**), oxida-

(118) T. Wagner-Jauregg and M. Häring, *Helv. Chim. Acta*, 41, 377 (1958).

(119) R. Mayer and K. Schaefer, *J. Prakt. Chem.*, 26, 279 (1964).
(120) D. L. Coffen and P. E. Garrett, *Tetrahedron Lett.*, 25, 2043 (1969).
(121) D. L. Coffen, J. Q. Chambers, D. R. Williams, P. E. Garrett, and N. D. Canfield, *J. Amer. Chem. Soc.*, 93, 2258 (1971).
(122) L. B. Brahde, *Acta Chem. Scand.*, 8, 1145 (1954).
(123) D. L. Coffen, K. C. Bank, and P. E. Garrett, *J. Org. Chem.*, 34, 605 (1969).

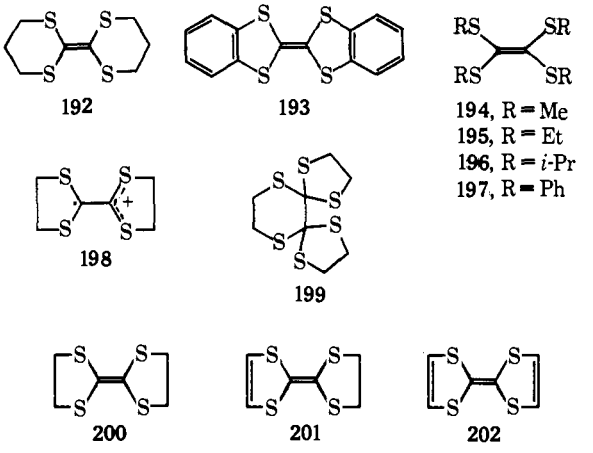


tion initially generates the 1,3-dithiolan-2-ylium ion (**190**) but subsequent rapid loss of proton generates the quinone **191**.[120]



Tetrathioethylene derivatives,[121] like their tetraaminoethylene counterparts, can be easily oxidized *via* successive discrete electron-transfer steps.[124-127] The similarity in behavior arises from the "electron-rich" double bond and the great stability of the cations resulting from one-electron oxidation. Recently, several electrochemical oxidations of tetrathioethylene derivatives have been reported.[121] Oxidation initially generates a cation radical, and the nature of these cations is of interest in this review. Polarographic oxidation potentials for the two tetrathioethylenes **192** and **193** at a rotating platinum electrode were reported by Hünig.[128,129] Geske and Merritt[130] reported the electrochemical oxidation of three tetraalkyltetrathioethylenes **194, 195,** and **196** as well as phenyl analog **197** and characterized the esr spectra of the cation radicals in terms of temperature-dependent intramolecular processes. Radical cation **198** has been identified as an intermediate in anodic oxidation of **199,** and its esr spectrum was reported.[131]

Finally, a thorough electrochemical study of **192, 197,** and **200–202** has been made, and all the recent electrochemical studies have been summarized.[121] Compounds **192, 197,** and **200–202** all are oxidized in two successive one-electron steps.[121] At slow sweep rates (<0.2 V sec^{-1}) both steps are electrochemically reversible for **192, 201,** and **202** but irreversible for **197** and **200**. At faster sweep rates (*ca.* 1 V sec^{-1}) the second wave in the cyclic voltammogram of **200** becomes reversible.[121]



Apparently the dications of **197** and **200** are so unstable that they react with solvent or residual water on the time scale of the experiment.

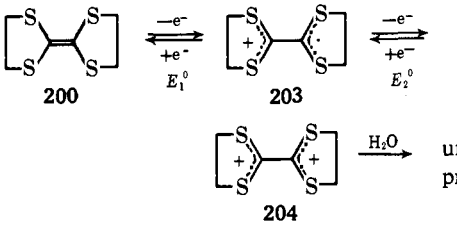
Table III lists the electrochemical potentials and both uv and esr data on **192, 197,** and **200–202**. As the π-electron system is extended going from **200** to **201** to **202,** the corresponding dications become less reactive. This extended conjugation results in a progressive decrease in the E_1^{01} values going from **200** to **202**. The E_1^{01} value for **192** and **200** are about the same. The difference in formal reduction potentials $E_2^{01} - E_1^{01}$ represents the E^{01} for coproportionation between the parent olefin and the dication. As can be seen, this potential is larger for the five- than for the six-membered ring system. The dications formed from **201** (10 π electrons) and from **202** (12 π electrons, electronically resembling biphenyls) are exceptionally stable. It should be remembered that Hart and Tomalia[73] were not able to generate oxygen analog **205** in several

Table III

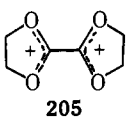
Electrochemical Potentials and Spectral Data for Compounds 192, 197, and 200–202

	192	200	201	202	197
E_1^{01} [a]	0.695	0.68	0.405	0.33	1.2
E_2^{01}	0.84	1.12	0.89	0.70	1.4[b]
$E_2^{01} - E_1^{01}$	0.145	0.44	0.485	0.37	0.2
λ_{max}[c]	391	568	470	435,580	488,611 unstable
ϵ[d]	7600	5050		22,500; 5910	
a_H		2.41	1.7	Single broad 3-G signal	Unresolved spectrum 2 G wide

[a] Formal reduction potentials in CH_3CN, 0.1 *M* TEAP (units, volts *vs.* sec). [b] Value was estimated from the second peak potential. [c] λ_{max} of the radical cation in nm. [d] Molar extinction coefficients in $cm^{-1}\ M^{-1}$.



(124) N. Wiberg and J. W. Buchler, *Angew. Chem., Int. Ed. Engl.*, 1, 406 (1962).
(125) D. M. Lemal and K. I. Kuwano, *J. Amer. Chem. Soc.*, 84, 1761 (1962).
(126) K. Kuwata and D. H. Geske, *ibid.*, 86, 2101 (1964).
(127) N. Wiberg, *Angew. Chem., Int. Ed. Engl.*, 7, 766 (1968).
(128) S. Hünig, *Pure Appl. Chem.*, 15, 109 (1967).
(129) S. Hünig, H. Schlaf, H. Kiesslich, and D. Schentzow, *Tetrahedron Lett.*, 2271 (1969).
(130) D. H. Geske and M. V. Merritt, *J. Amer. Chem. Soc.*, 91, 6921 (1969).
(131) N. D. Canfield, J. Q. Chambers, and D. L. Coffen, *J. Electroanal. Chem. Interfacial Electrochem.*, 24, A-7 (1970).

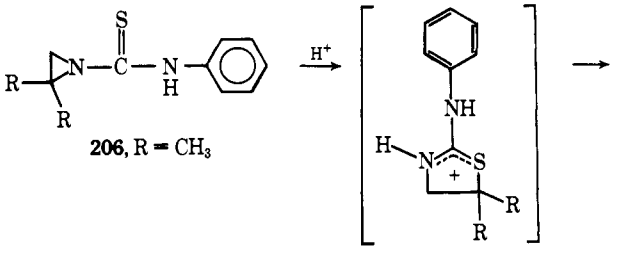


205

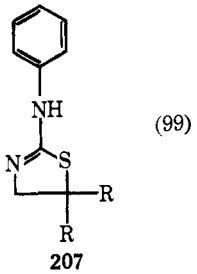
synthetic attempts and this agrees with the observation that its sulfur analog **204** is exceedingly reactive.

C. OXAZOLINIUM AND THIAZOLINIUM IONS

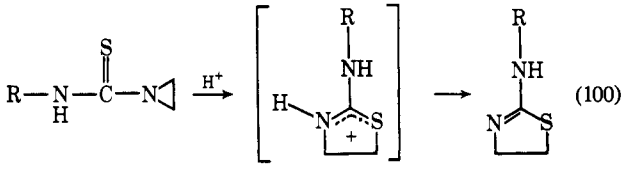
While the earliest examples of thiazolinium ions resulted from Gabriel's discovery of the acid-catalyzed isomerizations of 1-aziridinethiocarboxanilide into 2-anilino-2-thiazolines upon heating in concentrated HCl,[19] the salts of these heterocyclic compounds were not studied as such at that time. This acid-catalyzed reaction was perfected much later by Deutsch and Fanta[132] to give 90% yields of isolated 2-anilino-2-thiazolines. The reaction has been extended to substituted 1-aziridinethiocarboxyanilides (**206**),[133] 1-(*N*-cyclohexylthiocarbamyl)aziridine,[134,135] and 1-(*N*-benzylthiocarbamyl)aziridine[136] (see eq 99 and 100). Analogous sulfuric and phosphoric acid catalyzed



206, R = CH_3



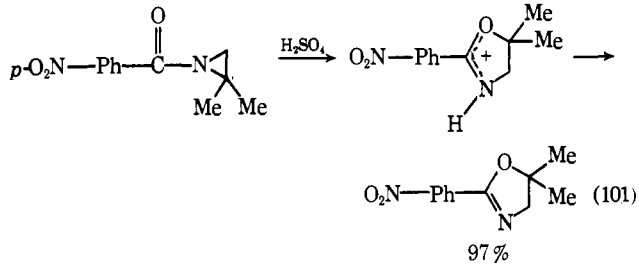
207 (99)



(100)

isomerizations of 1-(*N*-cyclohexylthiocarbamyl)aziridine and 1-(*N*-*m*-tolylthiocarbamyl)aziridine have been reported.[133] Unsymmetrical 1-(*N*-phenylthiocarbamyl)-2,2-dimethylaziridine (**206**) on treatment with hot concentrated HCl gives a 30% yield of 2-anilino-5,5-dimethyl-2-thiazoline (**207**).

In a very similar reaction, 1-aroylaziridines are isomerized to 2-aryl-2-oxazolines by $AlCl_3$ in refluxing heptane[136] and by

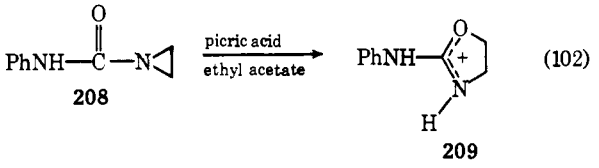


97%

(101)

concentrated H_2SO_4 at room temperature.[137] An example is shown in eq 101.[137]

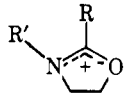
The isomerization of aziridine derivatives has been reviewed.[138] 1-Aziridinecarboxanilide (**208**) is converted into the



208 209 (102)

picrate of 2-anilino-Δ^2-oxazoline in refluxing ethyl acetate containing picric acid.[134] These reactions all have one thing in common, the presence of a thiazolinium or oxazolinium ion as an end product in the acid phase before neutralization and isolation of the parent heterocycle has been accomplished.

Oxazolines are weakly basic compounds which are easily converted to their corresponding oxazolinium salts. The lower members of the 2-oxazolines are water soluble and render water solutions alkaline to phenolphthalein. Their salts (**210**)



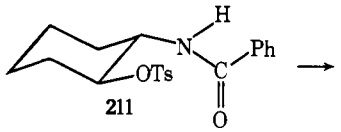
210a, R′ = H
b, R′ = COAr
c, R′ = Alk

include examples where R′ is hydrogen,[139] aroyl,[139] and alkyl.[140,141] While these salts have often been used in the identification of oxazolines, they are unstable toward hot water, owing to ring cleavage which usually generates the hydroxyamide. The hydrochloride salt of 2-oxazoline is particularly unstable and spontaneously hydrolyzes to *N*-(β-chloroethyl)formamide, but the higher members of the series are more stable. Owing to the potential use of 2-oxazolines and 4,5-dihydro-1,3-oxazines for local anesthetics,[142-145]

(132) A. S. Deutsch and P. E. Fanta, *J. Org. Chem.*, **21**, 892 (1956).
(133) M. Tisher, *Arch. Pharm.*, **291**, 457 (1958).
(134) Y. Iwakura and A. Nabeya, *J. Chem. Soc., Jap., Pure Chem. Sect.*, **77**, 773 (1956).
(135) Y. Iwakura and A. Nabeya, *Bull. Tokyo Inst. Technol.*, **42**, 69 (1961).
(136) H. W. Heine and Z. Proctor, *J. Org. Chem.*, **23**, 1554 (1958).
(137) H. W. Heine, M. E. Fetter, and E. M. Nicholson, *J. Amer. Chem. Soc.*, **81**, 2202 (1959).
(138) H. W. Heine, *Angew. Chem., Int. Ed. Engl.*, **1**, 528 (1962).
(139) A. A. Goldberg and W. Kelley, *J. Chem. Soc.*, 1919 (1948).
(140) F. M. Hamer and R. J. Rathbone, British Patent 541,330; *Chem. Abstr.*, **36**, 4767 (1942).
(141) I. G. Farbenindustrie, French Patent 848,028; *Chem. Abstr.*, **35**, 5716 (1941).
(142) M. Engelmann, U. S. Patent 2,027,031; *Chem. Abstr.*, **30**, 1519 (1936).
(143) M. Bockemuhl and R. Knoll, U. S. Patent 1,958,529; *Chem. Abstr.*, **28**, 4539 (1934).
(144) C. L. Rose, H. A. Schonle, and K. K. Chen, *Pharm. Arch.*, **11**, 81 (1940); *Chem. Abstr.*, **35**, 1522 (1941).
(145) R. Adams and M. T. Leffler, U. S. Patent 2,114,326; *Chem. Abstr.*, **32**, 4726 (1938).

antithyroid activity,[146] plant sprays,[147] analgesics,[148-149] central nervous system depressants,[150] antipyretics,[149] sedatives,[151] antitubercular activity,[152-154] antitumor activity,[155,156] anticorrosion agents,[157] passive components of azo dyes,[158,159] local antiseptics,[25] and many other uses, a large number of these compounds have been prepared and their salts isolated. No attempt will be made to review their preparation. While the hydrochloride salts were often used to isolate and identify 2-oxazolines and 4,5-dihydro-1,3-oxazines,[25,160-162] it has been the picrate salts which have been most often prepared.[24,162-171]

The chemistry of oxazolinium and other nitrogen-containing cations is not comprehensively treated here. Instead, a large part of this discussion parallels the treatment of the 1,3-dioxolan-2-ylium ions. The involvement of oxazolinium ions in solvolysis reactions where the leaving group has a neighboring amide function was first pointed out by Winstein, Goodman, and Boschan.[172] They showed that the solvolysis of *trans*-2-benzamidocyclohexyl tosylate ((**211**) in absolute ethanol proceeds 200 times faster than the corresponding *trans*-2-acetoxycyclohexyl tosylate where neighboring group participation had already been demonstrated. Solvolysis in ethanol or acetic acid generated the oxazolinium ion **212** which was isolated as both its *p*-toluenesulfonate and picrate salts or as the free oxazoline (**213**). Acylamino groups also participate in the *N*-bromosuccinimide bromination of *N*-*p*-methoxybenzoylallylamine (**214**). In a solvent of low nucleophilicity, such as acetic acid, oxazolinium bromides (*i.e.*, **215**) are the major products from the addition reaction.[173] It was



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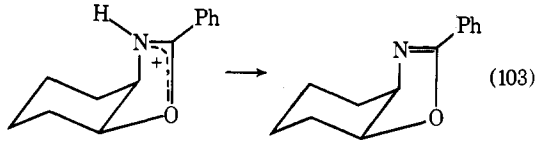
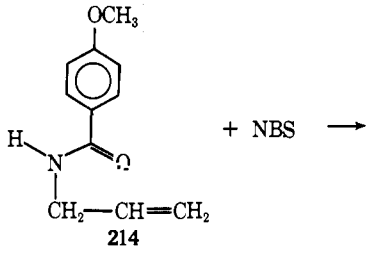
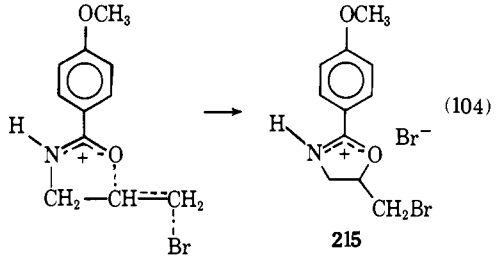


212 213 (103)

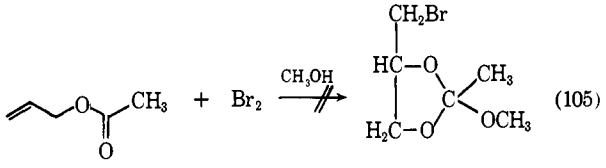


214



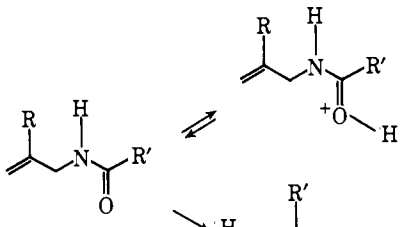
215 (104)

suggested that the participating ability of a neighboring benzamido group was greater than that of a neighboring acetoxy group since the bromination of allyl acetate gave no detectable cyclic ortho ester in methanol (eq 105).



(105)

In strong proton acids 2-substituted-5-methyl-2-oxazolines (**217a**) can be prepared from *N*-allylamides by heating.[174] The corresponding 5,5-dimethyloxazolines (**217b**) are rapidly formed from *N*-methallylamides without heating (see eq 107).[175] The product in the acid layer is the corresponding



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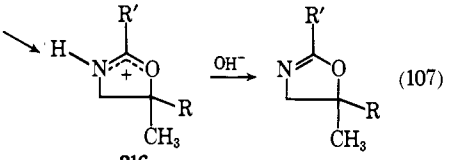

216 (107)

217a, R = H
b, R = CH_3

(146) W. H. Miller, R. O. Rublin, and E. B. Astwood, *J. Amer. Chem. Soc.*, 67, 2201 (1945).
(147) H. A. Bruson, U. S. Patent 2,282,931; *Chem. Abstr.*, 36, 6301 (1942).
(148) H. S. Mosher, M. B. Frankel, and M. Gregory, *J. Amer. Chem. Soc.*, 75, 5326 (1953).
(149) B. Y. Lesher and A. R. Surrey, *ibid.*, 77, 636 (1955).
(150) E. Test, L. Fontanella, G. Cristaini, and G. Gallo, *J. Org. Chem.*, 24, 1928 (1959).
(151) R. Fusco and E. Testa, *Farmaco, Ed. Sci.*, 12, 823 (1957); *Chem. Abstr.*, 52, 11853 (1958).
(152) T. Urbański, *Nature (London)*, 168, 562 (1951).
(153) T. Urbański, *Gruzlica*, 20, 157 (1952); 22, 681 (1954).
(154) T. Urbański, *et al.*, *Rocz. Chem.*, 26, 182 (1952); 28, 175 (1954); 29, 379 (1955).
(155) T. Urbański and B. Szczyciński, *ibid.*, 30, 1295 (1956).
(156) T. Urbański, *Nature (London)*, 187, 426 (1960).
(157) C. J. Schmidle, U. S. Patent 2,775,590; *Chem. Abstr.*, 51, 8811 (1957).
(158) W. Steinemann, U. S. Patent 2,901,473; *Chem. Abstr.*, 53, 22968 (1959).
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(160) M. Bergmann, *Z. Physiol. Chem.*, 137, 27 (1924).
(161) S. A. Karjala and S. M. McElvain, *J. Amer. Chem. Soc.*, 55, 2966 (1933).
(162) J. Takeda, *J. Pharm. Soc. Jap.*, No. 426, 691 (1917).
(163) S. Gabriel and J. Colman, *Ber.*, 47, 1866 (1914).
(164) E. Fromm, H. Barrenscheen, J. Frieder, L. Pirk, and R. Kapeller, *Justus Liebigs Ann. Chem.*, 442, 130 (1925).
(165) S. Gabriel and H. Ohle, *Ber.*, 54, 3158 (1921).
(166) M. Bergmann and A. Miekeley, *Z. Physiol. Chem.*, 140, 128 (1924).
(167) L. Birckenfach and M. Linhard, *Ber.*, 64, 1076 (1931).
(168) E. Fromm, R. Kapeller-Adler, W. Friedenthal, L. Stangel, J. Edlitz, E. Braumann, and J. Nussbaum, *Justus Liebigs Ann. Chem.*, 467, 240 (1928).
(169) P. Oxley and W. F. Short, British Patent 615,006; *Chem. Abstr.*, 43, 7512 (1948).
(170) M. W. Partridge and H. A. Turner, *J. Chem. Soc.*, 1308 (1949).
(171) A. F. McKay and R. O. Braun, *J. Org. Chem.*, 16, 1829 (1951).
(172) S. Winstein, L. Goodman, and R. Boschan, *J. Amer. Chem. Soc.*, 72, 2311 (1950).
(173) L. Goodman and S. Winstein, *ibid.*, 79, 4788 (1957).
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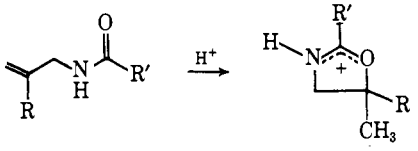
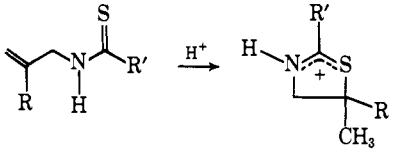
(175) S. P. McManus, J. T. Carroll, P. M. Grohse, and C. U. Pittman, Jr., *ibid.*, 1, 235 (1969).

oxazolinium ion, and its formation may be conveniently monitored by nmr until its yield has maximized.[174,175] At that point the acid layer may be neutralized to yield the heterocycle. A careful spectral study by McManus and Pittman[176] of oxazolinium (**218**) and thiazolinium (**219**) cations formed in strong acid cyclization reactions of *N*-allylamides, substituted *N*-allylamides, -urethans, -ureas, and -thioureas has now appeared.[176] Upon introduction into the acid, the



(108)

218

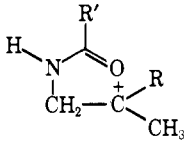


(109)

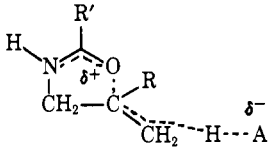
219

R = H, CH_3, C_6H_5
R = H, CH_3, C_6H_5, NH_2, p-$CH_3C_6H_4$, p-$NO_2C_6H_4$, OCH_3, NHC_6H_5

N-allyl derivatives were only O- or S-protonated at room temperature, but upon heating cyclization to the corresponding oxazolinium and thiazolinium ions occurred. When R = CH_3 or C_6H_5 cyclization occurred immediately. It was argued that the great difference in the rate of cyclization between the *N*-allyl and substituted *N*-allyl derivatives favors the intervention of a discrete carbonium ion intermediate (**220**) after protonation at the double bond and before cyclization.[176] Where a tertiary ion can be formed (R = CH_3, C_6H_5) the cyclization is very rapid, but where a secondary ion must be formed (R = H) cyclization is slow. If direct formation of the cyclic ions, by neighboring-group participation during C-protonation, occurred this should result in similar cyclization rates when R = H, CH_3, or C_6H_5. This follows because the R group in transition state **221** would not be ex-



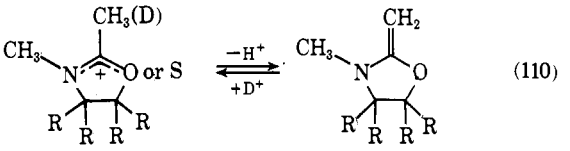
220



221

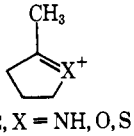
pected to contribute much to the stability of **221** if neighboring group participation is well developed in that transition state. The stabilizing effect of the developing oxazolinium ion should swamp out the effect of the methyl group.

The charge distributions in ions **218** and **219** were studied by nmr spectroscopy, and a discussion of these spectra can be found in section VII.A. Oxazolinium and thiazolinium ions did not undergo H–D exchange at the C-2 methyl group in 96% D_2SO_4 after 14 hr at 120° or in 65% D_2SO_4 after 10 min at 122°.[176] However, H–D exchange does occur in 0.005 and 0.1 *M* HI–D_2O solutions from the 2-methyl group of

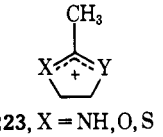


(110)

2,3,4,4-tetramethyl-2-oxazolinium iodide (eq 110).[177] When compared to other heteroatom stabilized cyclic ions, certain trends are evident. Five-membered ring cyclic carbonium ions (**222**) with a single adjacent heteroatom (O, N, S) incur H–D exchange among both the C-2 methyl hydrogens and the C-3 methylene hydrogens. Five-membered ring ions with two heteroatoms (**223**) are stabilized sufficiently by resonance that H–D exchange does not occur in strong acids.

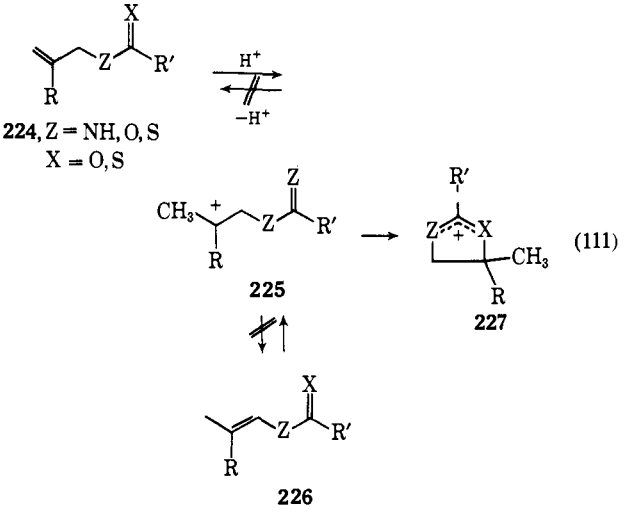


222, X = NH, O, S (NR)



223, X = NH, O, S; Y = NH, O, S

The stability of oxazolinium and thiazolinium ions is remarkable. In 96% H_2SO_4 they are stable at 130° for over an hour and do not degrade measurably in 24 hr at 122°.[175] Many remarkable similarities exist between oxazolinium, thiazolinium, and dioxolan-2-ylium ions. Studies in D_2SO_4, as summarized in eq 111, show the intermediate acyclic carbo-



(111)

224, Z = NH, O, S; X = O, S

225

226

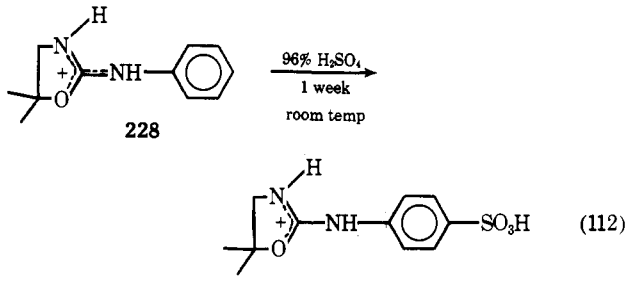
227

nium ion (**225**) is not in equilibrium with its starting allyl derivative (**224**) or vinyl derivative (**226**), but this ion must be captured by O (or S) before proton loss occurs.[175] The great resistance to H–D exchange at the 2-methyl group indicates the charge is very effectively localized over the two heteroatoms. The 2-amino-2-thiazolinium cation may be heated for a week to 90° in 71% H_2SO_4 without sign of degradation, and the ability of the heteroatoms to stabilize positive charge in this system is further illustrated by the para sulfonation of the phenyl ring in the 2-anilino-5,5-dimethyl-2-thiazolinium cation (**228**) after a week at 22° in 96% H_2SO_4 (eq 112).

The lack of cleavage of oxazolinium and thiazolinium ions in strong acids is in contrast to the behavior of analogous 1,3-dioxolan-2-ylium and 1,3-oxathiolan-2-ylium ions which

(176) S. P. McManus, J. T. Carroll, and C. U. Pittman, Jr., *J. Org. Chem.*, **35**, 3768 (1970).

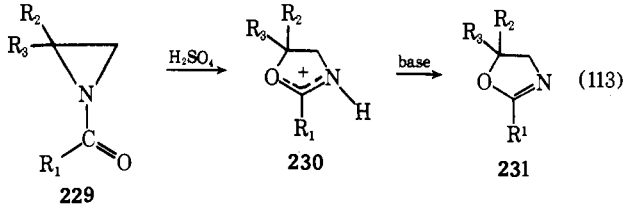
(177) P. Allen and J. Ginos, *ibid.*, **28**, 2759 (1963).



(112)

readily undergo A_{AL}-1 cleavage[87] at elevated temperatures. This suggests that the introduction of a nitrogen for an oxygen results in greater stability for the cation, a result in agreement with solvolysis studies of derivatives with neighboring benzamido *vs.* benzoyl groups.

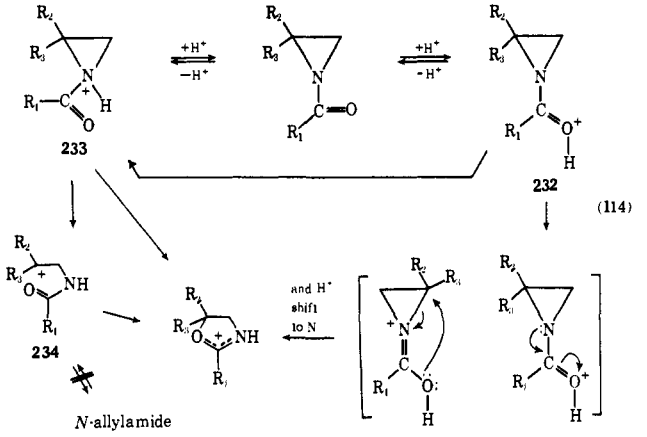
Pittman and McManus[178] and Heine and coworkers[137,138] have reported essentially quantitative conversion of *N*-acylaziridines to oxazolinium ions in sulfuric acid. This reaction appears remarkably similar to the acid-catalyzed rearrangement of cyclopropyl ketones which were discussed in detail in section IV.A (see eq 37). The conversion of 1-*p*-nitrobenzoyl-2,2-dimethylaziridine (**229f**) into 2-*p*-nitrophenyl-5,5-dimethyloxazoline[137] (**231f**) proceeds through oxazolinium ion **230f**. The nmr spectra of oxazolinium ions **230a–e** were



(113)

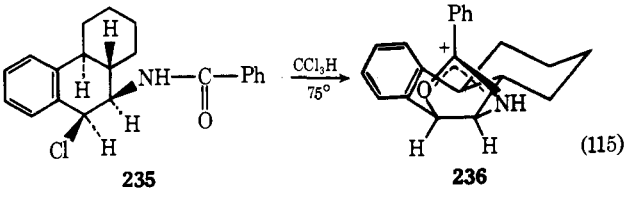
	R_1	R_2	R_3
a	CH_3	H	H
b	CH_3	CH_3	H
c	CH_3	CH_3	CH_3
d	C_6H_5	H	H
e	C_6H_5	CH_3	H
f	*p*-$O_2NC_6H_4$	CH_3	CH_3

obtained[178] and are discussed in section VII.A. By using FSO_3H–SbF_5–SO_2 at −55°, stable O-protonated 1-acylaziridines (**232**) could be observed,[178,179] but at higher temperature only rearrangement products are seen.[178] The potential mechanisms for this rearrangement to oxazolinium ions are presented in eq 114 below. O-Protonation of acylaziridines could be followed by concerted ring opening to an O-protonated oxazoline, which immediately converts into the observed oxazolinium ions by deprotonation–protonation. More likely, N-protonated acylaziridines (**233**) exist in equilibrium with O-protonated or unprotonated acylaziridines. The N-protonated species could rearrange by a direct concerted process to the oxazolinium ion or it could proceed through a short-lived acyclic carbonium ion **234**. N-Protonated *N*-acylaziridines have now been[179] directly observed and their existence lends credence to this route. The lack of H–D exchange during rearrangement[178] demonstrated that, if ion **234** has a discrete existence, its lifetime is too short to permit equilibration with the corresponding *N*-allylamide.



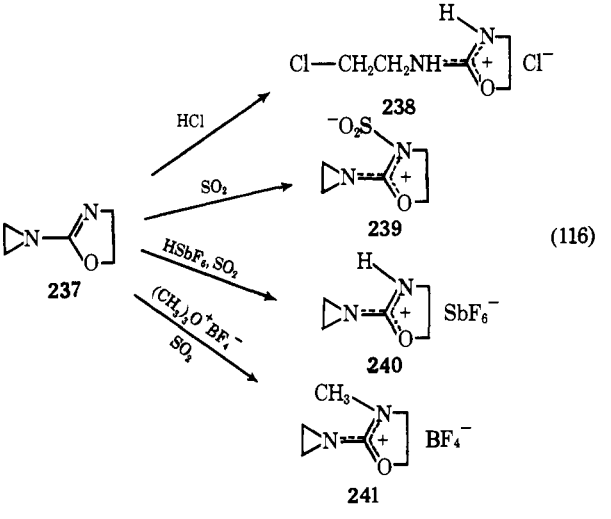
(114)

A few other observations of oxazolinium and thiazolinium cations and their salts are noteworthy. When a chloroform solution of 9(a)-chloro-10(e)-benzamido-1,2,3,4,4a,9,10,10a-(trans-4a,10a)octahydrophenanthrene (**235**) was warmed at 75° for 10–20 min, the formation of oxazolinium ion **236** was noted. The cis fusion was demonstrated by nmr.[180]



(115)

Tomalia, Ojha, and Thill[181] have prepared a series of 2-(1-aziridinyl)-2-oxazolinium ions (**238–241**) from 2-(1-aziridinyl)-2-oxazoline (**237**). The most basic site in this molecule



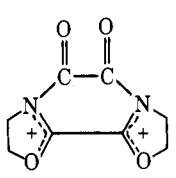
(116)

is the oxazoline nitrogen. Thus, protonation, methylation, and coordination with Lewis acid take place at that site as they did in the model compound 2-dimethylamino-2-oxazoline. Spectral data indicated significant delocalization of charge to the aziridine nitrogen, despite the fact that angle strain prevents the aziridine nitrogen from being sp^2 hybridized. It is interesting to note that aziridines are usually more basic

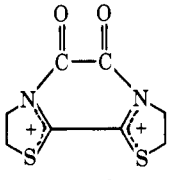
(178) C. U. Pittman, Jr., and S. P. McManus, *J. Org. Chem.*, **35**, 1187 (1970).
(179) G. A. Olah and P. J. Szilagyi, *J. Amer. Chem. Soc.*, **91**, 2949 (1969).
(180) W. L. Nelson and D. D. Miller, *J. Org. Chem.*, **35**, 1185 (1970).
(181) D. A. Tomalia, N. D. Ojha, and B. P. Thill, *ibid.*, **34**, 1400 (1969); also D. A. Tomalia, Dow Chemical Co., unpublished results, private communication with S. P. McManus, July 6, 1971.

than 2-oxazolines.[182,188] However, if protonation were to occur at the aziridine nitrogen in 2-(1-aziridinyl)-2-oxazolines, no delocalization of charge would be possible as is the case when protonation occurs at the oxazoline nitrogen.

Contrary to the results with dioxolan-2-ylium ions, oxazolinium and thiazolinium dications **242a** and **b** have been synthesized by Tomalia.[181] Their properties have not yet been published, but their very existence testifies to the great stability of oxazolinium (thiazolinium) ions.

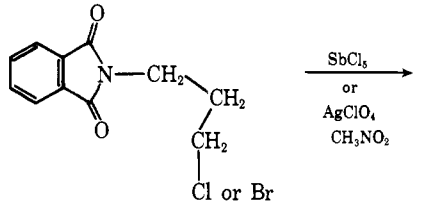


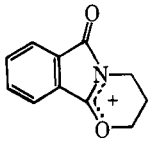
242a



242b

Treatment of *N*-(3-halopropyl)phthalimide with either $SbCl_5$ or $AgClO_4$ results[184] in the formation of the stable salt **243** in greater than 90% yields.

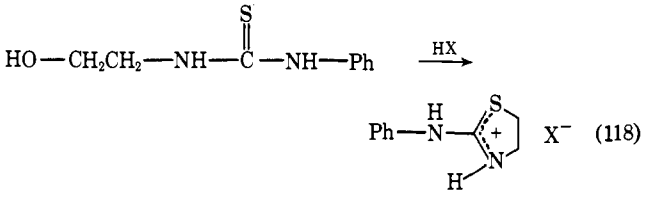




(117)

243

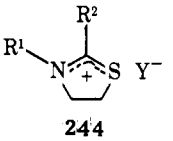
Thiazolinium salts have been prepared by the reaction o substituted phenyl isothiocyanates, such as *p*-tolyl isothio cyanate, with the hydrobromide salts of haloethylamines,[185] by the treatment (eq 118) of *N*-(2-hydroxyethyl)thioureas in



(118)

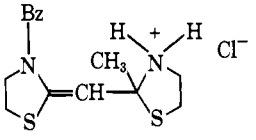
strong acids[186] and by simple protonation or quaternization of thiazolines.[187]

Clark and Sykes[187] recently prepared a variety of 2-substituted 2-thiazolinium salts (**244**) by direct quaternization of the corresponding 2-thiazolines with rigorous exclusion of moisture. With 2-methyl-2-thiazoline care had to be taken to avoid the formation of cyanine-type compounds. For example, the reaction of benzoyl chloride with 2-methyl-2-



244

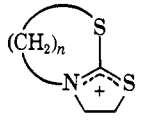
	R^1	R^2	Y
244a	$PhCH_2$	Me	Br
b	$PhCH_2$	Ph	Br
c	Me	MeS	I
d	p-$NO_2C_6H_4CH_2$	p-$NO_2C_6H_4CH_2S$	Br
e	$PhCH_2$	MeS	I
f	$PhCH_2$	$PhCH_2S$	Br
g	$PhCH_2$	$PhCH_2S$	Cl
h	PhCO	$PhCH_2S$	Br



245

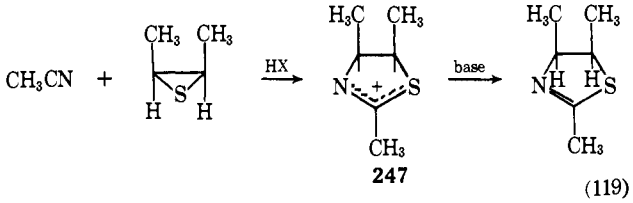
thiazoline gave azomethine salt **245**. By S-alkylation or -acylation of 2-thiazoline-2-thiol, both 2-alkyl- and 2-acylthio-2-thiazolinium salts can be prepared.[187-189] These salts are summarized by structure **244a-h**.

The reaction of 2-thiazoline-2-thiol with 1,2-dibromoethane and 1,3-dibromopropane gave the bicyclic salts **246a** and **246b** and not the expected bis salts. Treatment of 2-thiazo-



246a, $n = 2$
b, $n = 3$

line-2-thiol by acyl halides gives either *S*-acyl derivatives[190,191] or *N*-acyl derivatives,[192-194] but a definite interpretation of these results has not appeared. Helmkamp and coworkers[195] have reported a stereospecific route to a series of thiazoline salts consisting of the treatment of an episulfide with a nitrile in the presence of a strong acid. For example, the trinitrobenzenesulfonate salts of *trans*- and *cis*-2,4,5-trimethylthiazoline (**247**) were prepared, respectively, from *trans*- and *cis*-2-butene episulfide and acetonitrile (eq 119). The highest yields were obtained in sulfuric acid which was used in conjunction with acetonitrile, benzonitrile, and phenylacetonitrile. The mechanism suggested involves protonation of



247

(119)

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(184) S. Hünig and L. Geldern, *J. Prakt. Chem.*, **24**, 246 (1964).
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(189) J. C. Crawhall and D. F. Elliott, *J. Chem. Soc.*, 3094 (1952).
(190) J. B. Niederl and W. F. Hart, *J. Amer. Chem. Soc.*, **61**, 1145 (1939).
(191) A. H. Goddin and N. F. Searle, U. S. Patent 2,516,313; *Chem. Abstr.*, **45**, 810 (1951).
(192) L. B. Clapp and J. W. Watjen, *J. Amer. Chem. Soc.*, **75**, 1490 (1953).
(193) F. Runge, Z. El Heweki, H. J. Renner, and E. Taeger, *J. Prakt. Chem.*, **11**, 284 (1960).
(194) C. S. Dewey and R. A. Bafford, *J. Org. Chem.*, 30, 491 (1965).
(195) G. K. Helmkamp, D. J. Pettit, J. R. Lowell, Jr., W. R. Mabey, and R. G. Wolcott, *J. Amer. Chem. Soc.*, **88**, 1030 (1966).

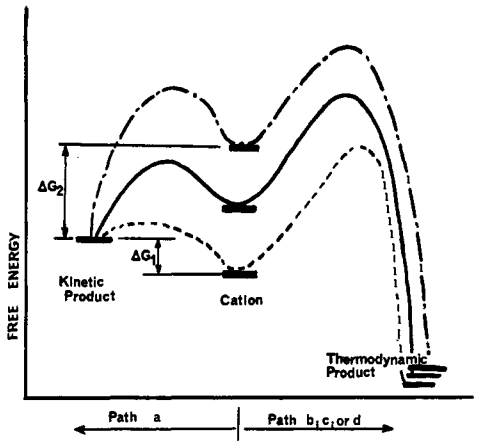
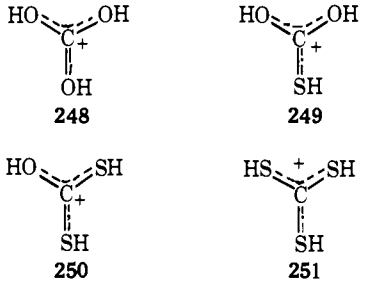


Figure 1. Effect of ambident cation stability.

the episulfide followed by nitrile nitrogen attack at the protonated episulfide carbon with ring opening to give a nitrilium ion. This is followed by nucleophilic attack by sulfur on carbon and a deprotonation–protonation sequence. When *sym*-dichloroacetone is treated with thiobenzamide, it gives thiazolinium chloride.[196]

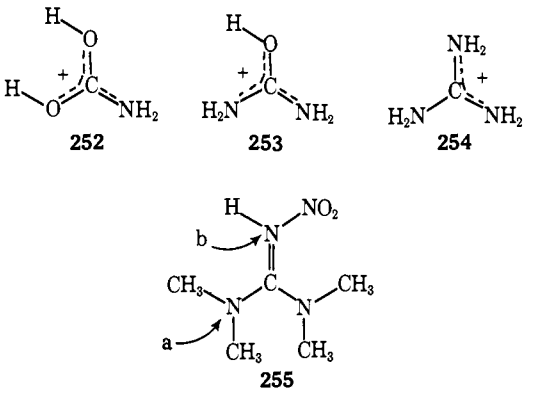
Open-chain analogs of 2-substituted-1,3-dioxolan-2-ylium and 1,3-dithiolan-2-ylium ions have been studied. These include protonated carbonic (**248**),[197] protonated thiocarbonic (**249**),[198] dithiocarbonic (**250**),[198] and trithiocarbonic (**251**)[198] acids.



248 **249**

250 **251**

The amino analogs have also been observed in acid media. Protonated carbamic acid **252**[199] and stable crystalline salts of protonated urea **253** and guanidine **254**[198,200–202] have all been observed in HSO_3F–SbF_5 by ^1H, ^{13}C, and ^{15}N magnetic resonance. Finally, from nmr studies, Price and coworkers[203] concluded that 1,1,3,3-tetramethyl-2-nitroguanidine (**255**) is protonated at the dimethylamino site (a) in strong acids and not at the imino nitrogen (b).



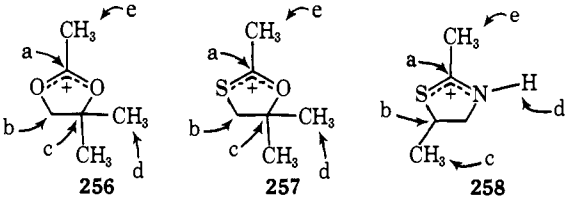
252 **253** **254**

255

V. Mechanisms of Reaction

A. AMBIDENT NATURE

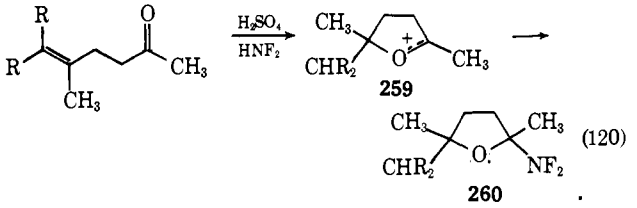
The ambident nature of 1,3-dioxolan-2-ylium and related cations is illustrated by structures **256–258** where bases or



256 **257** **258**

nucleophiles may react at positions a through e. In each case, reaction at position a involves the least bond reorganization, and this will tend to be the kinetic path. In **256** reaction at position b or c will regenerate an ester with its own resonance stabilization. However, bond reorganization will be extensive, and a higher $\Delta G^{\ddagger}$ is necessary. Thus, paths b and c in **256** and **257** will be thermodynamically favored but kinetically slower than path a. A base may also abstract a proton by path d. In **256** and **257** this leads to ring opening and formation of an ester (or thiolester) in a thermodynamic route. In **258** abstraction of a proton by path d gives the corresponding thiazoline. In each case, base may abstract a proton *via* path e, giving the heterocycle with an exo double bond.

The effect of the stability of the ambident cation on the course of the reaction may be illustrated in Figure 1. When the cation is more unstable (energy rich), the magnitude of ΔG_1, in an exothermic sense, is greater. As the cation is increasingly stabilized, the kinetic route becomes increasingly less attractive because the value of ΔG_1 is less exothermic (or more endothermic). Temperature also plays a major role in which pathway will be observed. Heating, of course, favors the thermodynamic paths, and running reactions at low temperatures may facilitate isolation of kinetic products. One example of these principles is the oxolan-2-ylium ion **259** (eq 120) which reacts with HNF_2 to capture NF_2^- by

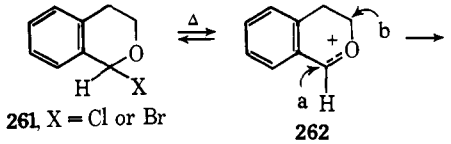


259 **260** (120)

(196) K. Brown and R. A. Newberry, *Tetrahedron Lett.*, 2797 (1969); also see *Quart. Rep. Sulfur Chem.*, 3 (4), 1968.
(197) G. A. Olah and A. M. White, *J. Amer. Chem. Soc.*, 90, 1884 (1968).
(198) G. A. Olah and A. M. White, *ibid.*, 90, 6087 (1968).
(199) G. A. Olah and M. Calin, *ibid.*, 90, 401 (1968).
(200) C. R. Redpath and J. A. S. Smith, *Trans. Faraday Soc.*, **58**, 462 (1962).
(201) R. Stewart and L. J. Muenster, *Can. J. Chem.*, **39**, 401 (1961).
(202) W. Kutzebrugg and R. Mecke, *Spectrochim. Acta*, **17**, 530 (1961).
(203) E. Price, R. D. Barefoot, A. S. Tompa, and J. U. Lowe, Jr., *J. Phys. Chem.*, 71, 1608 (1967).

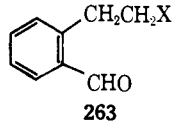
path a.[204] Ion **259** with only one heteroatom is energy rich, and ΔG_1 is large enough that kinetic product **260** can be isolated.

The thermal rearrangement of the 1-halogenoisochromans **261** *via* ambident cation **262** is another example.[205] At low temperatures the kinetic product (**261**) is stable, but at higher temperatures only *o*-halogenoethylbenzaldehyde (**263**) is obtained (eq 121). It is thought that oxolan-2-ylium ions all



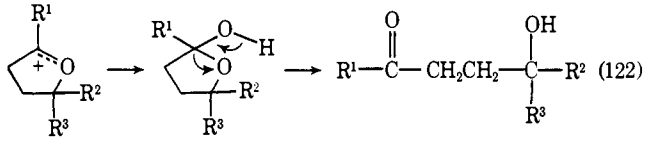
261, X = Cl or Br

262



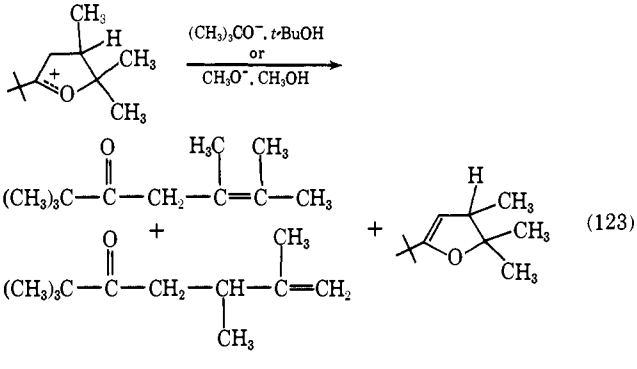
263 (121)

react by path a to give the observed γ-hydroxy ketone products which are obtained on adding the H_2SO_4 solutions to aqueous base (eq 122).[60] Steric hindrance can modify the



(122)

path. If path a is sterically retarded, ring opening to give the thermodynamic products can occur as illustrated by eq 123.[62]



(123)

Hünig[6] pointed out that the effect of the attacking nucleophile on the course of the reaction depends mainly on the energy of the resulting kinetic product, because the free energy of activation of the kinetic path is so much smaller than that for the thermodynamic route. This is illustrated in Figure 2 where the approximation has been made that the nucleophile's effects on ΔG_2 and $\Delta G_2^{\ddagger}$ are negligible in comparison. The kinetic product is usually more stable when strongly nucleophilic or basic reagents (CH_3O^- *vs.* CH_3OH, CN^- *vs.* I^-, or H^- *vs.* ^-OTs or ^-OBs) are used. Examples of this principle are listed in Table IV which summarizes the reaction of a representative series of ambident cations with various nucleophiles. This principle often, but not always, predicts the correct mode of opening. A few examples are discussed here including apparent violations of Hünig's rationale.

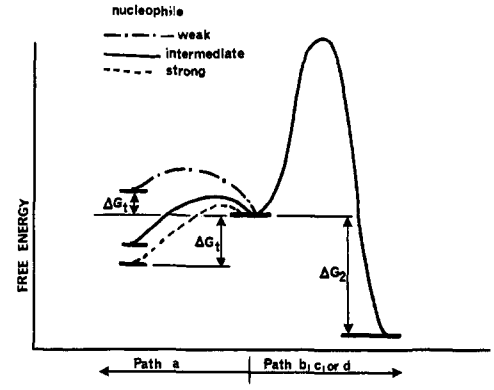
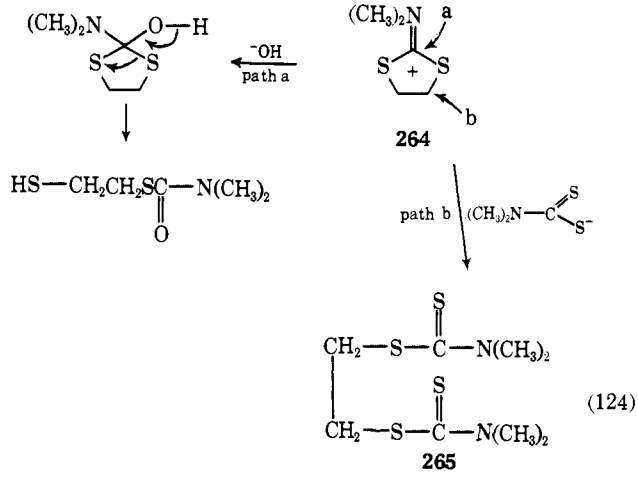


Figure 2. Effect of the nucleophile.

The 2-(dimethylamino)-1,3-dithiazolin-2-ylium ion (**264**) is an energy-poor (stable) ambident cation. Thus, it might be expected that only strongly basic reagents would offer any chance for reaction *via* path a. Nakai and coworkers[116,117] showed that ^-OEt and ^-OH would react by path a, but the more weakly basic dithiocarbamate anion attacks a neutral (sp^3) carbon at the 4 position (path b) to give ring open product **265** (see eq 124). The reaction of ^{18}O-labeled 2,3-di-



264

265 (124)

bromopropyl benzoate with weakly nucleophilic thiourea proceeds through 1,3-dioxolan-2-ylium ion (**266**) which opens by nucleophilic attack at C-5 (path b) as shown in eq 125.[206] Nucleophilic attack occurs at the least hindered position. Weakly nucleophilic bromide ion also opens **266** *via* path b.[207] It is noteworthy that ion **266** is more energetic than ion **264**, and reactions *via* path a should be more prevalent. In fact, path a is the mode by which water and alcohols react with 1,3-dioxolan-2-ylium ions. This has been shown in several studies[82,84] where the ring is fused to a six-membered ring (eq 126). On the other hand, the weakly nucleophilic acetate anion opens the ring by path b.[82,208,209] At first glance this rationale implies that thiourea, which causes **266** to open *via* path b, is a weaker base than water and alcohols which react with 1,3-dioxolan-2-ylium ions *via* path a. It is known that thiourea is more nucleophilic than water,

(204) K. Baum, *J. Amer. Chem. Soc.*, 90, 7083 (1968).
(205) E. Schmitz, *Chem. Ber.*, 91, 1133 (1958); A. Rieche and E. Schmitz, *ibid.*, 89, 1254 (1956).
(206) E. D. Sverdlvov, V. P. Zvolinskii, B. E. Zaitsev, and V. M. Fedoseev, *Dokl. Akad. Nauk SSSR*, 166, 1143 (1966).
(207) J. H. C. Nayler, *J. Chem. Soc.*, 189 (1959).
(208) K. B. Gash and G. U. Yuen, *J. Org. Chem.*, 34, 720 (1969).
(209) K. B. Gash and G. U. Yuen, *ibid.*, 31, 4234 (1966).

Table IV

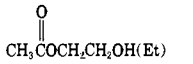
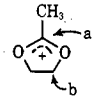
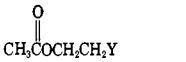
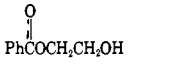
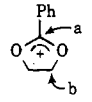
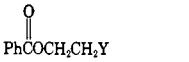
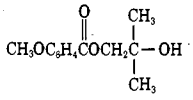
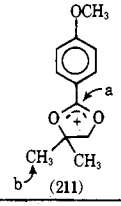
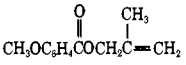
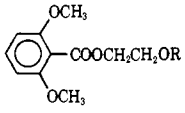
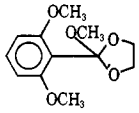
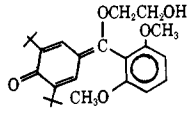
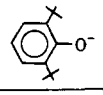
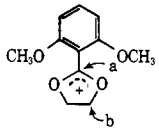
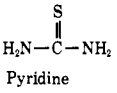
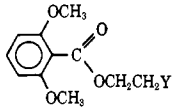
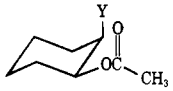
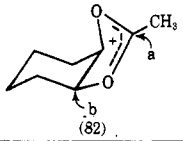
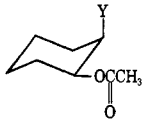
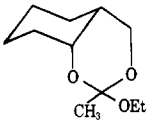
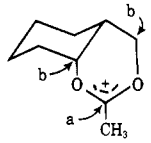
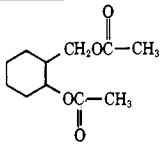
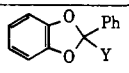
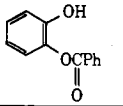
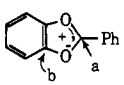
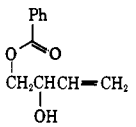
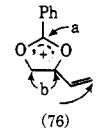
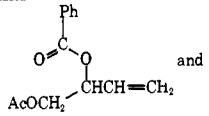
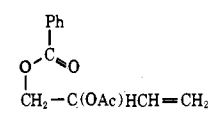
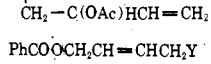
Product path a	*Nucleophile Y*	*Ambident cation (ref)*	*Nucleophile Y*	*Product path b*
 	CH_3O^- $C_2H_5O^-$ BuO^- CN^- H_2O EtOH	 (48)	I^-, Br^-, Cl^-, Et_3N	
 	EtO^- CN^- H_2O	 (48)	I^-, Et_3N	
	HO^-	 (211)	Pyridine	
 R = H, CH_3   	H_2O CH_3OH CH_3OH	 (68)	Br^- Thiophene  Pyridine	
	CH_3COOH H_2O	 (82)	CH_3COO^- ^-OTs Cl^-, Br^-	
	C_2H_5OH	 (85,86)	CH_3COOH CH_3COO^-	 mixture of *cis* and *trans*
 	PhMgBr EtO^- CH_3O^- H_2O	 (79)	Attack *via* path b prevented by reluctance of aromatic ring to undergo nucleophilic attack	
	H_2O	 (76)	CH_3COO^- CH_3CN C_6H_6	 and  

Table IV (Continued)

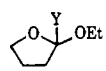
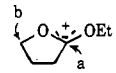
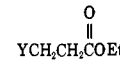
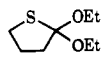
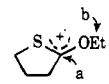
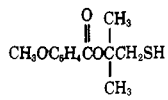
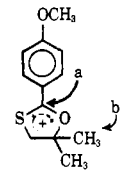
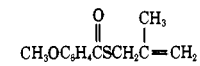
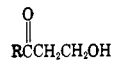
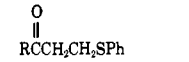
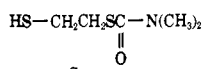
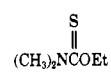
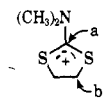
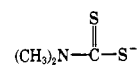
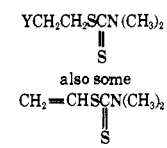
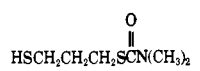
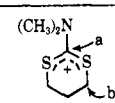
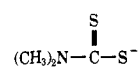
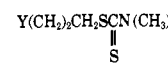
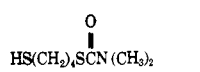
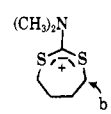
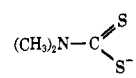
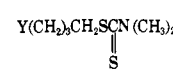
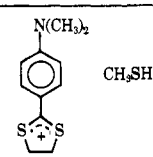
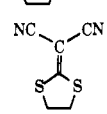
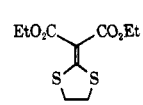
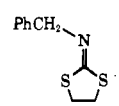
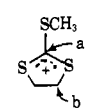
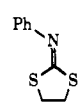
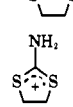
Product path a	*Nucleophile Y*	*Ambident cation (ref)*	*Nucleophile Y*	*Product path b*
	EtO^- NR_3	 (43)	I^-, Br^-, Cl^-, PhO^-, CH_3COO^- $ArNH_2$	
	EtO^-	 (43)	EtOH	
	^-OH	 (211)	$(CH_3)_3CO^-$	
	^-OH	 (63, 211)	PhS^-	
  	CN^- $H_2O, ^-OH$ EtO^-	 (116, 117)	RS^- Et_3N Bu_2NH 	
	^-OH	 (116, 117)		
	^-OH	 (116, 117)		
	$ArN(CH_3)_2$			
	$NCCH_2CN$			
	$CH_2(CO_2Et)_2$			
	$PhCH_2NH_2$	 (119)		
	$PhNH_2$			
	N_2H_4			

Table IV (Continued)

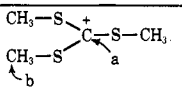
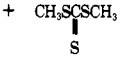
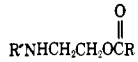
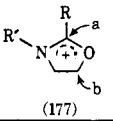
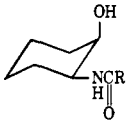
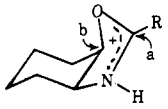
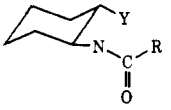
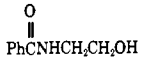
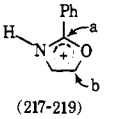
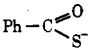
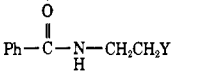
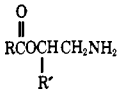
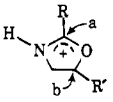
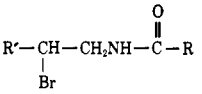
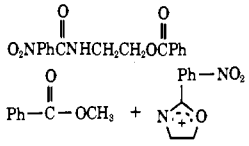
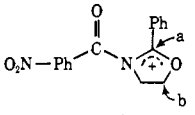
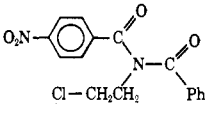
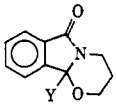
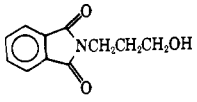
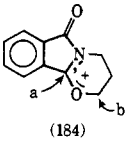
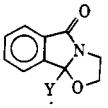
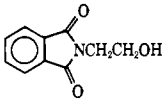
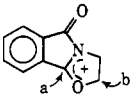
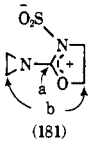
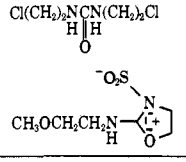
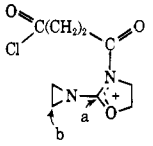
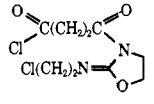
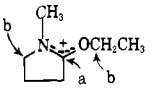
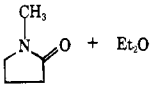
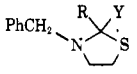
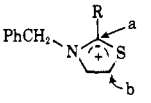
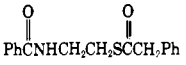
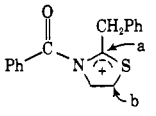
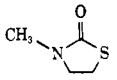
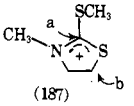
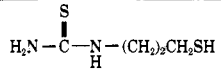
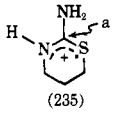
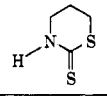
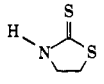
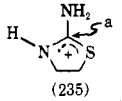
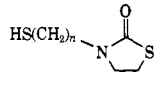
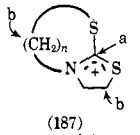
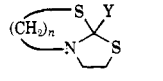
Product path a	*Nucleophile Y*	*Ambident cation (ref)*	*Nucleophile Y*	*Product path b*
	EtOH			
$(CH_3S)_2C{=}O$ $(CH_3S)_4C$	H_2O CH_3SH	 (105)	I^-, CN^-, Br^-, pyridine	YCH_3 + 
	H_2O	 (177)		
	H_2O	 (220)	CH_3COO^- ^-OTs Cl^-	
	^-OH	 (217-219)	HCl·EtOH  $O_2NC_6H_4CO_2^-$	
	1 mol of HBr	 (217)	Excess HBr	
	H_2O CH_3OH	 (223)	Cl^-	
 	CN^- EtO^- $^-CH_2NO_2$ pyridine H_2O	 (184)		
 	CN^- H_2O	 (184)		
		 (181)	HCl CH_3OH	
		 (181)	Cl^-	

Table IV (Continued)

Product path a	*Nucleophile Y*	*Ambident cation (ref)*	*Nucleophile Y*	*Product path b*
	EtO^-	 (43)	EtOH	
	PhS^- BH_4^- (in DMF)	 (187)		
	H_2O	 (187)		
	^-OH	 (187)		
	H_2S-H_2O	 (235)		
	H_2S-EtOH			
	H_2S-EtOH	 (235)		
	^-OH	 (187) $n = 2,3$		
	BH_4^- (H^-) PhS^-			

^-OH, and CH_3O^- toward methyl iodide. The separation of nucleophile strength and base strength in Hünig's approach is not always clear. The path b opening caused by thiourea in eq 125 could possibly be rationalized in terms of Pearson's hard and soft acid–base theory. In this view oxygen, which is a harder base than sulfur, would attack the ion at the hard acid site (carbon 2). On the other hand, the softer base sulfur could be envisioned as preferring attack at the softer acid site *via* path b. At present, neither approach alone seems to explain all the observed examples. The same modes of reactivity are exhibited by 1,3-dioxan-2-ylium ions fused to cyclohexane rings (**267**).[86,94,95,210] Bridged ion **268**, derived from the 6-substituted 3β-acetoxycholestan-5α-ol series,[94,95] undergoes attack by path a with water, hydroxyl ion, or pyridine. Another example of ring opening by path a involves the reaction of 1,3-oxathiolan-2-ylium ion (**269**) with aqueous $NaHCO_3$ to give ester **270**.[211] One example of a 1,3-dioxan-2-ylium ion reacting by path d involves the solvolytic rearrangement of 3β-tosyloxy-5α-acetoxy steroids to 3α-acetoxy-Δ⁵ derivatives (eq 128) reported by Plattner and Lang.[212] The reaction of halides with 1,3-dioxolan-2-ylium ions almost invariably leads to isolation of the most stable thermodynamic products. Some examples include the addition of HCl to ketene acetals,[213,214] the free radical bromination of *O,O'*-benzylidenecyclohexane-*cis*-1,2-diol to give *trans*-2-bromocyclohexyl

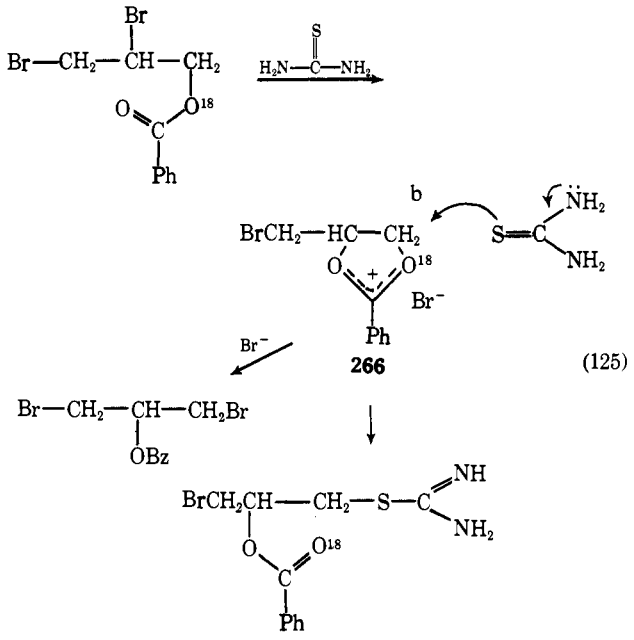
(210) L. J. Dolby and M. J. Schwarz, *J. Org. Chem.*, 30, 3581 (1965).

(211) C. U. Pittman, Jr., unpublished work.

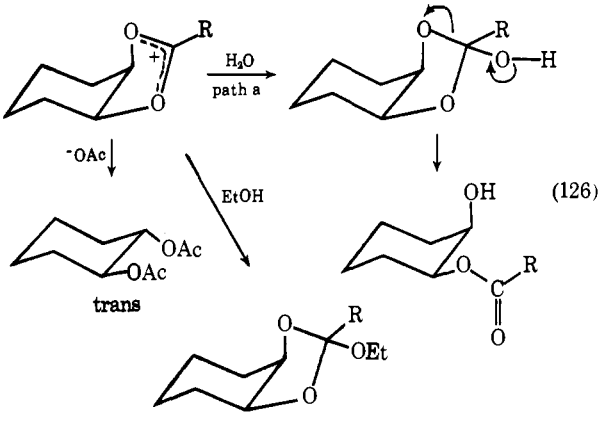
(212) P. A. Plattner and W. Lang, *Helv. Chim. Acta*, 27, 1872 (1944).

(213) S. M. McElvain and D. Kundiger, *J. Amer. Chem. Soc.*, 64, 254 (1942).

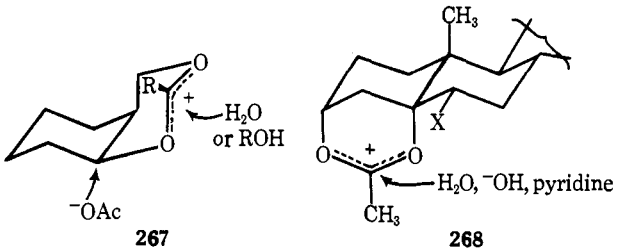
(214) S. M. McElvain and M. J. Curry, *ibid.*, 70, 3781 (1948).



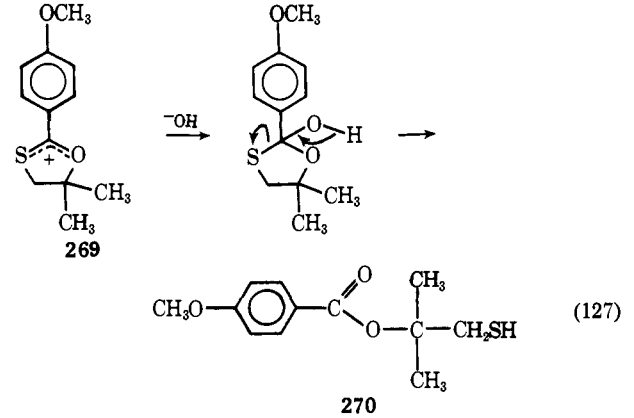
(125)



(126)

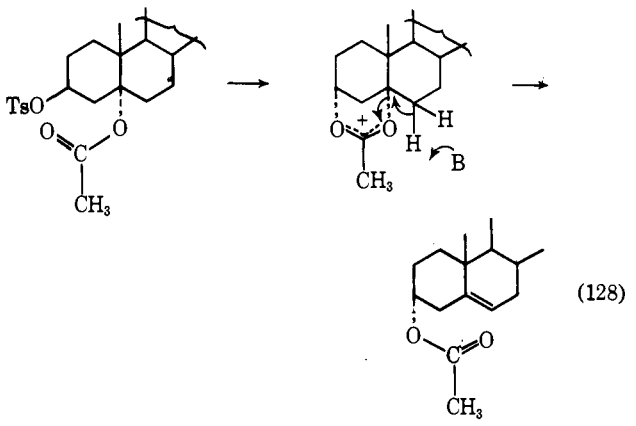


267 268

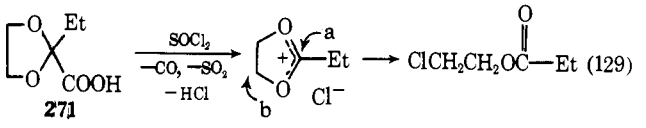


(127)

270



(128)

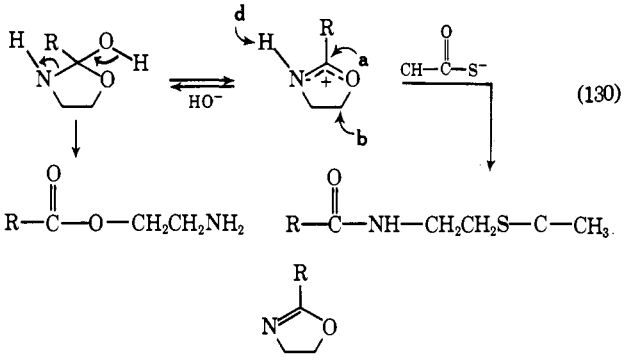


271

(129)

benzoates,[215] and the rearrangement of acid **271** on treatment with thionyl chloride (eq 129).[216]

The ambident nature of "energy-poor" oxazolinium ions was discovered as early as 1890 by Gabriel.[217] Many nucleophiles, while easily attacking the oxazolinium ion reversibly by path a, react to give products of path b. Nucleophiles like water and hydroxide ion, which after attack *via* path a can undergo prototropy and ring opening (see eq 130), give



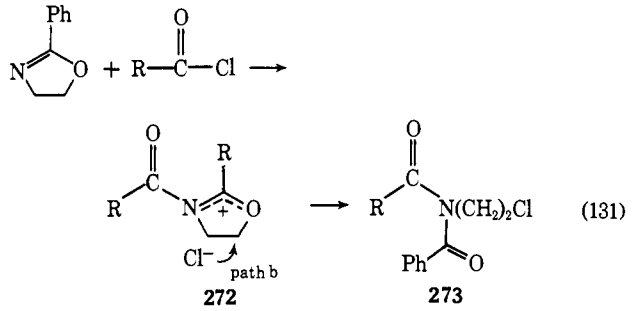
(130)

products from path a. The definitive stereochemical studies of Winstein and Boschan[220] confirm these results. They demonstrated that an oxazolinium ion, cis-fused to cyclohexane, opened up to the *cis*-hydroxyamide *via* path a with water, but opened *via* path b with acetate ion to give the trans amido ester. For most nucleophiles, path b is the normal route observed with oxazolinium ions.[217-219] This follows because these ions are very stable (energy poor) and, as per Figure 1, isolation of the kinetic product would be difficult. It should be noted that water or hydroxide ion also may react with oxazolinium cations *via* path d to give oxazolines as the product (eq 130).[174-176]

Reactions of oxazolinium ions which open the ring may

(215) A. Rieche, E. Schmitz, W. Schade, and E. Beyer, *Chem. Ber.*, **94**, 2926 (1961).
(216) S. M. McElvain and A. N. Bolstad, *J. Amer. Chem. Soc.*, **73**, 1988 (1951).
(217) S. Gabriel and T. Heymann, *Ber.*, **23**, 2495 (1890).
(218) E. M. Fry, *J. Org. Chem.*, **15**, 802 (1950).
(219) A. A. Goldberg and W. Kelly, *J. Chem. Soc.*, 1948 (1919).
(220) S. Winstein and R. Boschan, *J. Amer. Chem. Soc.*, **72**, 4669 (1950).

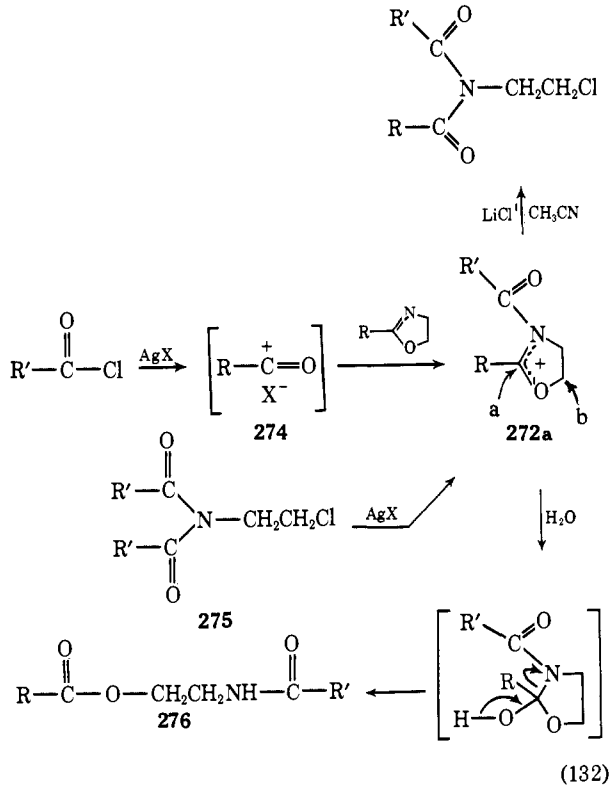
proceed to 2-substituted-*N*-alkylamide derivatives or less frequently to 2-aminoethyl esters.[3,221,222] The opening of the 2-phenyloxazoline ring by acid chlorides proceeds *via* oxazolinium ion **272** which is less stable than other oxazolinium ions by virtue of the carbonyl attached to nitrogen. In this case (eq 131) chloride ion attacks *via* path b to give **273**.[218]



(131)

272 **273**

Tomalia and Paige[223] recently synthesized a series of 3-(aroyl or acyl)-2-(aryl or alkyl)-2-oxazolinium salts (**272a**) by (1) trapping oxocarbonium ions (**274**) with oxazolines, and (2) by cyclization of the appropriate *N*-(2-chloroethyl)-*N*-aroyl- or -acylbenzamides (**275**) with silver tetrafluoroborate (eq 132). The salts, which were thoroughly identified by spectroscopic and chemical methods, exhibited ambident character. For example, 3-benzoyl-2-phenyl-2-oxazolinium tetrafluoroborate (**272a**, R, R′ = Ph) undergoes immediate ring opening with lithium chloride, *via* path b, in acetonitrile. Alternatively, water converts this cation in high yield to 2-benzamidoethyl benzoate (**276**, R, R′ = Ph) *via* path a (see eq 132).

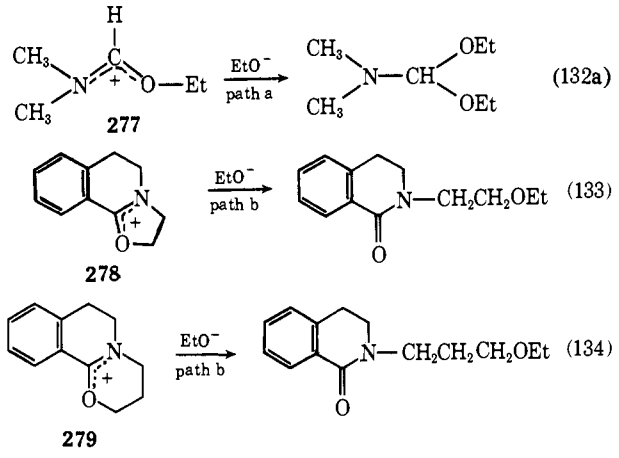


(132)

274 **272a** **275** **276**

(221) N. Seeliger and M. Lütke-Daldrup, French Patent 1,436,297 (1965).
(222) R. L. McKee, *Chem. Heterocycl. Compounds*, **17**, 341 (1962).
(223) D. A. Tomalia and J. N. Paige, in press. We thank Dr. Tomalia for making available preprints of this work.

The great stability of oxazolinium ions, without an *N*-acyl group, may be further emphasized by comparing the ambident reactivity of acyclic ion **277** to that of oxazolinium ion **278**. Meerwein[224] demonstrated that acyclic ion **277** adds ethoxide ion *via* path a to give the corresponding amide acetal (eq 132a). However, ion **278** gives only the stable amido ether (eq 133)[225] as a result of path b. Furthermore, use of the less strained dihydrooxazinium ion **279** also results in product



(132a)

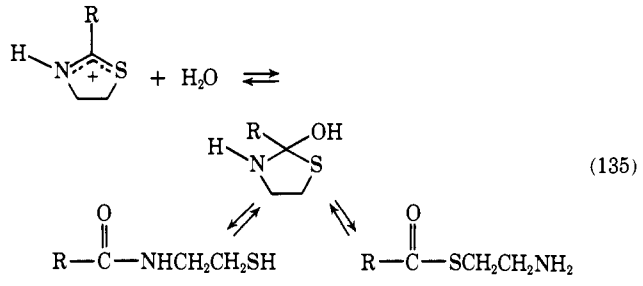
(133)

(134)

277 **278** **279**

from path b[226] as does the use of cyanide ion or lower temperature. Thus, this great stability makes it difficult to isolate path a products. In fact, perchlorate salts of **278** and **279** can be recrystallized unchanged from water!

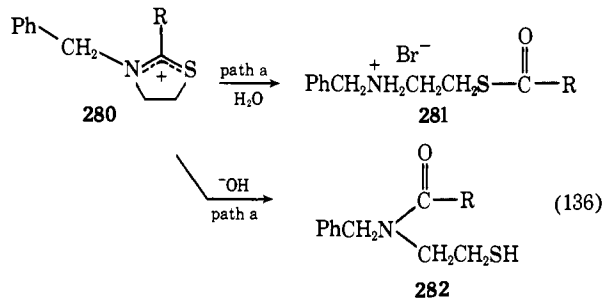
The mechanism of the thiazolinium ion's reaction with water has been the subject of intensive investigation,[227-230] partly because of its possible role in the mechanism of the intramolecular S to N acetyl transfer reaction of *S*-acetylmercaptoethylamine and in analogy to similar biological reactions. These hydrolysis reactions show bell-shaped pH–rate profiles. While the overall details of the mechanism are still being debated, it is apparent that the attack of water on the thiazolinium ion occurs *via* route a to give a tetrahedral C-2 intermediate which can then open to a thiolamide or to an amino thiolester (eq 135). Water converts 3-benzyl-2-alkyl-



(135)

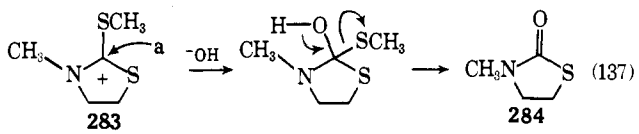
(or aryl-) 2-thiazolinium bromides (**280**) to their respective *S*-acylthioalkylammonium salts (**281**) *via* path a, but the direction of ring opening is pH dependent[187] (eq 136). In cold

(224) H. Meerwein, W. Florian, N. Schön, and G. Stopp, *Justus Liebigs Ann. Chem.*, **641**, 1 (1961).
(225) W. Schneider and B. Müller, *Chem. Ber.*, 93, 1579 (1960).
(226) See ref 6, footnotes 53 and 54, p 557.
(227) R. B. Martin, R. I. Hedrick, and A. Parcell, *J. Org. Chem.*, 29, 3197 (1964).
(228) G. L. Schmir, *J. Amer. Chem. Soc.*, **87**, 2743 (1965).
(229) R. Barnett and W. P. Jencks, *ibid.*, 90, 4199 (1968).
(230) R. B. Martin and R. I. Hedrick, *J. Org. Chem.*, 29, 3197 (1964).



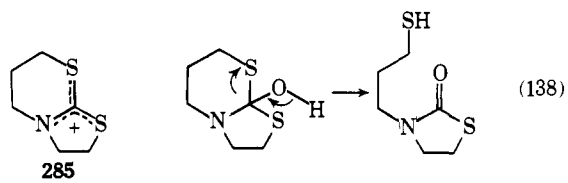
(136)

base ($^-$OH) these same salts underwent ring opening to give the acylamino derivative **282**.[187] The action of base on *N,S*-dialkylthiazolinium salt **283** gave 3-alkylthiazolidin-2-one (**284**) *via* path a. In the very interesting case of bicyclic ion



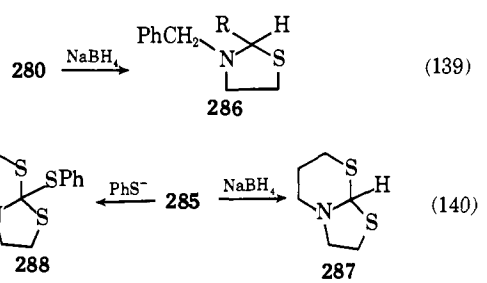
(137)

285, reaction with hydroxide ion, *via* path a, resulted only in opening of the six-membered ring (eq 138).[187] The 3-benzyl-



(138)

2-methyl- (or phenyl-) 2-thiazolinium ions (**280**) are reduced by sodium borohydride to the corresponding thiazolidines **286** in DMF, and bicyclic ion **285** gave the corresponding bicyclic thiazolidine **287** (eq 139 and 140). Attack by the

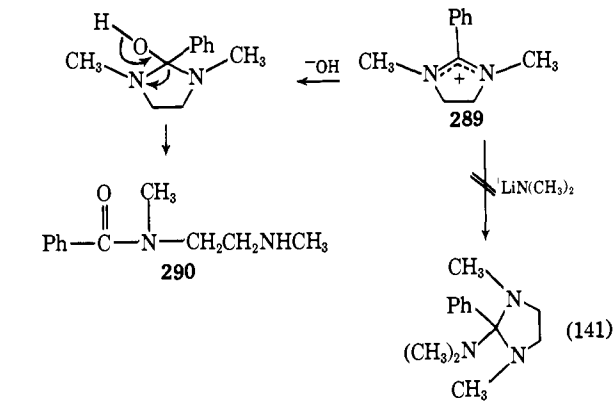


(139)

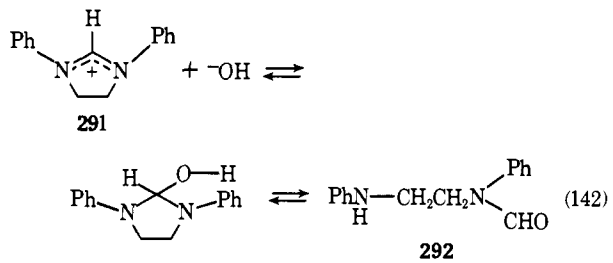
(140)

benzenethiolate anion in anhydrous ethanol on **285** results in path a adduct **288** (eq 140). Adduct **288** is exceedingly susceptible to traces of moisture which result in ring-open products.[187] Since **285** is a very stable cation, its propensity to react *via* path a with H^-, $^-$OH, and $^-$SPh must in part be due to the lack of stability of the C=S function which would need to be formed by attack *via* path b.

Ambident cations with two nitrogens are more stable than any of the heterocyclic ions discussed so far. This should (Figure 1) result in a marked decrease in the ability to isolate their reaction products from path a (where prototropy is not occurring). This principle is illustrated by the lack of reactivity of ion **289** (eq 141) with lithium dimethylamide in boiling ether.[231] Small concentrations of hydroxide ion results in ring opening (eq 141) to give amide **290**. The hydrolysis of the 1,3-diphenyl-2-imidazolinium ion (**291**) by water to *N*-(2-anilinoethyl)formanilide (**292**) (eq 142) has been investigated



(141)



(142)

by Robinson and Jencks.[232] Detailed rate and other studies indicated that a tetrahedral intermediate was first formed in the reaction. This was supported by the direct spectrophotometry of this intermediate[233] which then decomposed in a pH-dependent fashion. The same behavior was found in the hydrolysis of methenyltetrahydrofolic acid.[234,235]

B. STEREOCHEMICAL CONSIDERATIONS

The nucleophilic opening of 1,3-dioxolan-2-ylium ions by path b always results in inversion at C-4 or C-5 in bimolecular reactions. Opening *via* path a, of course, results in retention of configuration at C-4 and C-5. Studies of 1,3-dioxolan-2-ylium ions fused to six-membered rings have been of great importance in elucidating the stereochemical details of ring openings. The work of King and Allbutt[96,97,236] is especially valuable in this respect. They fused the dioxolan-2-ylium ion to anchored six-membered rings where conformational inversion was impossible. Specifically, conformationally rigid ions **293**, **294**, and **295** were prepared. Each of these ions was treated with a solution of tetraethylammonium bromide to give the corresponding halohydrin esters.[96,236] The trans-diaxial products greatly predominated for ions **293** and **295** (by a factor of about 20) clearly showing axial attack of Br^- to give preferential diaxial ring opening. Table V summarizes these results. The diaxial:diequatorial opening ratio was insensitive to both total yield and solvent. Similarly, variation of the attacking nucleophile did not affect the reaction appreciably (as long as it was a path b nucleophile). For example, diaxial opening was strongly favored by Cl^-, CF_3COO^-, and $PhCOO^-$ as well as Br^-. Thus, the opening of a dioxolan-2-ylium bridge resembles ring openings of ep-

(231) H. Böhme and F. Soldan, *Chem. Ber.*, 94, 3109 (1961).

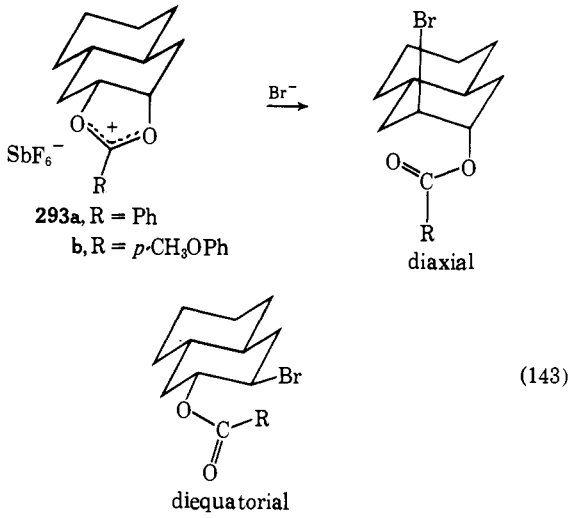
(232) D. R. Robinson and W. P. Jencks, *J. Amer. Chem. Soc.*, 89, 7088 (1967).

(233) D. R. Robinson, *Tetrahedron Lett.*, 5007 (1968).

(234) D. R. Robinson and W. P. Jencks, *J. Amer. Chem. Soc.*, 89, 7098 (1967).

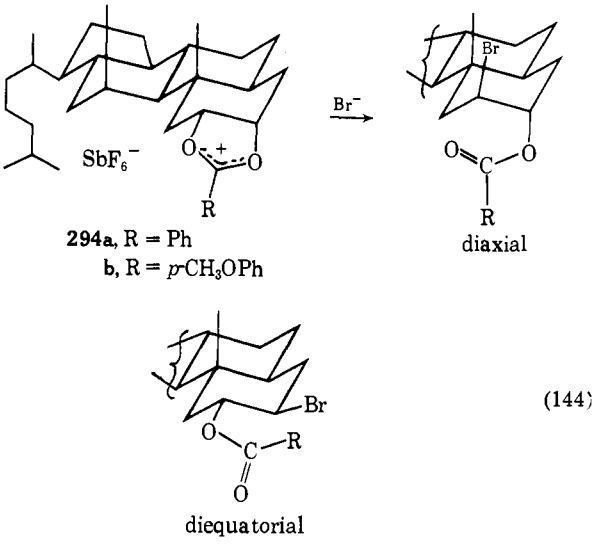
(235) D. L. Klayman and P. T. McIntyre, *J. Org. Chem.*, 33, 884 (1968).

(236) J. F. King and A. D. Allbutt, *Chem. Commun.*, 14 (1966).



293a, R = Ph
b, R = *p*-CH_3OPh

(143)



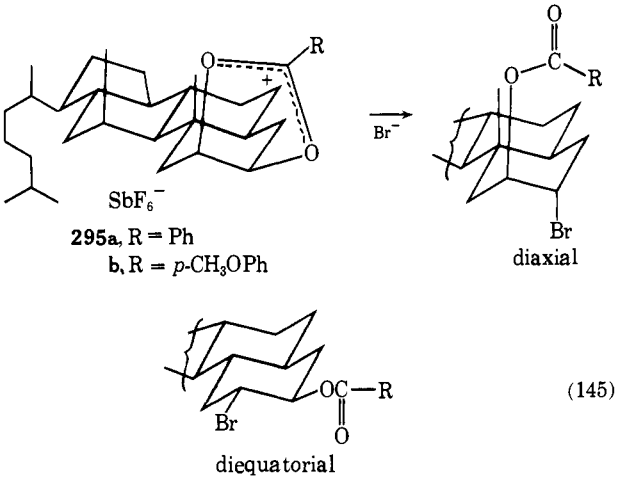
294a, R = Ph
b, R = *p*-CH_3OPh

(144)

Table V

Reaction of Conformationally Rigid 1,3-Dioxolan-2-ylium Ions with Nucleophiles *via* Path b

1,3-Dioxolan-2-ylium salt	*Nucleophile*	*Solvent*	*Total yield of ring-opened products*	*Diaxial:diequatorial opening ratio*
293b	Br^-	CH_2Cl_2	99	19:1
293b	Cl^-	CH_2Cl_2	92	16:1
293b	CF_3COO^-	CH_2Cl_2	64	Only diaxial product detected
293a	$PhCOO^-$	CH_2Cl_2	69	7:1
295b	Br^-	CH_2Cl_2	83	49:1
295a	Br^-	CH_2Cl_2	72	Only diaxial product detected
294b	Br^-	CH_2Cl_2	94	0.5:1
294b	Br^-	CH_3CN	78	0.5:1
294b	Br^-	CH_3NO_2	90	0.7:1



295a, R = Ph
b, R = *p*-CH_3OPh

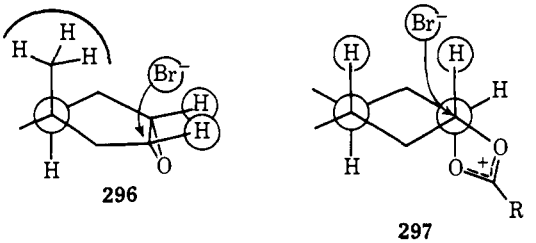
(145)

oxides fused to six-membered systems where the "diaxial opening rule" holds.[237] This rule also applies to halonium ion,[238] ethylenimmonium ion,[239] and episulfonium ion[240] ring openings.

The reaction of salt **294** did not show the same strong preference for diaxial ring opening. However, a bromide ion attacking ion **294** in the axial mode would experience a strong steric repulsion from the angular (C-19) methyl group. This strong repulsion, without counterpart in the diequatorial mode, would raise the transition state energy of the diaxial opening, and now equatorial bromide ion attack competes favorably (by a factor of 2). It should be noted that ring opening of the corresponding epoxide, 5α-cholestane 2α,3α-epoxide, with hydrobromic acid gave diaxial product. Does this mean that the angular methyl group increases the activation energy of the diaxial dioxolan-2-ylium ion opening more than it does in the case of the epoxide, or does this indicate a greater inherent tendency for the epoxide to open diaxially? Since the $\Delta G_E^{\ddagger} - \Delta G_A^{\ddagger}$ values for the two systems without an angular methyl group are very similar,[96] it appears that the angular methyl group increases the transition state energy for axial attack by bromide more for a fused dioxolan-2-ylium ion than for an epoxide. Referring to structures **296**, **297**, and **298**, the relatively greater openness of the epoxide system is emphasized.

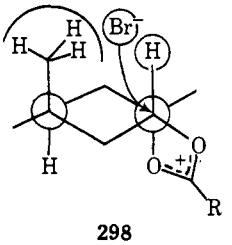
King explained the normal preference for diaxial ring opening in the dioxolan-2-ylium systems in terms of transition state structures **300** amd **301** (eq 146).[96] It was argued that in the transition state for diequatorial opening (**301**) the dioxolan-2-ylium ring system must be severely puckered with a consequent loss of resonance stabilization. This puckering is a direct result of the dihedral angle change between α-cis substituents which must occur when the axial group is the one which is leaving while still tied into a fused ring system with the neighboring equatorial substituent. When bromide attacks from the axial direction (**300**), the dihedral angle between the α-cis substituents closes and the ring actually becomes more planar—a situation which is favorable for increased resonance stabilization in the transition state. It also reduces the strain associated with the five-membered rings puckering in the starting ion **299**.

(237) A. Fürst and P. A. Plattner, *Proc. Int. Congr. Pure Appl. Chem.*, 12, 409 (1951).
(238) D. H. R. Barton and R. C. Cookson, *Quart. Rev., Chem. Soc.*, 10, 44 (1956).
(239) A. Hassner and C. Heathcock, *J. Org. Chem.*, 30, 1748 (1965); *Tetrahedron Lett.*, 393 (1963).
(240) J. F. King, K. Abikar, D. M. Deaken, and R. G. Pews, *Can. J. Chem.*, 46, 1 (1968).



296

297



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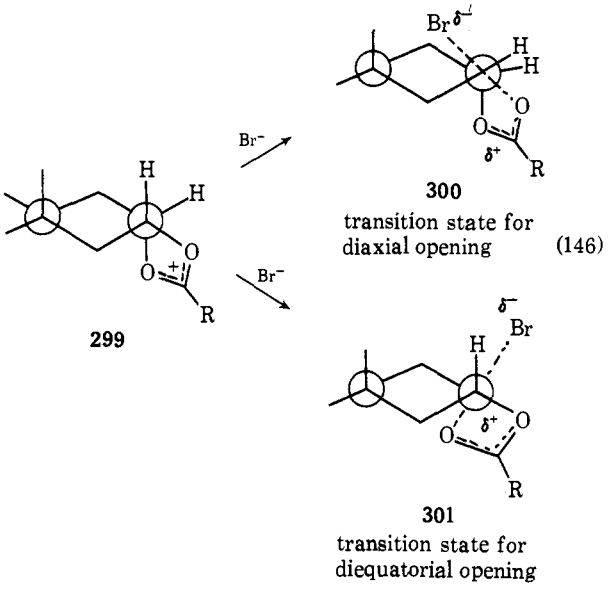


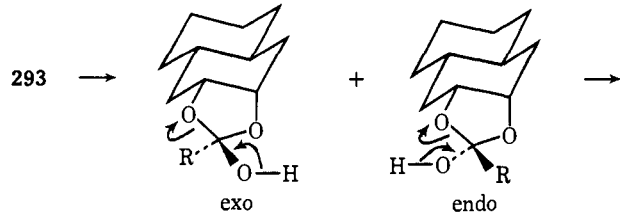
299

300
transition state for
diaxial opening

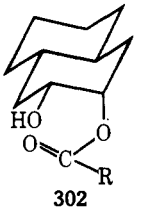
301
transition state for
diequatorial opening

(146)

Anchoring 1,3-dioxolan-2-ylium ions to rigid six-membered ring systems also made it possible to examine stereochemical details of hydrolysis in water. Hydrolysis, as shown previously, proceeds *via* path a to an "ortho acid" which decomposes *via* prototropy to a hydroxy ester. King and Allbutt[97] demonstrated that the hydroxy ester with the ester function axial and the hydroxyl group equatorial is formed almost exclusively. This was demonstrated on the three rigid systems **293**, **294**, and **295**, and the reactions are summarized in eq 147–149. For example, 9β,10α-decalin-2β,-3β-(2′-anisyl-1′,3′-dioxolan-2′-ylium) hexafluoroantimonate (**293b**) hydrolyzes (eq 147) to generate the equatorial alcohol **302** which constitutes more than 99.5% of the hydroxy ester product. Ion **294** also selectively gives hydroxy ester **303** in greater than 99.5% isomeric purity. To conclusively demonstrate that the observed axial esters were kinetic, not thermodynamic products, hydroxy ester **303** was equilibrated with sulfonic acid catalysts, and the equatorial ester (**305**) was shown to predominate at equilibrium (eq 150). Water hydrolysis of ion **295** selectively generates axial ester **304**, which is also the thermodynamically less stable isomer. Thus, there exists a very strong propensity to produce the axial ester on water hydrolysis.

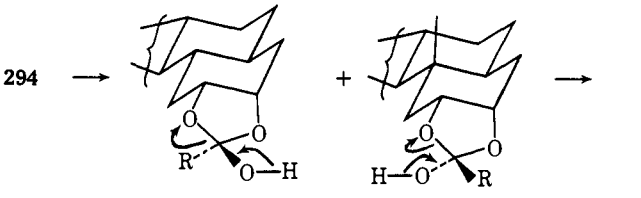


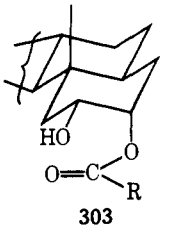
exo endo



302

(147)





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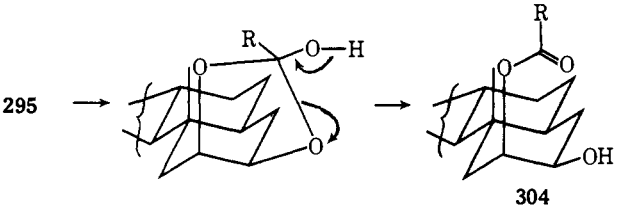
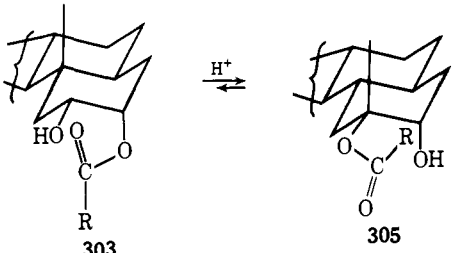
(148)



304

(149)

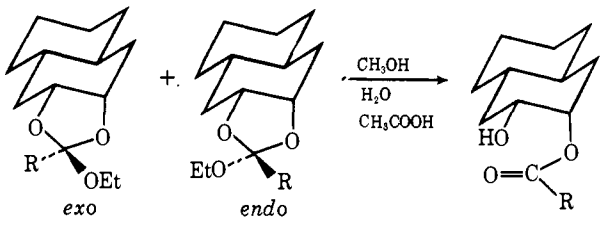


303 305
predominates

(150)

Next, King and Allbutt[97] demonstrated that ortho esters of this series (for example, **306a–c**) hydrolyzed in methanol–aqueous acetic acid solutions to selectively produce the corresponding hydroxy ester with the ester function axial (eq 151). Thus, ortho ester hydrolyses gave the same results as the dioxolan-2-ylium ion hydrolyses which they must greatly resemble. The only exception was the orthoformate (**306a**) which gave 40% equatorial and 60% axial formate. It should be noted that the exo ortho esters always predominated whatever synthetic method was used to prepare them.[97,241] For example, Lemieux and Cipera[241] found the exo ortho esters

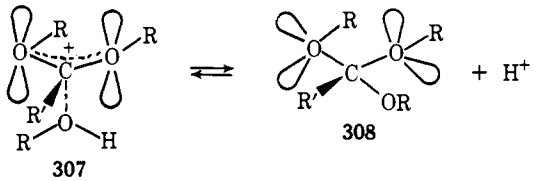
(241) R. U. Lemieux and J. D. T. Cipera, *Can. J. Chem.*, **34**, 906 (1956).



306a, R = H
b, R = CH_3
c, R = Et (151)

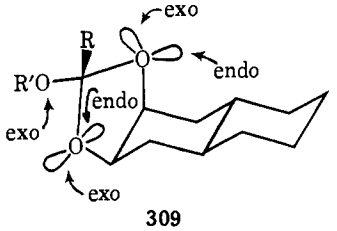
predominated when fused 1,3-dioxolan-2-ylium ions in the pyranose system were treated with alcohols.

To explain the origin of the stereoselectivity observed in the hydrolyses of all the ions and ortho esters (except in the case of formate **306a**), King invoked a combination of steric and stereoelectronic effects. Consider **307** as representing



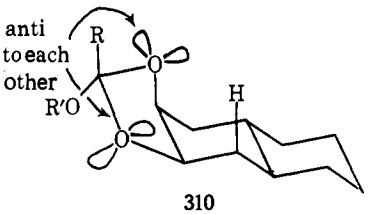
307 308

the transition state of attack of ROH on a dioxolan-2-ylium ion or the loss of RO^- from an ortho ester. In order to achieve maximum stabilization of the positive charge on carbon by the electrons on the two adjacent oxygen atoms, one free electron pair on each oxygen must be anti (or at least antiperiplanar) to the leaving group.[242] Considering a specific 1,3-dioxolan-2-ylium ion fused to an anchored six-membered ring, it may be concluded from inspection of models that this fusion restricts the means by which a conformation such as **307** may be achieved. In fact, to achieve a conformation in which a free electron pair on each oxygen is antiperiplanar with the leaving group is difficult. The endo electron pair on the axial oxygen (of model system **309**) can become anti-



309

periplanar with the equatorial oxygen (which is the leaving group in the formation of the equatorial alcohol–axial ester product) only by introducing severe steric strain *via* ring distortion or by flipping the six-membered ring into a boat conformation. Moreover, the exo electrons of the equatorial oxygen can become antiperiplanar to the axial oxygen only by introducing significant strain. However, the exo electrons of the axial oxygen can become antiperiplanar to the equatorial oxygen as shown in **310**. Alternatively, as shown in **311**, the endo electrons of the equatorial oxygen and the axial oxygen can be arranged antiperiplanar *if in doing so the endo substituent on C-2 (i.e., R) moves very close to the nearest*



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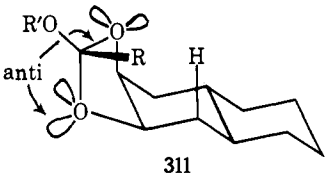
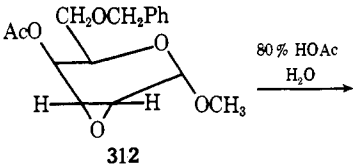


311

axial cyclohexane ring hydrogen. If the R group is reasonably large (alkyl, aryl, alkoxyl, or hydroxyl), the interaction of this endo R group with the axial hydrogen would raise the energy of the transition state obtained from **311** much higher than that obtained from **310**. Since the transition state from structure **311** leads to the equatorial ester while the lower energy transition state from **310** leads to the axial ester, it follows that the axial ester should be the kinetic product except when R is very small (such as when R = H in the formate hydrolysis.)

In agreement with these ideas, Buchanan and Fletcher[243] converted anhydro sugars **312** and **315** to **314** and **317**, respectively, *via* 1,3-dioxolan-2-ylium ions **313** and **316**. Again, the strong preferential formation of the axial esters is apparent. Unfortunately, no formates were studied.



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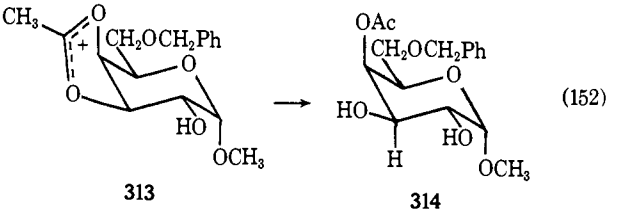
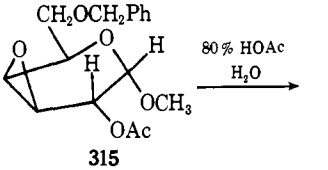
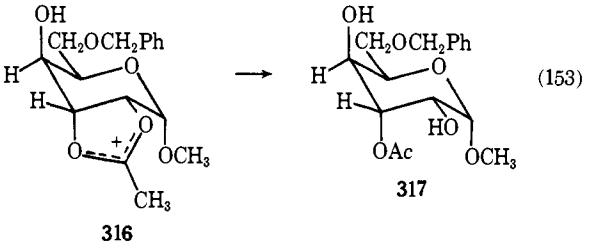


313 314 (152)



315



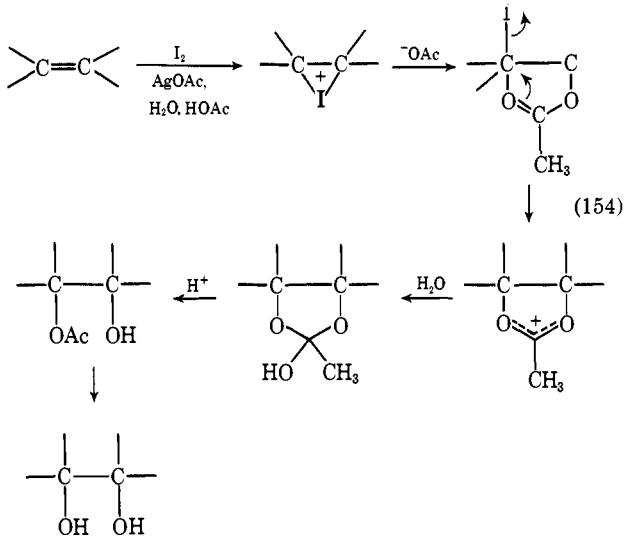
316 317 (153)

(242) E. L. Eliel and F. Nader, *J. Amer. Chem. Soc.*, 91, 536 (1969).

(243) J. G. Buchanan and R. Fletcher, *J. Chem. Soc.*, 6316 (1965).

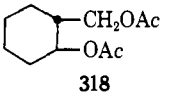
C. OCCURRENCE IN ORGANIC REACTIONS

The heterocyclic ions covered in this review have been invoked as intermediates in a variety of reactions. Dioxolan-2-ylium ions will be covered first. The Woodward–Prevóst reaction,[244-246] where an olefin reacts with iodine and silver acetate in wet acetic acid, is believed to proceed through 2-methyl-1,3-dioxolan-2-ylium ions (see eq 154). If this is



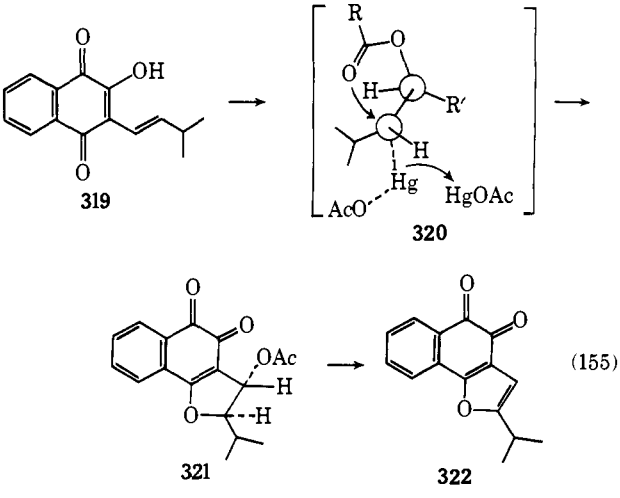
(154)

so, the intermediate hydroxy acetate, formed before hydrolysis to the glycol, should have an axial acetate group in rigid systems such as decalin. King and Allbutt[97] demonstrated this was the case when *trans*-2-octalin was subjected to this procedure. Dialkoxycarbonium ions, including 1,3-dioxolan-2-ylium ions, etc., have long been regarded as intermediates in the acid-catalyzed hydrolysis of ortho esters. The amount of study which has been expended on this reaction is immense and would take an entire review alone to cover. Such a review of the supporting evidence has been provided by Cordes.[247] Criegee[248] postulated the intermediacy of 1,3-dioxolan-2-ylium ions in the lead tetraacetate oxidations of some olefins, and there is still support for this view in some instances.[249,250] While it was suggested that 1,3-dioxolan-2-ylium ions could be involved[251] in the Prins reactions, it has now been shown[210] that the Prins reaction on cyclohexene gave trans isomer **318**, while hydrolysis of independently prepared **267** gave the cis isomer. Other studies also now agree that the Prins reaction does not go through such bridged



318

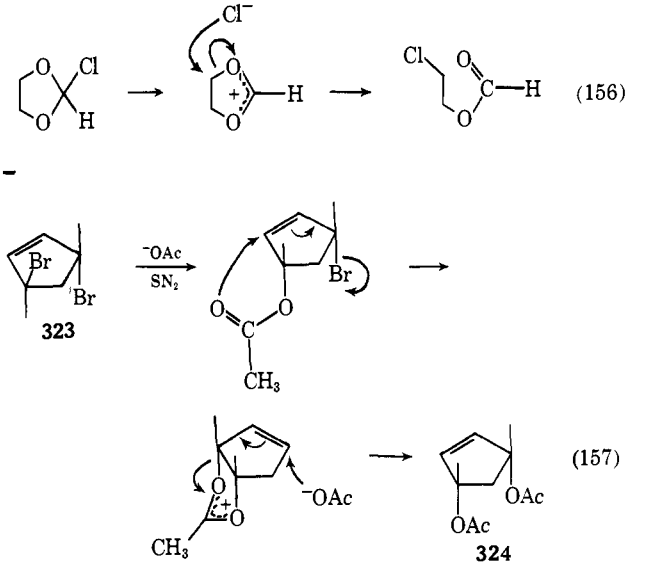
ions.[252,253] A 1,3-dioxolan-2-ylium ion has been suggested[254] as an intermediate in the mercuric acetate oxidation of isolapachol (**319**) which proceeds *via* **320** and **321** to α-isopropylfurano-1,2-naphthoquinone (**322**). The chlorination



(155)

of 1,3-dioxolane gives β-chloroethyl formate, presumably by rearrangement of 2-chloro-1,3-dioxolane as shown in eq 156.[255,256]

A very interesting reaction (eq 157) of *trans*-3,5-dibromo-

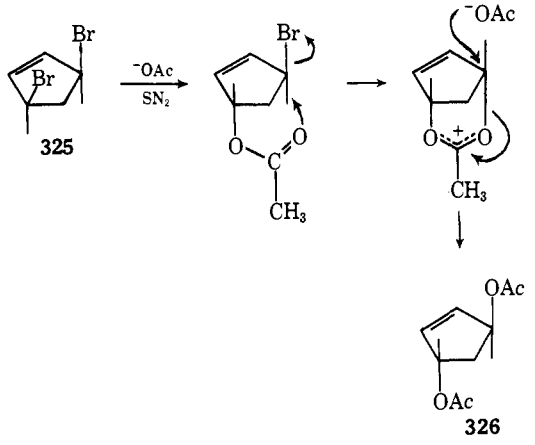


(156)

(157)

cyclopentene (**323**) with acetate ion was first investigated by Owen and Smith.[257] They assigned the wrong stereochemistry to the products,[258] but this has now been clarified by Saegebarth.[259] The *trans*-dibromide (**323**) gives *cis*-diacetate (**324**). Furthermore, as shown in eq 158, the *cis*-di-

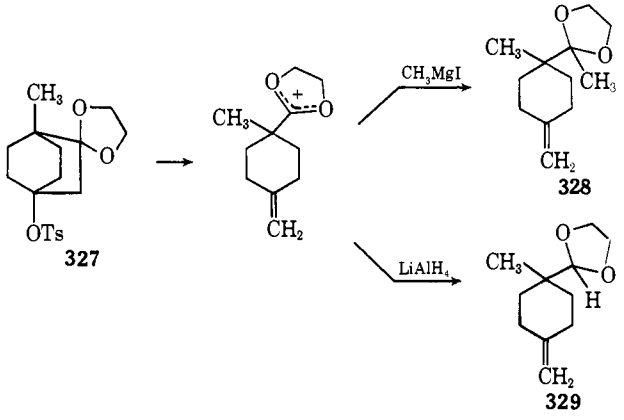
(244) R. B. Woodward and F. V. Brutcher, Jr., *J. Amer. Chem. Soc.*, 80, 209 (1958).
(245) C. Prevóst, *C. R. Acad. Sci.*, 196, 1129 (1933).
(246) C. Prevóst and J. Wiemann, *ibid.*, 204, 700 (1937).
(247) E. H. Cordes, *Progr. Phys. Org. Chem.*, 4, 1 (1967).
(248) R. Criegee, *Angew. Chem.*, 70, 173 (1958).
(249) R. Criegee, "Oxidation in Organic Chemistry," Part A, K. B. Wiberg, Ed., Academic Press, New York, N. Y., 1965. Chapter 5.
(250) R. O. C. Norman and C. B. Thomas, *J. Chem. Soc. B*, 604 (1967).
(251) L. J. Dolby, C. N. Lieske, D. R. Rosencrantz, and M. J. Schwarz, *J. Amer. Chem. Soc.*, 85, 47 (1963).
(252) O. Kovacs and I. Kovari, *Acta Chim. Acad. Sci. Hung.*, 48, 147 (1966).
(253) C. Agami and C. Prevóst, *C. R. Acad. Sci., Ser. C.*, 263, 153 (1966).
(254) K. H. Dudley and H. W. Miller, *J. Org. Chem.*, 32, 2341 (1967).
(255) H. Baganz and L. Domaschke, *Chem. Ber.*, 91, 653 (1958).
(256) L. A. Cort and R. G. Pearson, *J. Chem. Soc.*, 1682 (1962).
(257) L. N. Owen and P. N. Smith, *ibid.*, 2449 (1952).
(258) W. G. Young, H. K. Hall, and S. Winstein, *J. Amer. Chem. Soc.*, 78, 4338 (1956).
(259) K. A. Saegebarth, *J. Org. Chem.*, 25, 2212 (1960).



(158)

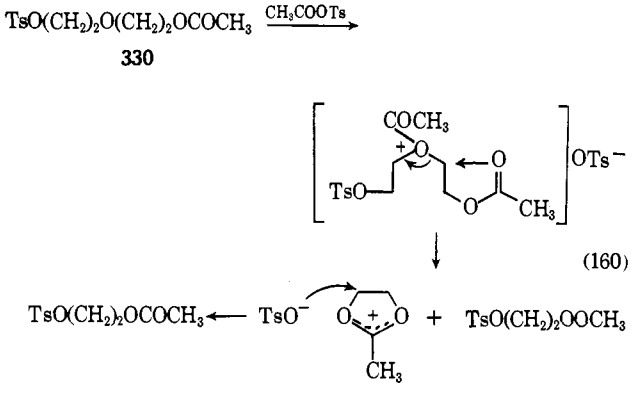
bromide (**325**) produces the *trans*-diacetate (**326**).

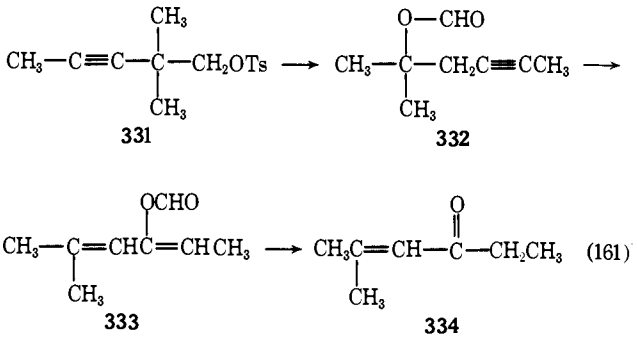
Kraus and Chassin[260] described 1,3-dioxolan-2-ylium cation intermediates in the novel solvolytic rearrangement of bridgehead bicyclic tosylate **327** to give dioxolane derivatives **328** and **329** (see eq 159).



(159)

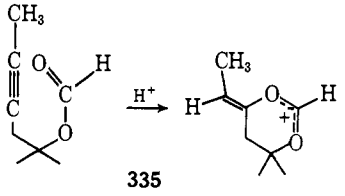
Wilson[261] has recently found that compound **330** in the presence of the acylating agent, acetyl tosylate, formed products which were best rationalized as having occurred, in part, by means of an acylation and displacement to form the intermediate dioxolan-2-ylium cation shown in eq 160. The formolysis of homopropargylic tosylate (**331**) was shown to proceed sequentially through **332** and **333** prior to





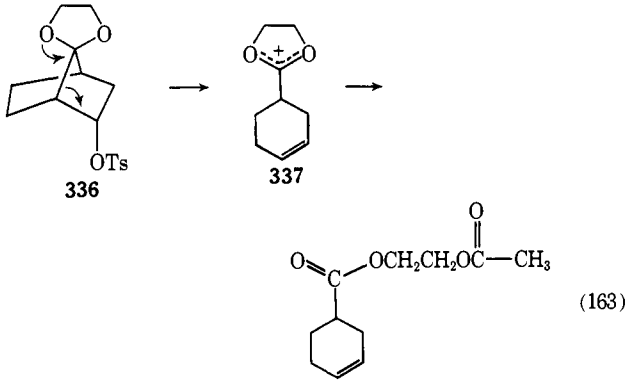
(161)

formation of product **334**. Of the several mechanisms considered for the conversion of **332** → **333**, one invoked 1,3-dioxan-2-ylium ion (**335**) (eq 162).[261] The solvolysis of *endo*-2-



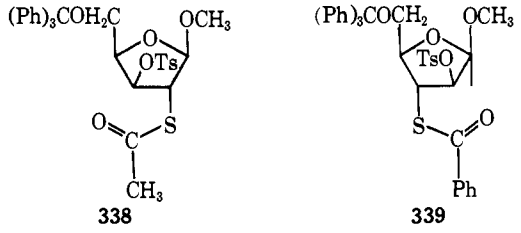
(162)

norbornyl *p*-toluenesulfonate (**336**) was shown by Gassman[262] to be only 11 times slower than the exo derivative. This remarkably low exo/endo rate ratio was rationalized by formation of 1,3-dioxolan-2-ylium ion (**337**) as an intermediate (eq 163). AcO-6 participation apparently occurs in the sol-

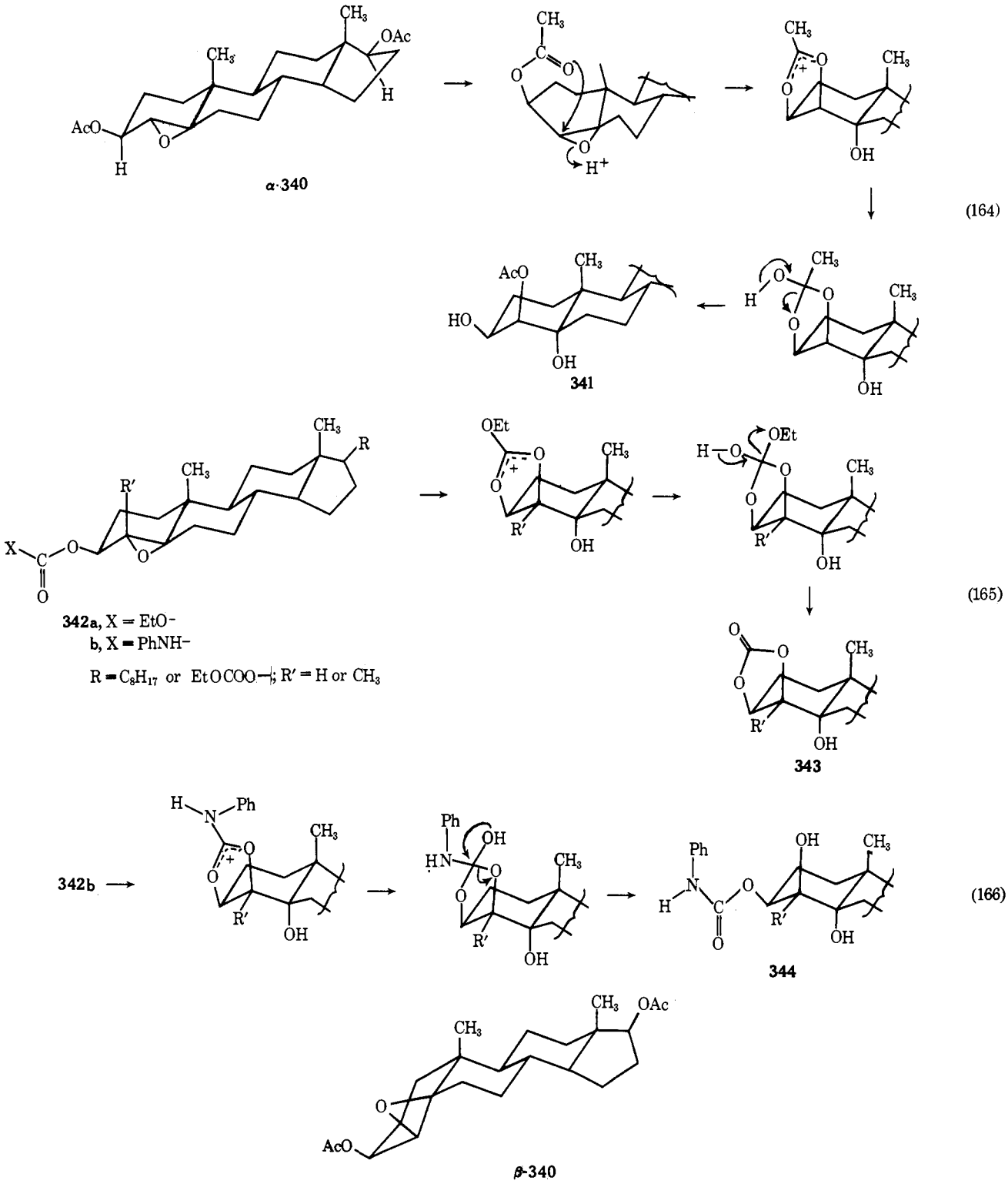


(163)

volysis of 3-acetoxy-3-phenylpropylmercuric acetate which reacts 18 times faster than 3-phenylpropylmercuric acetate. Introducing a *p*-methoxy group resulted in a further 510-fold increase in rate.[263] Instead of oxygen participation, sulfur participation occurs in the reaction of compounds **338** and **339** with sodium benzoate in DMF for reasons which are not entirely clear.[264]



(260) W. Kraus and C. Chassin, *Tetrahedron Lett.*, 539 (1970).
(261) J. W. Wilson, *J. Amer. Chem. Soc.*, 91, 3238 (1969).
(262) P. G. Gassman and J. G. Macmillan, *ibid.*, 91, 5527 (1969).
(263) R. J. Ouellette and R. D. Robins, *Tetrahedron Lett.*, 397 (1968).
(264) K. J. Ryan, E. M. Acton, and L. Goodman, *J. Org. Chem.*, 33, 3727 (1968).



(164)

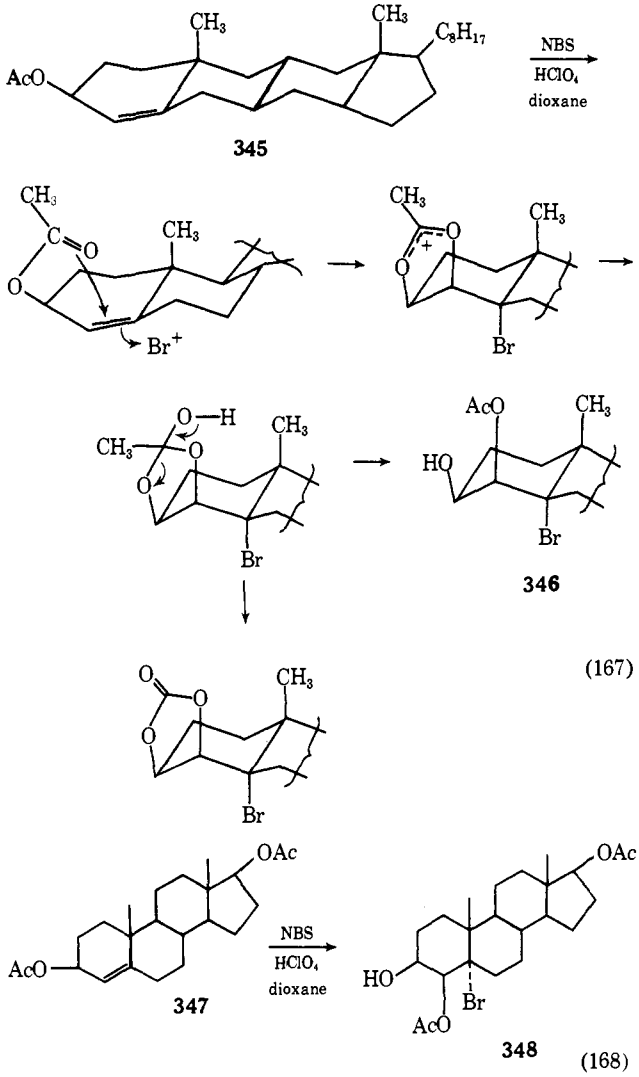
(165)

(166)

The intervention of 1,3-dioxolan-2-ylium and 1,3-dioxan-2-ylium ions in the reaction of steroids has been increasingly recognized in the past decade. Examples include the mineral acid catalyzed transformation[265] of 3β,17β-diacetoxy-4α,5α-epoxyandrostane (α-**340**) into 4β,17β-diacetoxyandrostane-3β,5α-diol (**341**) in eq 164, and the conversion of **342a** to **343** in eq 165 and **342b** to **344**. However, on acetolysis, epoxide β-**340** does not proceed through a bridged ion (eq 166). It is interesting to note that **341** has the ester function in the expected axial position despite the 1,3-diaxial interaction with the angular methyl group. However, in eq 166 the product **344** has the hydroxyl group in the axial position. Julia and Fürer[266] have transformed steroids **345** and **347** into **346** and **348**, respectively, using *N*-bromosuccinimide in perchloric

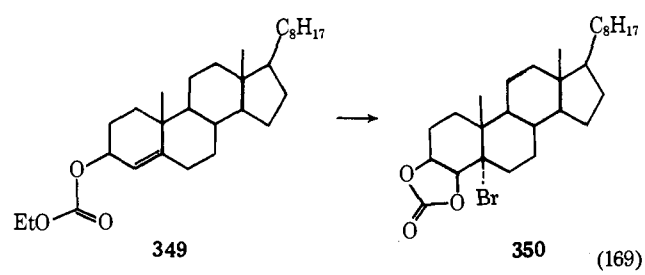
(265) S. Julia and B. Fürer, *Bull. Soc. Chim. Fr.*, 1106 (1966).

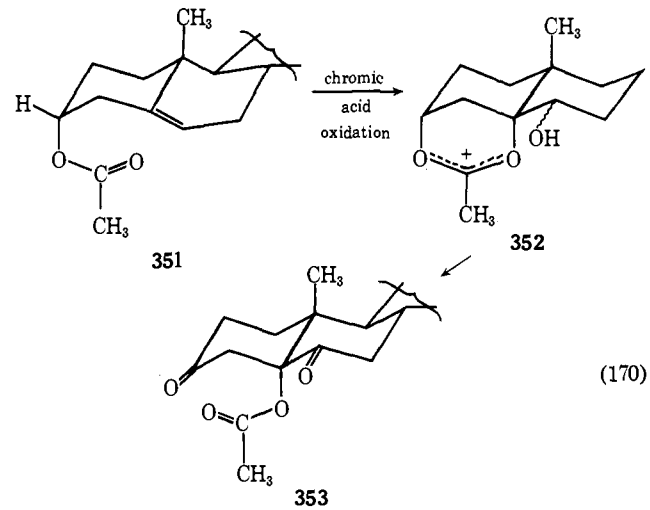
(266) S. Julia and B. Fürer, *ibid.*, 1114 (1966).



acid–dioxane solutions. These reactions proceed through cyclic ions as shown in eq 167.

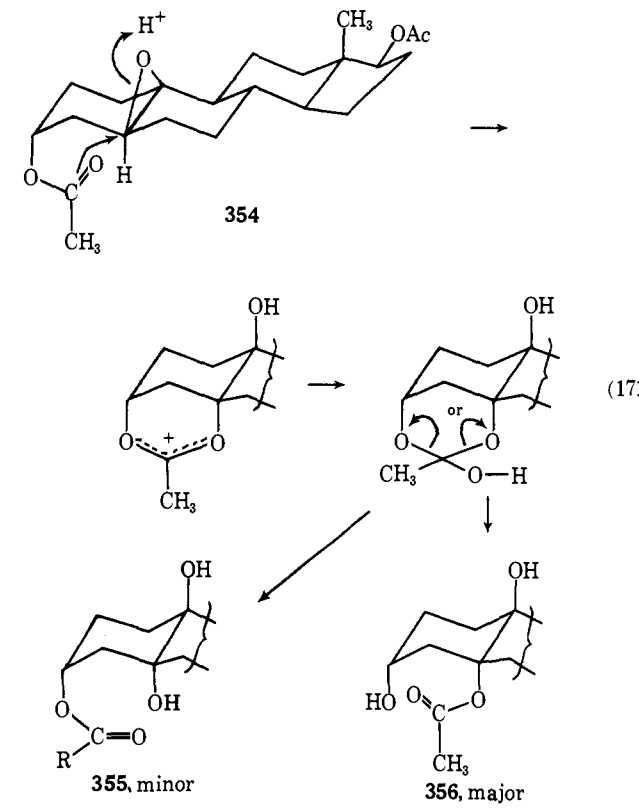
In eq 167 the 1,3-dioxolan-2-ylium ion opens by water attack by path a followed by opening to give the cis hydroxy acetate **346**, which has equatorial hydroxy and axial ester functions. This is another example of the stereochemical generalizations established by King (see eq 147 and 148). Under these same conditions 3-cholest-4-ene ethyl carbonate (**349**) gave the cyclic bromocarbonate **350**. Again a cyclic ion is required. Chromic acid oxidation of epicholesteryl acetate (**351**) produced two products, one of which is 5α-acetoxycholestane-3,6-dione (**353**) *via* 1,3-dioxan-2-ylium cation (**352**).[267] The





acetate group in the product was the same one present at the 3α position in the starting material. This was demonstrated by using propionic acid as a solvent and showing that no propionoxy group is incorporated into **353**. Comparable acyloxy migrations in several systems are well known.[212,268,269] Exposure of estrane-3α,17β,diol 5β,10β-epoxide diacetate (**354**) to 2 *N* H_2SO_4 furnished the 3α,17β-diacetoxyestrane-5α,10β-diol (**355**) (minor product) and 5α,17β-diacetoxyestrane-5α,10β-diol (**356**) (major product). This reaction also proceeds *via* a 1,3-dioxan-2-ylium ion (eq 171).[270]

As a final example in the steroid series, the conversion of 5β,6β-epoxy-6α-methylcholestane derivative (**357**) to diene

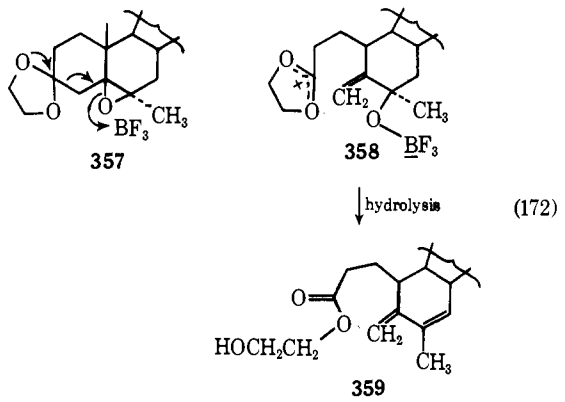


(267) E. J. Tarlton, M. Fieser, and L. F. Fieser, *J. Amer. Chem. Soc.*, 75, 4423 (1953).

(268) V. Petrow, O. Rosenheim, and W. W. Starling, *J. Chem. Soc.*, 135 (1943).

(269) M. F. C. Paige, *ibid.*, 437 (1943).

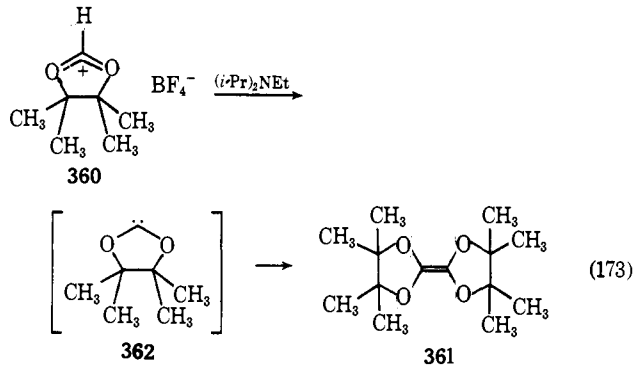
(270) A. D. Cross, E. Denot, R. Acevedo, R. Urquiza, and A. Bowers, *J. Org. Chem.*, **29**, 2195 (1964).



(172)

ester **359** was envisaged as proceeding *via* cyclic ion **358** with subsequent ring opening and dehydration.[271]

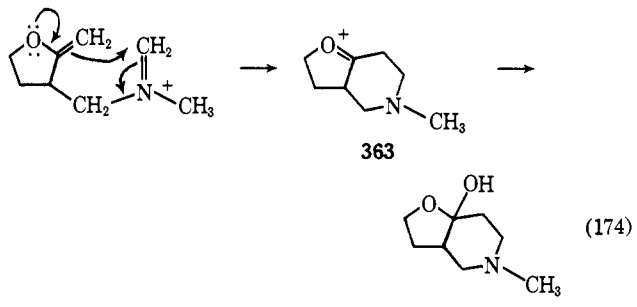
The conversion of 4,4,5,5-tetramethyl-1,3-dioxolan-2-ylium tetrafluoroborate (**360**) to its dimer **361** on treatment with diisopropylethylamine was said to proceed through a carbene intermediate **362**.[70] If this mechanism can be substantiated,



(173)

it would add another mode of reactivity to those listed in section V.A. The base must be powerful enough to abstract the proton, but it must not preferentially react with other electrophilic sites on the cation. Attack by mode b or c (see structure **256**) would be very hindered in **360**.

Oxolan-2-ylium ions are also involved in many reactions. Husson, *et al.*,[272] invoked the intermediacy of ion **363** in the Clarke-Eschweiler cyclization shown in eq 174, and this reaction was applied to steroid syntheses. Baddeley and coworkers[273] demonstrated O-5 participation in the solvolysis of 1-bromo-5-acetyl-*trans*-decalin. The high rate of solvolysis



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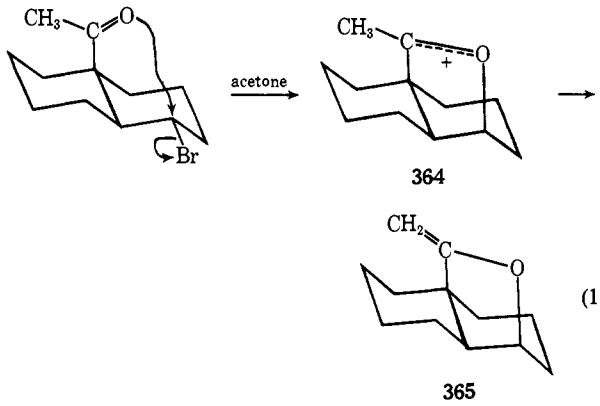
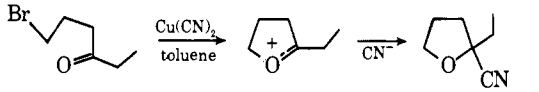


(175)

coupled with the isolation of tricyclic ether **365** points toward ion **364** as the intermediate.

Product analysis suggests oxolan-2-ylium ion involvement in the reaction of 6-bromo-3-hexanone with cupric cyanide in toluene.[274] Participative solvolysis of this halide, followed by cyanide attack *via* path a, led to 2-cyano-2-ethyltetrahydrofuran (eq 176). Several kinetic studies of O-5 and O-6 participation of halo ketones are discussed in section VI. Other tetrahydrofuran derivatives have been formed by acid-catalyzed ring closure of 4-hydroxyolefins and 5-hydroxyolefins, and oxolan-2-ylium ion intermediates must be assumed.[275-277] In this connection, Brouwer[61] suggested that the acid-catalyzed formation of furans from 1,4-diketones proceeds by intramolecular O-alkylation of the mono-O-protonated cation **366** followed by acid-catalyzed elimination of water from the intermediate oxolan-2-ylium ion **367** shown in eq 177. Stork and Borch[278] made use of carbonyl participation



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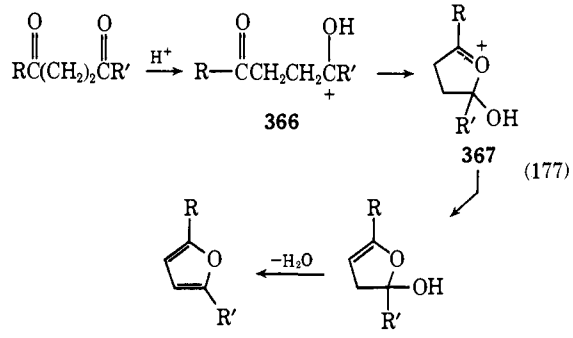
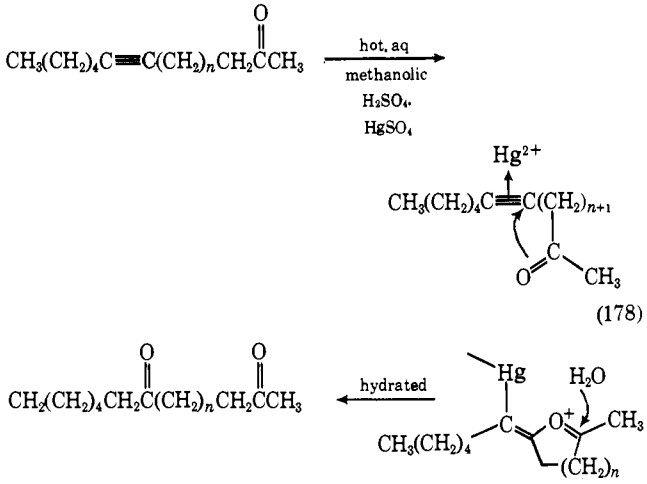


(177)

in the mercury-catalyzed hydration of acetylenic ketones in their diketone synthesis which gives γ- or δ-diketones in yields of 80 to 85% (eq 178). The O-participation is much faster in the preparation of five-membered rings than with their six-membered analogs. This reaction was crucial in the total synthesis of *cis*-jasmone[279] where it was necessary to find con-

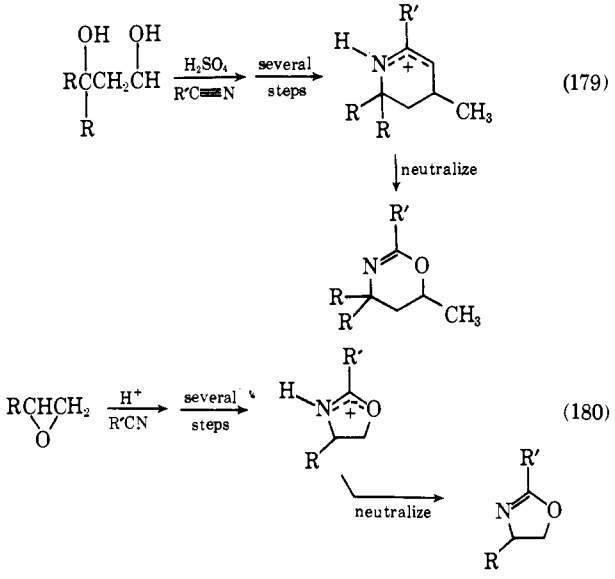
(271) J. W. Blunt, M. P. Hartshorn, and D. N. Kirk, *Chem. Commun.*, 545 (1965).
(272) H. P. Husson, P. Potier, and J. LeMan, *Bull. Soc. Chem. Fr.*, 948 (1966).
(273) G. Baddeley, E. K. Baylis, B. G. Heaton, and J. W. Rasburn, *Proc. Chem. Soc., London*, 451 (1961).
(274) H. Normant, *C. R. Acad. Sci.*, **232**, 1942 (1951).
(275) R. Paul and H. Normant, *ibid.*, **216**, 689 (1948).
(276) H. Normant, *ibid.*, **226**, 733 (1948).
(277) O. Riobe, *Justus Liebigs Ann. Chem.*, **512**, 593 (1949).
(278) G. Stork and R. Borch, *J. Amer. Chem. Soc.*, **86**, 935 (1964).
(279) G. Stork and R. Borch, *ibid.*, **86**, 936 (1964).



(178)

ditions which did not cause isomerization of a cis double bond. Other examples of oxolan-2-ylium intervention in organic mechanisms range from cyclic hemiacetal formation[280] to alkylation at acyl oxygen in dinuclear manganese carbonyls[281] to the Van Slyke determination of nitrogen in glutamine.[282]

An immense number of organic reactions involve oxazolinium, thiazolinium, and related cations at some point in their mechanisms. Some representative examples are selected here. Oxazolinium and 5,6-dihydro-1,3-oxazinium ions are certainly formed in the Ritter reaction[4,5,283] regardless of the other details of the mechanism. Of the many mechanisms discussed[4,5,283-286] the 2-oxazoline or 5,6-dihydro-1,3-oxazine product ends up in the acidic medium as its corresponding N-protonated cation (eq 179 and 180). The Ritter reaction has been extended to produce both 5,6-dihydro-1,3-thiazines and 1,3-thiazolines (eq 181 and 182).[284,285] By reacting meth-



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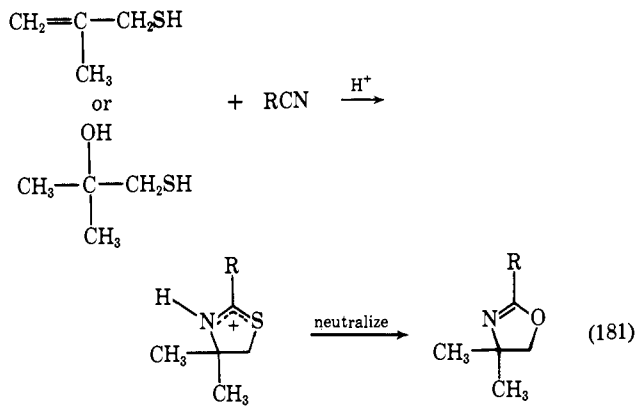

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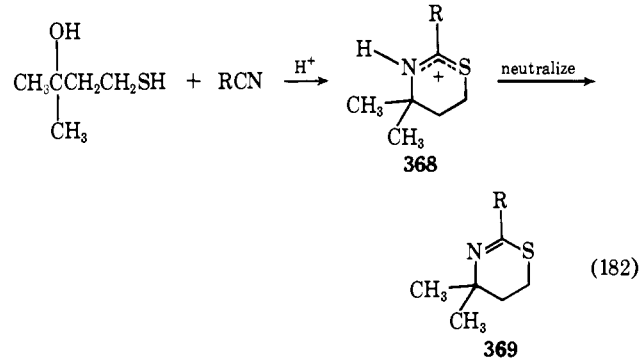

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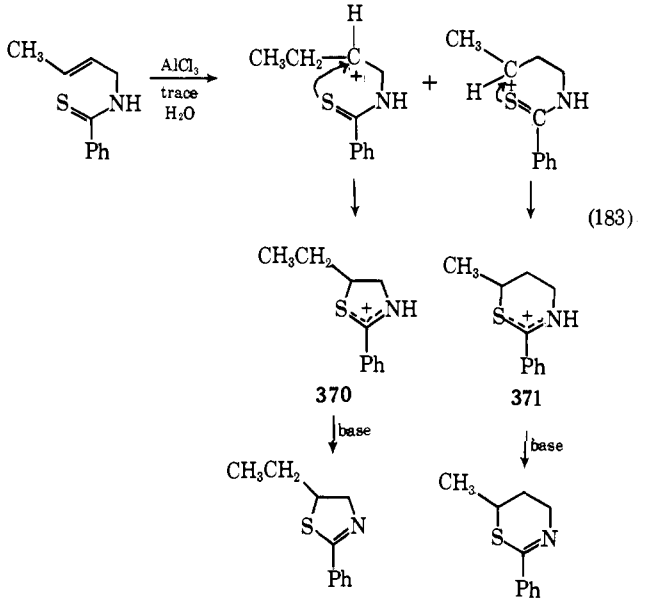
(182)

369

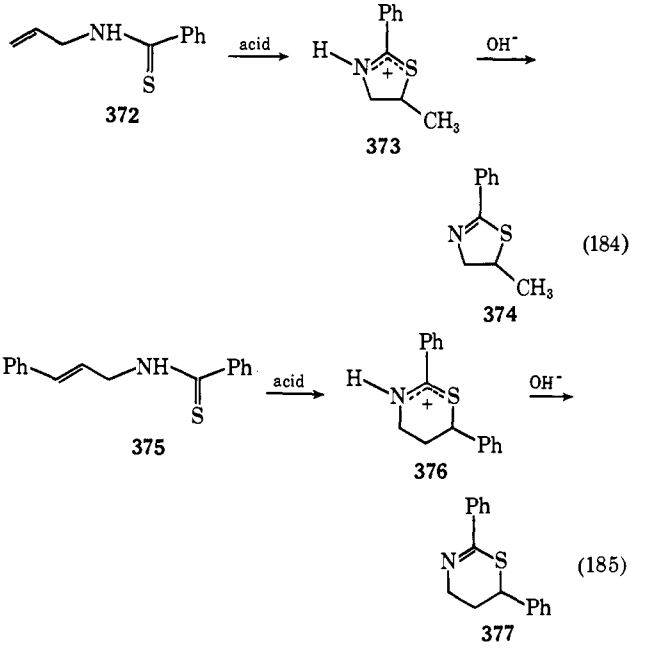
allyl mercaptan or 2-methyl-2-hydroxypropanethiol with nitriles in strong acids, a thiazolinium ion is formed (eq 181).[284,285] Another example is the reaction of 3-hydroxy-3-methylbutanethiol with nitriles in acid media to give 5,6-dihydro-1,3-thiazinium ion (**368**) from which the corresponding dihydrothiazine **369** is isolated (eq 182). The use of α,ω-dinitriles in these reactions leads to the production of α,ω-bis-(heterocyclyl)alkanes *via* the bis cations.[287]

N-Alkenylthioamides have been cyclized to thiazolines and dihydrothiazines[288] by a path involving protonation of the alkene function with (1) neighboring group S-participation or (2) subsequent trapping of the resulting alkyl cation by sulfur (eq 183). Intermediate ions **370** and **371** exist in the acidic medium before work-up of the heterocycles. It is again found that cyclization to the five-membered ring predominates by an 8:1 ratio. The question of five- *vs.* six-membered ring formation was examined[288] by comparing the acid-catalyzed ($SnCl_2$, BF_3, H_2SO_4, and $AlCl_3$) cyclizations of *N*-allylbenzthioamide (**372**) and *N*-cinnamylbenzthioamide (**375**) to the *N*-crotyl derivative of eq 183. With **372** only the thiazoline **374** was obtained (eq 184) through ion **373**. However, with

(280) C. F. Wilcox and D. L. Nealy, *J. Org. Chem.*, **28**, 3450 (1963).
(281) C. P. Casey and R. L. Anderson, *J. Amer. Chem. Soc.*, 93, 3554 (1971).
(282) A. T. Austin and J. Howard, *Chem. Ind. (London)*, 1413 (1959).
(283) E. J. Tillmanns and J. J. Ritter, *J. Org. Chem.*, **22**, 839 (1957).
(284) A. I. Meyers and J. J. Ritter, *ibid.*, **23**, 1918 (1958).
(285) A. I. Meyers, *ibid.*, **25**, 1147 (1960).
(286) R. Oda, M. Okano, S. Tokiura, and F. Misumi, *Bull. Chem. Soc. Jap.*, **35**, 1219 (1962).
(287) A. I. Meyers, *J. Org. Chem.*, **25**, 2231 (1960).
(288) P. A. S. Smith and J. M. Sullivan, *ibid.*, 26, 1132 (1961).



(183)



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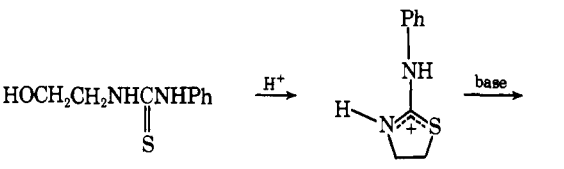

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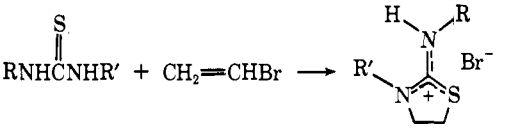

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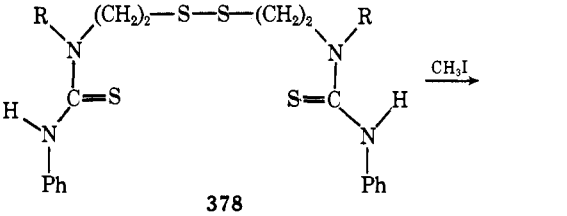
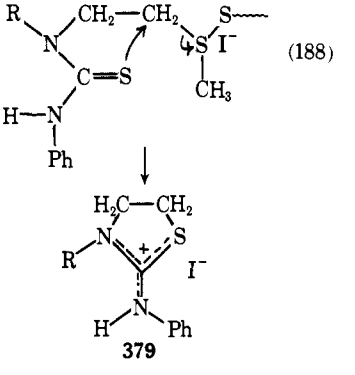
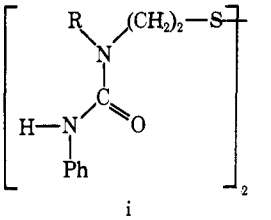




(188)

375 the dihydrothiazine was formed to the exclusion of the five-membered ring (eq 185). Thiazolinium ions are also formed in the mineral acid catalyzed cyclization of 1-(2-hydroxyethyl)thioureas.[186,289] A large number of 2-substituted iminothiazolidines, such as the example in eq 186, have been prepared in this way. The reaction of 1,3-disubstituted thioureas with ethylene bromide gives 2-substituted amino-1,3-thiazolinium bromides[290-292] represented by the general case in eq 187. A similar reaction of bis(1-substituted-1-(2-thioethyl)-3-phenylthiourea) (**378**) with excess methyl iodide in refluxing ethanol gives 2-phenylimino-3-substituted thiazolidinium hydriodides (**379**) by the route shown in eq 188.[293] The conversion appears unique to thioureas having a disulfide substituent. Attempts to extend this reaction to the bis urea analog i gave unchanged starting material as did the use of the thiol monomers.



i

The ability to form oxazolinium ions from esters of *N*-acylphenyl and *p*-nitrophenylserinates is dependent upon the

(289) E. Cherbuliez, B. Baehler, S. Jaccard, H. Jindra, G. Weber, G. Wyss, and J. Rabinowitz, *Helv. Chim. Acta*, 49, 807 (1966).

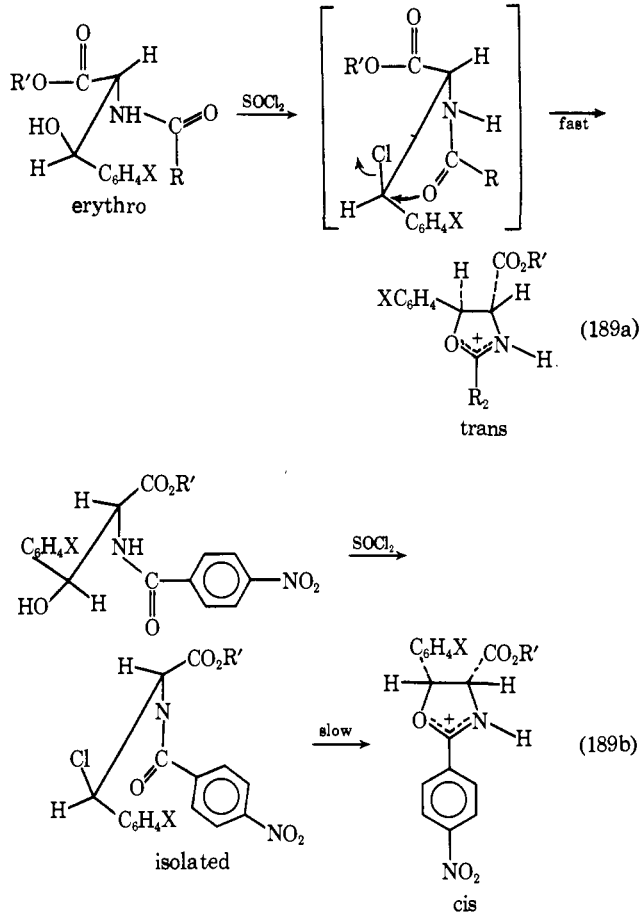
(290) L. Dashen and R. Q. Brewster, *Trans. Kans. Acad. Sci.*, **40**, 103 (1937); *Chem. Abstr.*, **33**, 5394 (1939).

(291) H. Erlenmeyer, H. Schulthess, and H. Bloch, *Helv. Chim. Acta*, **30**, 1336 (1947).

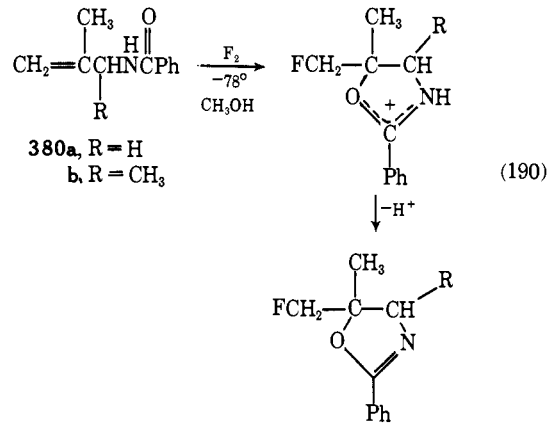
(292) C. K. Bradsher, F. C. Brown, and E. F. Sinclair, *J. Amer. Chem. Soc.*, **78**, 6189 (1956).

(293) O. L. Salerni, J. I. Morrison, W. L. Budde, and C. W. Stanley, *Tetrahedron Lett.*, 5307 (1968).

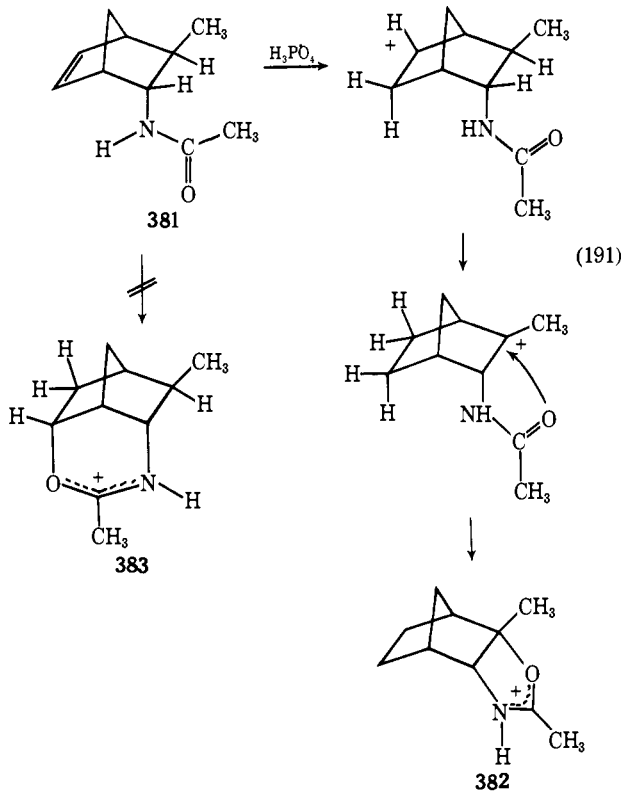
stereochemistry of these serinates.[294] The erythro isomers rapidly cyclize to the hydrochloride salts of the trans oxazolines when treated with thionyl chloride (eq 189a). Conversely, the *threo*-phenylserinates give *threo*-β-chloro derivatives without oxazolinium ion formation, although the *threo*-*p*-nitrophenyl analogs may be slowly converted to the *cis*-oxazolines as in eq 189b. This provides the usual stereochemical evidence that back-side O-participation is occurring during the loss of chloride ion. In the threo isomer, approach to the transition state requires a progressively greater eclipsing of the CO_2R' and C_6H_4X groups. This, in turn, increases the activation energy for the reaction and decreases its rate. The kinetics of a large number of similar erythro and threo systems have been studied, and erythro:threo rate ratios were found to vary widely as a function of the size of such eclipsing groups.[295]



Oxazolinium ion formation occurs in the direct fluorination of *N*-methallylbenzamide (**380a**) and *N*-(1,2-dimethyl-2-propene)benzamide (**380b**).[296] The fluorinations, conducted at −78° in solvents at least as polar as methanol, generated transient β-fluorocarbonium ions which were trapped by neighboring group participation (eq 190). These fluorocyclizations would only occur when the β carbon can provide a tertiary carbonium ion. In polyphosphoric acid *endo*-2-acetamido-*exo*-3-methylbicyclo[2.2.1]hept-5-ene (**381**) generates

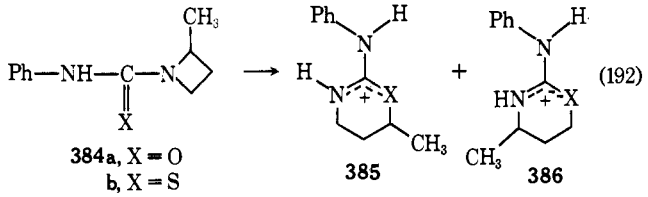


protonated 2,4-dimethyl-3-oxa-5-aza-*endo*-tricyclo[5.2.1.$0^{2,6}$]-dec-4-ene (**382**) and not the 5,6-dihydro oxazinium ion **383** which would result from neighboring amide group participation during olefin protonation.[297] Capture of the carbonium ion by the amide function occurs after molecular rearrangement (eq 191).

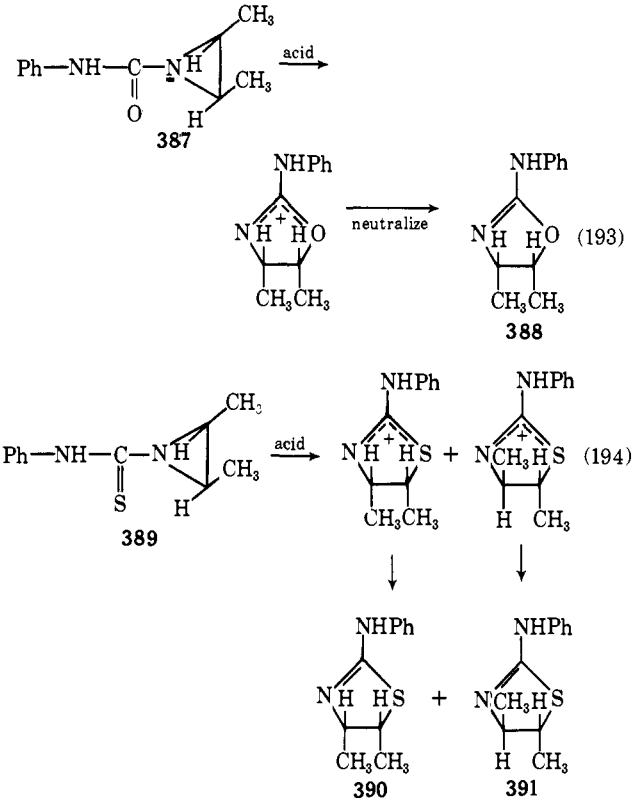


Iwakura and coworkers[298,299] reported the interesting isomerization of 1-(*N*-phenylcarbamyl)-2-methylazetidine (**384a**) and its thiocarbonyl analog (**384b**). In picric or *p*-toluenesulfonic acid–toluene solutions **384a** ring opens to give only the 2-anilino-6-methyl-5,6-dihydrooxazinium ion (**385**). However, the sulfur analog **384b** gave the 2-anilino-4-methyl-5,6-dihydrothiazinium ion (**386**) as the major product with some **385**. Since the solvent was so weakly nucleophilic that addition–elimination mechanisms were ruled out, the rearrange-

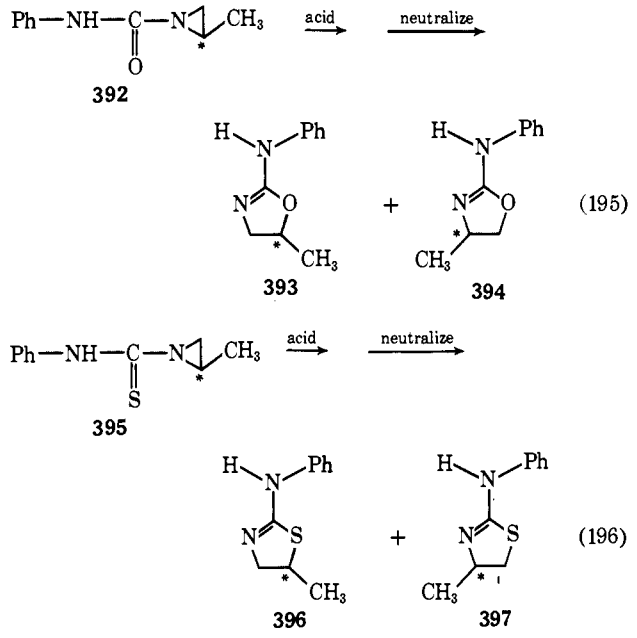
(294) S. H. Pines, M. A. Kozlowski, and S. Karady, *J. Org. Chem.*, **34**, 1621 (1969).
(295) M. Pankova and J. Sicher, *Collect. Czech. Chem. Commun.*, **30**, 388 (1965).
(296) R. F. Merritt, Rohm and Haas Co., private communication, 1969.
(297) S. P. McManus, *Chem. Commun.*, 235 (1969).
(298) Y. Iwakura, A. Nabeya, T. Nishiguchi, and K. Ohkawa, *J. Org. Chem.*, **31**, 3352 (1966).
(299) Y. Iwakura, A. Nabeya, T. Nishiguchi, and Y. Ichikawa, *ibid.*, **30**, 3410 (1965); *cf.* M. Tisler, *Arch. Pharm.*, **293**, 621 (1960).



ments of **384b** were thought to be more SN2-like (internal S attack), while for **384a** more SN1-like character was suspected. Upon neutralization the corresponding heterocycles were isolated. This same group has now reported their very extensive mechanistic studies of the acid-catalyzed isomerization of 1-acyl- and 1-thioacylaziridines which lead to oxazolinium and thiazolinium ions in the acid media before neutralization.[300,301] In a variety of acid systems and solvents, *cis*-1-(*N*-phenylcarbamyl)-2,3-dimethylaziridine (**387**) gave only the *cis*-4,5-dimethyloxazoline (**388**). On the other hand, *cis*-1-(*N*-phenylthiocarbamyl)-2,3-dimethylaziridine (**389**) gave both cis and trans thiazolines **390** and **391** in some acids and

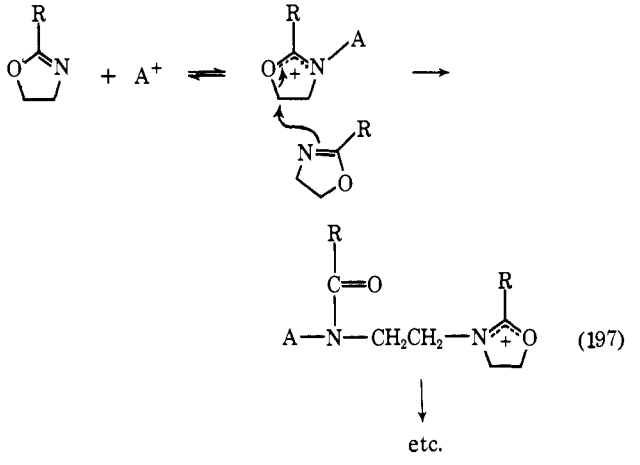


only the cis in others. The mechanisms invoked included both addition–elimination (two inversions of configuration) and internal SN-1 types. Further studies[301] with optically active aziridines **392** and **395** gave optically active products **393**, **394**, **396**, and **397** in eq 195 and 196. The amount of retention and inversion was determined in each case, and from these studies of the stereochemical details and the direction of ring opening, it was clear that free carbonium ions are not formed. Instead some O-participation is taking place in the ring opening leading to oxazolinium ions in nonnucleophilic solvent media.



Similar conclusions were reached for S-participation. Other earlier studies of these systems have been published.[302-304]

The acid-catalyzed polymerizations of oxazolines and dihydrooxazines proceed through their corresponding oxazolinium and dihydrooxazinium cations to produce high molecular weight *N*-acylpolyethylenimines and -polytrimethylenimines.[305-309] In these polymerizations, acid adds to the ring nitrogen producing the ion which is attacked nucleophilically at the 5 position (*via* path b) by the nitrogen of another ring. This is shown in eq 197. When a 2-substituted oxazoline is also substituted in both the 4 and 5 position, polymerization is prevented.



(300) T. Nishiguchi, H. Tochio, A. Nabeya, and Y. Iwakura, *J. Amer. Chem. Soc.*, 91, 5835 (1969).
(301) T. Nishiguchi, H. Tochio, A. Nabeya, and Y. Iwakura, *ibid.*, 91, 5841 (1969).
(302) V. B. Schatz and L. B. Clapp, *ibid.*, 77, 5113 (1955).
(303) D. H. Powers, Jr., V. B. Schatz, and L. B. Clapp, *ibid.*, 78, 907 (1956).
(304) J. E. Earley, C. E. O'Rourke, L. B. Clapp, J. O. Edwards, and B. C. Lawes, *ibid.*, 80, 3458 (1958).
(305) T. Kagiya, S. Narisawa, T. Maeda, and K. Fukui, *J. Polym. Sci., Part B*, 4, 441 (1966).
(306) I. T. G. Bassiri, A. Levy, and M. Litt, *ibid.*, 5, 871 (1967); A. Levy and M. Litt, *ibid.*, 5, 881 (1967).
(307) A. Levy and M. Litt, *J. Polym. Sci., Part A-1*, 6, 57, 63 (1968).
(308) D. A. Tomalia and D. P. Sheetz, *ibid.*, 4, 2253 (1966).
(309) W. Seeliger and W. Thier, *Angew. Chem., Int. Ed. Engl.*, 5, 612 (1966).

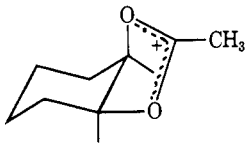
VI. Stability

A. KINETIC MEASUREMENTS

In this section we shall consider the stability of cations. Since no heats of formation of 1,3-dioxolan-2-ylium or related ions from the elements are known, an indirect measure of their thermodynamic stability is all that can be obtained. Heats of formation of some of these ions from various precursors are available. This allows the stability of the ion *relative to the specific precursor used* to be obtained. There are also much kinetic data available which can be used as an index of cation stability. What is measured is the difference in energy between the ion precursor and the transition state leading to the ion. Again, all energies are relative to that of the precursor. To the extent that the ion and the transition state leading to it resemble each other, the solvolysis rate constants will reflect the energy difference between the ion and its precursor, provided cation formation is the rate-determining step. Using both thermodynamic and kinetic techniques, we can get information on the effect of structural and solvent changes on the energy difference between a cation and its precursor.

In this section our attention will be limited to nonaromatic five- and six-membered cyclic cations containing one oxygen or sulfur or two heteroatoms (either nitrogen, oxygen, or sulfur) in the 1,3 positions. Since our fundamental interest is in cation stabilities, participation by anions to give these heterocyclic systems will not be discussed, since no information on cation stabilities can be obtained from them. Much of the early work on the systems to be discussed here is covered in Capon's review.[9]

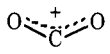
The first thoroughly studied neighboring group yielding a heterocyclic cation of interest here was the acetoxy group. Product studies discussed earlier indicated that an intermediate having the structure shown in **398** is present in the



398

acetolysis of *trans*-2-acetoxycyclohexyl *p*-toluenesulfonate. The kinetic data in Table VI show a large acceleration due to neighboring group participation.[37,39,40]

Two interesting observations stand out in Table VI. One is that participation by acetoxy has little effect on $\Delta S^{\pm}$. The other is that phenoxy is not as effective as acetoxy. A small ρ value (-1.003) for this reaction (see Figure 3) indicates that charge is dispersed into the aromatic ring.[208] However, a large ρ is not expected since the charge is highly delocalized over the



system. It may be that the phenyl group stabilizes the ground state more than the transition state and in this way reduces the rate constant for the acetolysis.

Recently the formation of 1,3-dioxan-2-ylium ions (**399**) by anchimeric assistance has been investigated.[84] The acetolysis rate constants of the compounds studied and some model compounds are shown in Table VII. Since **400** could be isolated from the solvolysis of **403** but not from the other isomers, it was concluded that only the former goes through a

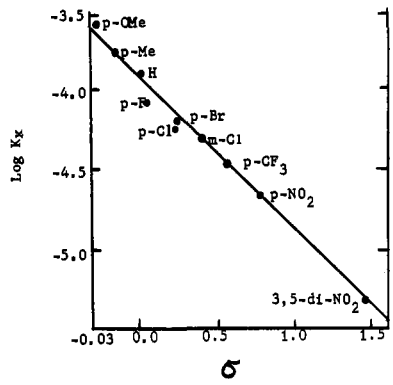
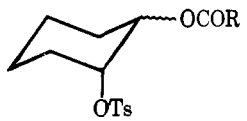


Figure 3. Plot of log $k_{99.7°}$ against σ for the acetolysis of *trans*-2-tosyloxycyclohexyl meta- and para-substituted benzoates.

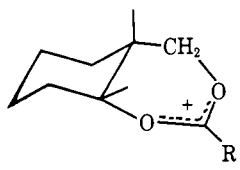
Table VI

Rate Constants at 99.7° for Acetolysis of

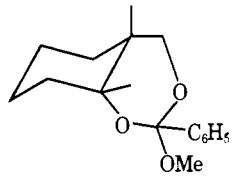


R	$k \times 10^5$ sec^{-1}	Additive concn, M	$\Delta H^{\pm}$, kcal/mol	$\Delta S^{\pm}$, eu	Ref
H	64.2	DPG[a] [0.095]			40
trans-CH_3	21	DPG [0.100]			40
trans-CH_3	20.3	KOAc [0.0995]			40
trans-CH_3	52[b]	H_2O [0.36]	26	−4.2	37
cis-CH_3	0.053	DPG [0.108]			40
cis-CH_3	0.097[b]	Ac_2O [0.046]	30.9	−3.5	37
trans-C_6H_5	16	KOAc [0.116]			39

[a] Diphenylguanidinium acetate. [b] Brosylate leaving group.



399



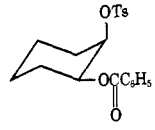
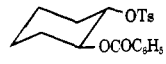
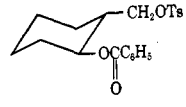
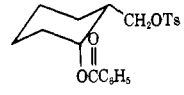
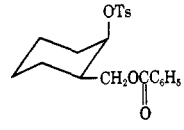
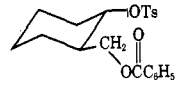
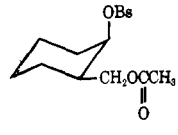
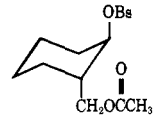
400

1,3-dioxan-2-ylium ion intermediate. Starting from **403**, the assisted reaction is 52 times faster than the unassisted solvolysis. However, when **405** and **406** are the starting materials, the assisted pathway is *slower* by a factor of 2.3. It is difficult to reconcile this fact with participation by the benzoyloxy group unless one realizes that *cis*-2-alkylcyclohexyl tosylates solvolyze much faster than the corresponding trans isomers. For example, the cis/trans rate ratio for solvolysis of 2-methylcyclohexyl tosylates and 2-isopropylcyclohexyl tosylates are 68 and 44, respectively.[312] Participation by neighboring acetoxy has also been observed in steroids.[313] From the data in Table VII it might be concluded that $-CH_2OOCCH_3$ is a better neighboring group than $-CH_2OOCC_6H_5$. However,

(310) O. Kovacs, G. Schneider, and L. K. Lang, *Proc. Chem. Soc., London*, 374 (1963).
(311) L. J. Dolby and M. J. Schwarz, *J. Org. Chem.*, 30, 3581 (1965).
(312) G. Schneider, personal communication.
(313) G. Schneider and I. Weisz-Vinze, *Kem. Kozlem.*, 31, 383 (1969).

Table VII

Rate Constants for Acetolysis at 100°

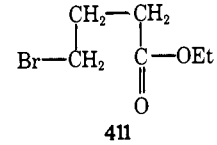
No.	Compound	$k \times 10^5\ sec^{-1}$	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, eu	Ref
401		0.03			84.
402		17.3			84
403		179			84
404		3.45			84
405		19.7			84
406		8.57			84
407		64.2			310
408		0.51			310
409		43.4[a,b]	24.9 ± 0.7	− 6.4 ± 1.8	311
410		46.4[b]	26.7 ± 1.2	− 6.4 ± 3.3	311

[a] Does not go through a 1,3-dioxan-2-ylium ion. [b] $T = 94°$.

when the benzoyloxy group is replaced by an acetoxy group, the rate enhancement is fairly small, and in the examples cited the leaving group has been changed. This same order is observed in the formation of 1,3-dioxolan-2-ylium ions. This is consistent with greater stabilization of the starting ester than of the cation by the benzene ring.

The intermediacy of a 1,3-dioxan-2-ylium ion in the solvolysis of **410** and the absence of this intermediate in the solvolysis of **409** were shown using O^{18} labeling. About 80% of the products resulting from **410** goes through the 1,3-dioxan-2-ylium ion intermediate.[311] The rate constants and activation parameters for the two compounds are quite similar. As pointed out earlier, since the trans isomer is expected to solvolyze slower than the cis, this observation is consistent with anchimeric assistance.

The solvent dependence of participation by the acetoxy group has been reported in an important communication by



411

Kwart.[314] The dependence of the rate constant for solvolysis of ethyl γ-bromobutyrate (**411**) on solvent is shown in Table VIII. The solvent dependence is that expected[315] for a reaction in which charge is being created. It is noteworthy and important that the reaction does not occur in the gas phase, emphasizing the great difference between even a hydrocarbon solvent and the gas phase.

(314) H. Kwart and M. T. Waroblah, *J. Amer. Chem. Soc.*, **89**, 7145 (1967).

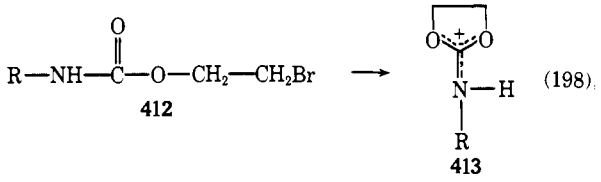
(315) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," 2nd ed, Cornell University Press, Ithaca, N. Y., 1969, pp 463–468.

Table VIII

Rate Constants for Lactonization of Ethyl γ-Bromobutyrate at 200°

Solvent	*Dielectric constant*	$k \times 10^5$ sec^{-1}
Acetonitrile	37.5	8500
Dimethyl phthalate	20	3200
Chlorobenzene	5.7	350
1,3-Dimethyl-5-ethyl-adamantane	1.9	27
Gas phase	1+	

Participation by the carbonyl group of carbamates (**412**) to give heterocyclic cations (**413**) has been studied.[316] The



(198)

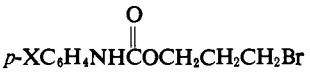
effect of solvent on this reaction is small, as emphasized by the data in Table IX. As occurs so often, the activation en-

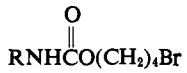
Table IX

Kinetics of Solvolysis of 2-Bromoethyl Phenylcarbamate (412, R = C_6H_5) in Aqueous Ethanol at 50°[316]

% ethanol (v/v)	$k \times 10^5$ sec^{-1}	$\Delta H^{\pm}$, *kcal/mol*	$\Delta S^{\pm}$, *eu*
100	0.76	18.9	−23.7
95	1.38	19.3	−21.1
90	1.66	21.7	−13.3
80	2.52	22.4	−10.4
70	2.92	22.4	−10.0
60	3.72	22.5	−9.4
50	4.68	22.8	−7.9
40	5.43	22.9	−7.1

thalpy and entropy change in opposing directions as the solvent varies. The effect of varying the carbamate's R group in both five- and six-membered ring series is shown in Table X. The six-membered rings result from solvolysis of **414**.[317]





As we have seen before, replacing an alkyl group by a phenyl group conjugated to the carbonyl of the neighboring group results in a rate decrease. Increasing the size of the ring from five to six also reduces the rate. A severe drop occurs on going to a seven-membered ring. Interestingly, the rate reduction on going from a five- to a six-membered ring transition state is due almost completely to an increase in $\Delta S^{\pm}$. This suggests that a greater increase in structure is necessary to arrive at a transition state of essentially the same stability (equal $\Delta H^{\pm}$) in the formation of the six-membered ring. A complete dis-

Table X

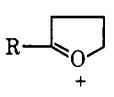
Rate Constants for the Solvolysis of Some β- and γ-Bromo Carbamates ($RNHCOO(CH_2)_nX$) in 80% Aqueous Ethanol

Compound	$k \times 10^6$ sec^{-1}	*T, °C*	$\Delta H^{\pm}$, *kcal/mol*	$\Delta S^{\pm}$, *eu*	*Ref*
R = Et	9.0	50			318
R = α-naphthyl	3.36	50			318
R = phenyl	2.56	50			318
R = α-naphthyl	0.18	50			318
R = α-naphthyl	0.0023	50			318
X = CH_3CH_2O	1.94	75	19.7	−23.6	317
X = CH_3	1.69	75	20.5	−21.5	317
X = H	1.40	75	19.6	−24.7	317
X = Cl	0.99	75	20.7	−22.2	317
X = NO_2	0.17	75	20.9	−25.1	317
p-$EtOC_6H_4$	45.9	75	21.7	−11.6	319
p-MeC_6H_4	45.6	75	22.3	−10.2	319
C_6H_5	33.2	75	22.4	−10.4	319
p-ClC_6H_4	21.6	75	22.6	−10.7	319
p-$NO_2C_6H_4$	6.2	75	23.8	−9.7	319

cussion of the effects of ring size on anchimeric assistance is given in Capon's review.[9] For both five- and six-membered ring transition states in carbamate solvolyses, the ρ values are small and similar, −0.88 and −0.92, respectively.[317-319] This value is also close to that observed for neighboring ArCOO–, which is surprising since resonance delocalization of charge onto nitrogen should contribute strongly to stabilization of the ion. The data in Table X indicate that most of the substituent effect is due to changes in $\Delta S^{\pm}$, the reactions being nearly isoenthalpic.

The participation of the unsubstituted carbonyl group in solvolysis reactions has been studied. When γ- and δ-ketoalkyl tosylates are solvolyzed in trifluoroacetic acid, the stable cations **416** and **417** are observed.[59] As shown by the data in Table XI, the formation of the five-membered ring is faster, owing principally to a greater $\Delta S^{\pm}$.

The participation of the carbonyl group in the silver ion assisted solvolysis of a variety of chloro ketones has been



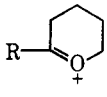


Table XI

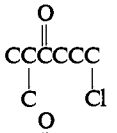
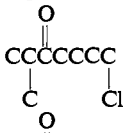
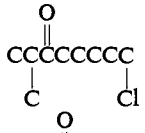
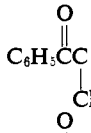
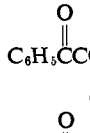
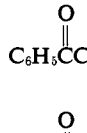
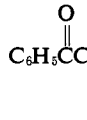
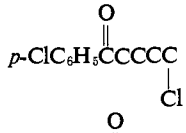
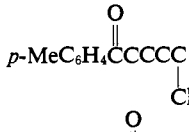
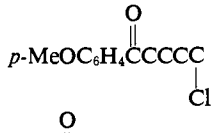
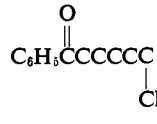
Rate Constants for the Trifluoroacetolysis of Some Ketobrosylates at 30°[59]

Compound	$k \times 10^5$ sec^{-1}	E_a, *kcal/mole*	$\Delta S^{\pm}$, *eu*
$CH_2(CH_2)_2\overset{O}{\overset{\|}{C}}C_6H_5$ OBs	1920	17.4	−11.0
$CH_2(CH_2)_3\overset{O}{\overset{\|}{C}}C_6H_5$ OBs	49	17.8	−17.0

(316) F. L. Scott, E. J. Flynn, and D. F. Fenton, *J. Chem. Soc. B*, 277 (1971).
(317) F. L. Scott and D. F. Fenton, *Tetrahedron Lett.*, 685 (1970).
(318) F. L. Scott, R. E. Glick, and S. Winstein, *Experientia*, **13**, 183 (1957).
(319) F. L. Scott and E. Flynn, *Tetrahedron Lett.*, 1675 (1964).

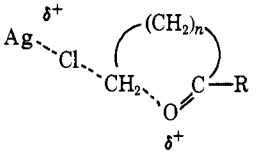
Table XII

Solvolysis of ω-Chloro Ketones in 80% Aqueous Ethanol with Silver Perchlorate at 56.28°[320]

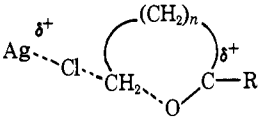
No.	Compound	$k \times 10^5$ mol^{-1} min^{-1}	$\Delta H^{\pm}$, kcal/mol	$\Delta S^{\pm}$, eu	k_{rel}
418	$CH_3(CH_2)_3Cl$	0.211			1.00
419		114	16.2	−18.2	537
420		4.54	18.7	−20.8	21.5
421		0.755	19.3	−22.6	3.6
422		0.265	11.7	−45.3	1.3
423		1.66	20.9	−16.0	7.9
424		161	18.0	−15.8	759
425		4.52	20.5	−20.4	21.3
426		0.567	19.2	−20.5	10.3
427		2.17	14.4	−17.9	28.7
428		6.07	19.0	−18.5	39.2
429		8.29	19.1	−23.1	2.7

thoroughly investigated.[320] The relevant data are contained in Table XII. For compounds **419**, **420**, and **421** it was suggested that five-, six-, and seven-membered rings formed since in all three cases the rate constants are greater than that of *n*-butyl chloride. There are few claims in the literature of anchimeric assistance through a seven-membered ring.[9] The evidence in this case is marginal. As expected, there is a decrease in $\Delta S^{\pm}$ of 1.8 eu going from the six- to the seven-membered ring, but this is just outside the experimental error of 1.2 eu. The difficulty in interpreting such changes in $\Delta S^{\pm}$ is illustrated by compounds **425–428**, when $\Delta S^{\pm}$ varies by 2.6 eu, probably due to solvation changes. On the other hand, both compounds **421** and **429** show rate constant increases, and $\Delta S^{\pm}$ decreases, consistent with the formation of a seven-membered ring in the transition state.

It has been pointed out in several systems that the replacement of an aliphatic group by a phenyl group conjugated to a participating carbonyl reduces the rate constant for the solvolysis. With ketones, this substitution has only a small effect. A Hammett plot using σ is linear. In these cases ρ is close to −1, as observed in other systems. On the basis of these observations, it was suggested that the p–π electrons of the carbonyl group were not involved. That is, resonance structure **430** was the principal contributor, not **431**. This is in excellent



430



431

agreement with conclusions drawn from the structure of protonated ketones. Studies[2] show that the double bond is still intact and a protonated ketone is best represented as $R_2C{=}O^+{-}H$. Because of this phenomenon, little charge is delocalized into the aromatic ring in the halo ketone solvolyses. This picture is consistent with the small negative ρ value, though interpretation of a ρ value this small is somewhat risky. The observed facts are also consistent with greater resonance stabilization of the starting ketone than that of the ion by the phenyl substituent. A substituent on a phenyl ring would exert its normal effect, although the effect would be comparatively small. The substitution of phenyl for methyl would lead to a rate reduction. Finally, to the extent that this interaction is smaller in a ketone than in an ester, the rate reduction by phenyl in a ketone should be less. This is as observed.

The mercuric ion assisted solvolysis of a variety of bromo ketones, bromo esters, and bromo ethers has also been studied.[321] These data are shown in Table XIII. The increase in rate constant accompanying 1,3-dioxolan-2-ylium ion formation from compound **435** is quite apparent. The isolated carbonyl group is a more reactive neighboring group than is the carbonyl group in an ester. Using the data in Tables XIII and XIV, a comparison of the reactivity of the carbonyl group and the ether oxygen[322] can be made. It is seen from the data in Table XIV that an ether oxygen is a much better nucleophile than an ester alkyl oxygen when both form a five-membered ring. From the data in Table XIII, it appears that an aryl ketone's carbonyl oxygen is more effective than an ester's carbonyl oxygen. Thus, neither oxygen in an ester is as effective as its isolated analog. This may be due to the greater loss of resonance energy in the ester when the group participates in a reaction as a nucleophile.

The participation of the *o*-carbomethoxy and -carbophenoxy group in the solvolysis of benzyl halides has been investigated thoroughly. There is a small difference in the ability of RCOO– and ROOC– to participate as neighboring groups in solvolysis reactions.[323] The former shows no evidence for participation when ortho to a benzylic halide, while the latter seems to participate. Also, participation by ROOC– seems

(320) D. J. Pasto and M. P. Serve, *J. Amer. Chem. Soc.*, **87**, 1515 (1965).

(321) S. Oae, *ibid.*, 78, 4030 (1956).

(322) S. Oae, *ibid.*, 78, 4032 (1956).

(323) A. Singh, L. J. Andres, and R. M. Keefer, *ibid.*, **84**, 1179 (1962).

Table XIII

Rate Constants of Mercuric Ion Assisted Solvolysis in 30% Aqueous Dioxane at 40.05°[321]

No.	Compound	$k \times 10^3$ l. mol^{-1} sec^{-1}
432	$CH_3CH_2CH_2CH_2Br$	4.2
433	$C_6H_5CCH_2Br$ (O)	0.23
434	$C_6H_5CCH_2CH_2Br$ (O)	1.3
435	$C_6H_5CCH_2CH_2CH_2Br$ (O)	78.3[a]
436	$CH_3CH_2OCCH_2Br$ (O)	0.13
437	$CH_3CH_2OCCH_2CH_2Br$ (O)	0.43
438	$CH_3CH_2OCCH_2CH_2CH_2Br$ (O)	5.2
439	$CH_2COCH_2CH_2Br$ (O)	2.0
440	$CH_3COCH_2CH_2CH_2Br$ (O)	2.0
441	$CH_3CO(CH_2)_4Br$ (O)	2.2
442	$CH_3CH_2OCH_2CH_2CH_2Br$	1.4
443	$CH_3CH_2O(CH_2)_4Br$	33.8
444	$CH_3CH_2O(CH_2)_5Br$	5.0

[a] At 25°, too fast to be measured at 40°.

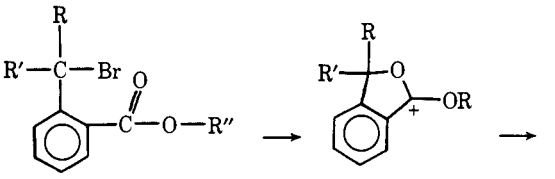
Table XIV

Rate Constants for Solvolysis in 78.5% Formic Acid (w/w) at 85°[322]

Compound	$k \times 10^5$ sec^{-1}
$CH_3CHBrCH_3$	6.37
$CH_3CH_2CHBrCH_3$	6.74
$CH_3CH_2CH_2CHBrCH_3$	6.50
$CH_3OCH_2CH_2CH_2CHBrCH_3$	189
$CH_3COO(CH_2)_3CHBrCH_3$	6.4

more effective (higher k_{ortho}/k_{para} ratio) when R is phenyl rather than methyl.[323,324] However, since the two groups being compared are reacting in different systems (see Tables XV and XVI),[323,325-328] this conclusion is tentative.

The data in Tables XV and XVI permit a comparison to be made of the ability of an ortho -COOR group to participate as the methyl group prevents the ring and benzyl carbonium ion from becoming coplanar, hindering resonance stabilization of the ion. Not only is the stabilization prevented, but also the carbon is placed in a conformation with the open

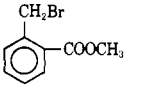
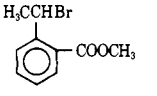
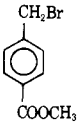
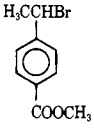
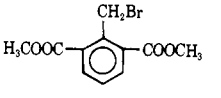
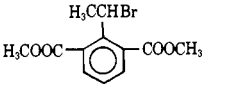
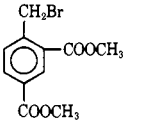
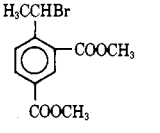


(199)

445, R = R′ = H
446, R = H; R′ = CH_3
447, R = R′ = CH_3
448, R = H; R′ = C_6H_5

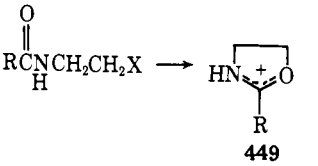
Table XV

Relative Rate Constants for Solvolysis in Aqueous Dioxane at 70.7°[325]

Compound	Rel rate	Compound	Rel rate
	1.0		64.5
	1.4		6.9
	0.40		0.89
	0.30		7.9
	0.55		1.8

"face" of the ion toward the carbonyl group facilitating participation. This effect increases in compound **448**, when the phenyl group very effectively interferes sterically. This argument is strongly supported by the absence of participation in 4-carbomethoxy-9-bromofluorene, where this favorable conformation is impossible.[326] Significant participation, however is not observed in compound **447**, and this has been attributed to steric factors.[37,39,40,208]

The participation by neighboring benzamido groups to give oxazolinium ion **449** has been studied thoroughly. As



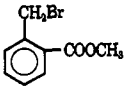
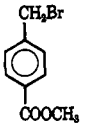
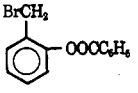
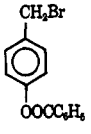
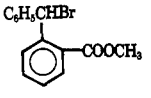
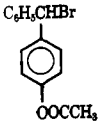
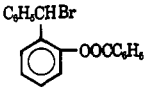
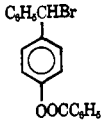
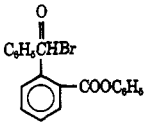
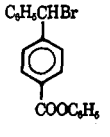
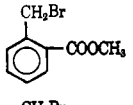
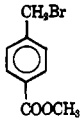
(200)

449

(324) M. J. Strauss, L. J. Andres, and R. M. Keefer, *J. Amer. Chem. Soc.*, 90, 3473 (1968).
(325) M. J. Strauss, I. Horman, L. J. Andres, and R. M. Keefer, *J. Org. Chem.*, 33, 2194 (1968).
(326) R. E. Louis, L. J. Andres, and R. M. Keefer, *J. Amer. Chem. Soc.*, 84, 3959 (1962).
(327) J. L. Cotter, L. J. Andres, and R. M. Keefer, *J. Org. Chem.*, 28, 1917 (1963).
(328) E. A. Jeffery, R. K. Bansal, L. J. Andrews, and R. M. Keefer, *ibid.*, 29, 3365 (1964).

Table XVI

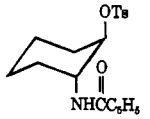
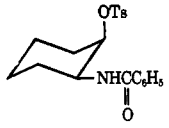
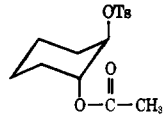
Rate Constants for Solvolysis of Some Benzylic Bromides[323,328]

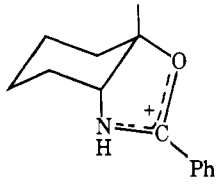
Compound	Solvent	Temp, °C	$k \times 10^5$ sec^{-1}	E_a kcal/mole	$\Delta S^{\ddagger}$, eu
	80% aq dioxane	71.4	1.88		
			2.67	21.4 ± 0.6	−19.7 ± 1.7
			0.74	17.0 ± 0.7	−35.1 ± 2.0
			0.548	19.8 ± 0.4	−27.6 ± 1.2
			2.61	20.2 ± 0.5	−23.2 ± 1.5
	90% aq acetone	25	16.4		
			2.23		
			41.7		
			0.68	17.4 ± 0.4	−18.8 ± 1.3
			26.7	21.2 ± 0.2	−16.1 ± 0.7
			14.4		
			0.167		
	50% aq acetone	45	1.40		
			0.78		

stated earlier, work on this series was done first by Winstein,[172,173,329] who studied the solvolysis of 2-benzamidocyclohexyl tosylates. It can be seen from the data in Table XVII that benzamido is about 200 times better as a neighboring group than acetoxy. Indeed the oxazolinium ion formed (**450**) is so stable that it can readily be isolated as the tosylate salt.[329] The trans isomer solvolyzes *ca.* 1000 times faster than the cis isomer, similar to the rate ratio for neighboring acetoxy. It has been reported[330] that amide participation in the acid-catalyzed hydrolysis of **451** causes a rate increase of at least 10^4. Studies[331,332] of solvent effects on the solvolysis of 2-benzamidoethyl bromide (**452**) have yielded some interesting results. The reactions are only slightly effected by solvent as shown by the data in Table XVIII.[331] At 50° the *m* value is 0.139 in aqueous ethanol, less than *m* for ethyl bromide and consistent with an SN2 reaction. The SN2 character of this reaction was firmly established first by Pocker.[332] In addition to studying the solvent dependence, he studied the effects of added salts and nucleophiles on the reaction, both of which were consistent with an internal SN2 displacement.

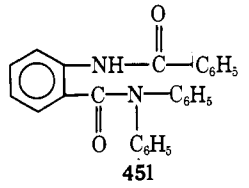
Table XVII

Rate Constants for Solvolysis of Some 2-Substituted Cyclohexyl Tosylates[329]

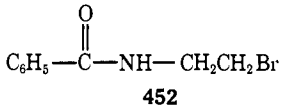
Compound	Temp, °C	Solvent	KOAc, $M \times 10^3$	$k \times 10^5$ sec^{-1}
	74.51	EtOH	30.2	179
	49.61	EtOH	28.2	12.3
	74.72	HOAc	0	0.249
	75.04	EtOH	0	0.995



450



451



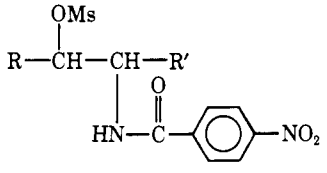
452

Table XVIII

Kinetics of Solvolysis of 2-Benzamidoethyl Bromide (452) in Aqueous Ethanol[331,332] and Other Solvents

Solvent	$k \times 10^5$ sec^{-1}	Temp, °C	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, eu
C_2H_5OH–H_2O, % (v/v)				
100	5.75	50	21.7	−6.4
90	8.51		20.8	−8.2
80	11.0		20.6	−8.4
70	13.9		21.4	−5.6
60	16.1		21.6	−4.7
50	20.6		22.0	−3.1
40	22.3		22.8	−0.2
30	25.6		23.2	3.2
$C_6H_5CH_2OH$	8.06	25		
CH_3NO_2	6.65			
CH_3CN	5.36			
$C_6H_5NO_2$	5.32			
C_6H_5CN	4.91			
CH_3COCH_3	3.84			
CH_3OH	3.22			
CH_3CH_2OH	2.42			
i-PrOH	1.86			
$CHCl_3$	1.74			
EtOH–CH_3OH (1:1, v/v)	6.44			

The rate constants for participation by neighboring benzamido has been used to probe steric interactions in a number of systems. The erythro and threo isomers of **453** were solvolyzed in ethanol[295] (see Table XIX). As expected the rate constants in the threo series are more sensitive to the size of the alkyl groups than those in the erythro series. Branching in the α position has a particularly pronounced effect. As the transition state is reached and the oxazolinium ion is being formed, R and R′ will begin to seriously eclipse one another (see **454**). The effect of para substituents when R or



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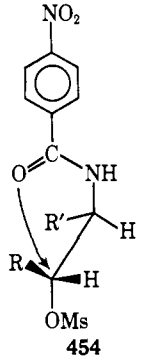
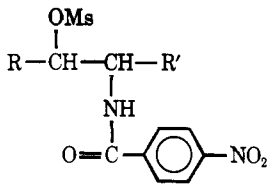


454

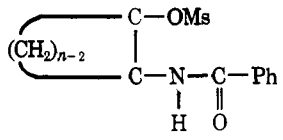
(329) S. Winstein and R. Boschan, *J. Amer. Chem. Soc.*, 72, 4669 (1950).
(330) T. Cohen and J. Lipowitz, *ibid.*, 86, 5611 (1964).
(331) F. L. Scott, E. J. Flynn, and D. F. Fenton, *J. Chem. Soc. B*, 277 (1971).
(332) Y. Pocker, *ibid.*, 2319 (1959).

Table XIX

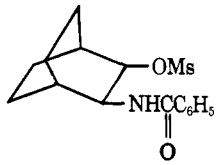
Rates of the Ethanolysis of



A



B,445



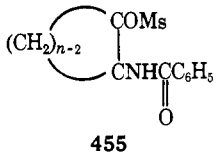
C

	R	R′	Temp, °C	$k \times 10^5$ sec^{-1}	$\Delta H^{\ddagger}$,[a] kcal/mol	$\Delta S^{\ddagger}$[a]
			Structure A			
erythro	CH_3	CH_3	30.10	9.05	21.8	−5.1
threo			29.90	2.40	23.2	−3.1
erythro	*n*-C_3H_7	*n*-C_3H_7	30.10	14.0	21.0	−6.8
threo			30.10	3.27	22.6	−4.4
erythro	*n*-C_4H_9	*n*-C_4H_9	30.00	1.43	20.7	−8.0
threo			30.00	3.53	22.2	−5.7
erythro	*i*-C_4H_9	*i*-C_4H_9	29.90	6.67	20.6	−9.7
threo			39.85	8.13	21.9	−7.2
erythro	$C_6H_{11}CH_2$	$C_6H_{11}CH_2$	29.90	7.51	19.8	−12.2
threo			35.00	5.53	22.3	−5.5
erythro	CH_3	C_6H_{11}	29.90	36.3	21.2	−4.2
threo			39.85	3.51	22.8	−6.3
erythro	C_6H_{11}	CH_3	29.90	1.90	22.6	−5.6
threo			49.80	2.09	23.8	−6.4
erythro	C_6H_{11}	C_6H_{11}	30.10	15.8	21.7	−4.2
threo			69.75	2.22	25.7	−5.1
erythro	*i*-C_3H_7	*i*-C_3H_7	30.00	12.6	21.0	−6.9
threo			69.75	2.09	25.3	−6.3
			Structure B (**455**)			
	n					
trans	5		20	91.2	19.1	−5.6
cis	6		60	0.0775	27.0	−5.5
trans	6		60	26.3	24.5	−1.4
cis	7		60	2.96	23.6	−8.4
trans	7		35	133	20.7	−4.4
cis	8		60	2.73	23.3	−9.7
trans	8		60	121	22.3	−5.0
cis	9		60	1.02	24.6	−7.5
trans	9		60	28.1	23.4	−4.8
cis	10		60	1.52	24.4	−10.7
trans	10		60	61.0	21.5	−8.8
cis	11		60	0.948	24.1	−9.2
trans	11		60	16.9	23.1	−6.6
cis	12		60	0.233	25.9	−6.6
trans	12		60	48.8	24.8	−3.9
cis	13		60	3.53	23.1	−9.7
trans	13		60	87.9	21.4	−8.5
cis	14		60	4.02	23.2	−9.3
trans	14		60	35.3	23.9	−2.8
cis	15		60	22.9	21.4	−11.0
trans	15		50	67.4	22.0	−4.9
cis	16		60	35.7	21.7	−9.3
trans	16		60	141	22.0	−5.7
cis	20		50	86.4	20.9	−8.0
trans	20		50	101	21.0	−5.7
cis	26		40	96.0	21.9	−2.4
trans	26		40	35.5	21.0	−7.3
			Structure C			
cis			90	4.01	25.6	−8.4
trans			60	6.84	24.4	−4.4

[a] At 60°.

R′ is aryl has been determined. It was argued that the rate ratio for the benzene and *p*-nitrobenzene derivatives (k_H/k_{NO_2}) will be close to one when there is little or no participation and will increase as participation becomes more important. Consistent with this k_H/k_{NO_2} was always found to be greater for the erythro compound than for the threo isomer.

The effect of the ring size as shown in structure **455** on the

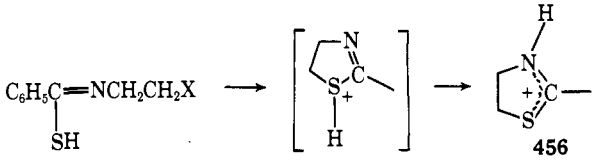


455

participation by the benzamido group has been very thoroughly examined[333,334] (see Table XIX). The ratio k_{trans}/k_{cis} decreases steadily as ring size increases. The rate constants for the trans isomers show a decrease from the 20- to 26-membered ring, while the rate constants for the cis isomers increase steadily from a ring size of 12 through 26. Indeed in the 26-membered ring the cis isomer reacts faster. The rate constant for the trans isomer in the 16- and 20-membered rings is close to that of the open-chain compound.[335] The very high reactivity of both five- and seven-membered rings is striking. The $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ values for this reaction seem to be coupled, with $\Delta H^{\ddagger}$ becoming larger when $\Delta S^{\ddagger}$ is least negative. A transition state involving a large amount of participation will be more highly ordered and more stable than one with less participation. This should result in a lower $\Delta H^{\ddagger}$ and a more negative value for $\Delta S^{\ddagger}$. These data have also been discussed in a review of the stereochemistry of large ring systems.[336] The effect of boat–chair equilibrium on the extent of participation in substituted cyclohexanes has also been investigated.[337] Finally the methanolysis of some *N*-2-bromoethylbenzamides has been studied and shown to proceed through an oxazolinium ion.[338]

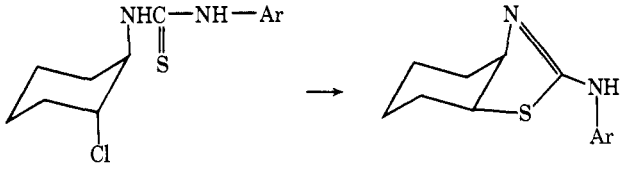
(333) J. Sicher and M. Sroboda, *Collect. Czech. Chem. Commun.*, 23, 2094 (1958).
(334) M. Sroboda and J. Sicher, *ibid.*, 30, 2948 (1965).
(335) J. Sicher, M. Pankova, J. Jonas, and M. Sroboda, *ibid.*, 24, 2727 (1959).
(336) J. Sicher, *Progr. Stereochem.*, 3, 203 (1962).
(337) J. Sicher, M. Tichy, F. Sipos, and M. Pankova, *Collect. Czech. Chem. Commun.*, 26, 2418 (1961); *Proc. Chem. Soc., London*, 384 (1960).
(338) H. W. Heine, *J. Amer. Chem. Soc.*, 79, 908 (1957).

There have been only a few studies of the kinetics of reactions leading to the formation of nonaromatic five- and six-membered heterocycles containing sulfur. Thiazolinium ions (**456**) have been detected in reaction 201.[339,340] The *N*-arylthioureido group (**457**) is an extremely effective neighboring group as shown by the data in Table XX.[341] Substi-



456

(201)



457

(202)

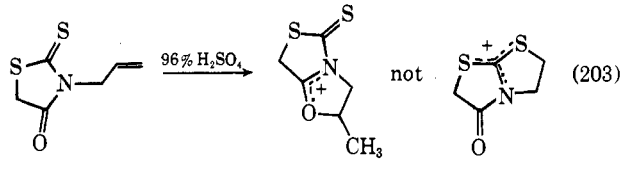
Table XX

Rate Constants for Solvolysis of Trans Para-Substituted Phenylthioureidocyclohexyl Chlorides (457) in 80% Aqueous Ethanol at 75°

Para substituent	$k \times 10^5$ *sec*$^{-1}$	$\Delta H^{\pm}$, *kcal/mol*	$\Delta S^{\pm}$, *eu*
CH_3O	55.0	24.3	−3.87
CH_3	53.6	24.3	−3.92
H	50.6	24.3	−4.07
Cl	44.3	24.3	−4.32
Br	43.6	24.3	−4.35
NO_2	22.5	24.3	−5.78

tution in the aryl group leads to a ρ value of −0.26 in aqueous ethanol at 75°. This is quite consistent with the existence of the extremely stable cation. The reaction has a nearly constant $\Delta H^{\pm}$, the substituent effect being due to changes in $\Delta S^{\pm}$. The formation of a 1,3-dithiolan-2-ylium ion has also been reported;[116] however, the rate constants for ion formation have not been measured.[116]

The sole reaction at oxygen rather than sulfur has been determined in the cyclization of *N*-allylrhodamine (eq 203) in concentrated sulfuric acid.[342] While one might not predict this result because of the higher nucleophilicity of sulfur generally, and the presence of a second sulfur atom to help

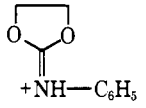


(203)

stabilize the carbonium ion, it is only cyclization at oxygen which is observed. This may be another manifestation of the hard–soft acid–base theory.

It is possible to use the kinetic data discussed here to compare the relative stabilities of the heterocyclic cations. To do this it is necessary to know the rate constants for the formation of the cations under the same conditions (solvent, temperature, and leaving group). The most convenient reaction is acetolysis at 75° with bromide as the leaving group. The data in Table XXI were calculated from data given earlier in this review using the Grunwald–Winstein mY treatment to correct for solvent changes.[343] Corrections for different leaving groups were made using data from Streitwieser's review.[344]

The rate decrease on going from a five- to a six-membered ring (ions **398** → **399** and **413** → **458**) has been discussed thoroughly before.[9] The large increase in rate constant between ions **398** and **413** is at first glance surprising. It is probably due in part to the greater stability of the latter due to contributions from resonance forms such as **463**. However, the fact



463

that the ion is not fused to a six-membered ring is also important as shown by the data for ions **449** and **450**. Indeed if this factor is considered, the amine substituent increases the rate constant by only a factor of 3. It seems unlikely that fusion to a six-membered ring greatly destabilizes a 1,3-dioxolan-2-ylium ion. It seems more likely that the rate of formation of ion **398** is slowed by steric effects. The trans coplanar transition state will involve two axial groups and will therefore be destabilized. The very large rate constant for ion **459** is also noteworthy. It seems likely that this high rate constant is due to formation of the very stable benzhydryl cation or to stabilization of an electron-deficient transition state by the phenyl rings. The relative "stability" of 1,3-dioxolan-2-ylium and oxazolinium ions can be roughly evaluated by comparing rate constants for formation of ions **398** and **450**. As expected, the oxazolinium ion is much more stable. Note that the 2 substituent is methyl in **398** and phenyl in **450**. The thiazolinium ion (**460**) is even more stable. The fact that ion **461**, stabilized by a 2-amino substituent, is formed faster than ion **449** is again a consequence of the resonance delocalization of charge to the nitrogen atom. Direct comparison under different conditions gives the same results.[318]

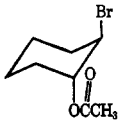
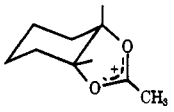
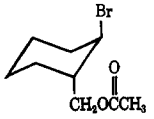
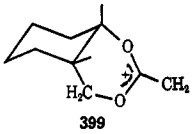
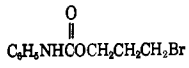
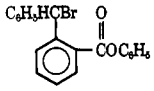
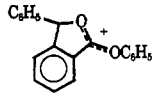
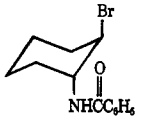
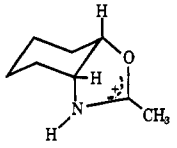
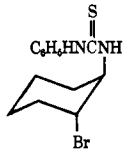
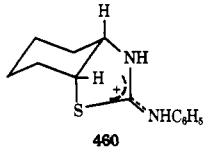
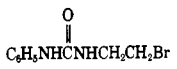
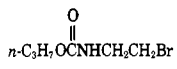
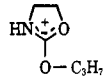
B. THERMODYNAMIC MEASUREMENTS

There is a regrettable lack of data on the thermodynamic stability of heterocyclic cations. Heats of formation have been obtained for a series of acyclic heteroatom stabilized carbonium ions in the gas phase by mass spectrometry. Although data are not available for 1,3-dioxolan-2-ylium ions, enough data are available to demonstrate the great stabilizing ability of adjacent oxygen atoms. As can be seen in Table XXII,

(339) E. Cherbuliez, B. Baehler, O. Espejo, E. Frankenfeld, and J. Rabinowitz, *Helv. Chim. Acta*, 49, 2608 (1966).
(340) E. Cherbuliez, H. Jindra, and J. Rabinowitz, *ibid.*, 49, 1951 (1966).
(341) F. L. Scott and C. V. Murphy, *Tetrahedron Lett.*, 1731 (1970).
(342) S. P. McManus, P. M. Grohse, K. Y. Lee, and C. U. Pittman, Jr., unpublished results.
(343) J. E. Leffler and E. Grunwald, "Rates and Equilibria of Organic Reactions," Wiley, New York, N. Y., 1963.
(344) A. Streitwieser, Jr., "Solvolytic Displacement Reactions," McGraw-Hill, New York, N. Y., 1962.

Table XXI

Rate Constants for Cation Formation from Alkyl Bromide in Acetic Acid at 75°

Compound	*Ion*	$k \times 10^5$ *sec*$^{-1}$	$H^{\pm}$, *kcal/mol*	$S^{\pm}$, *eu*	*m*	k_{Br}/k_X
	 398	0.076	26.[a]	−4.2[a]		0.0182
	 399	0.0093	26.7[a]	−6.4[a]		0.0182
	 413	12.5	22.4[b]	−10.4[b]	0.257	
	 458	0.53	19.6[b]	−24.7[b]	0.257	
	 459	1850	19.2[c,d]	−11.3[d]	0.503	
	 450	~14			~0.2	
	 449	743	20.6[b]	−8.4[b]	0.139	
	 460	~1800			~0.2	
	 461	~300				
	 462	2				

[a] Values are given for the tosylate. [b] In 80% ethanol–water (v/v). [c] In trifluoroacetic acid. [d] E_3, not $\Delta H^{\pm}$.

oxygen atoms are far more efficient stabilizers of adjacent positive charge than any of the halogens, alkyl groups, or sulfur and about the equivalent of an adjacent nitrogen. Table XXIII presents the effect of the substituent in terms of a stabilization energy relative to CH_3^+. *In solution this order cannot be used necessarily, other than to emphasize the great stabilizing ability of oxygen.*

There is a good review[345] of the ionization constants of

(345) A. Albert, *Phys. Methods Heterocycl. Chem.*, 1, 1 (1963).

Table XXII

Gas-Phase Stabilities of Selected Cations

Cation	Heat of formation, kcal/mol	Ref
CH_3^+	258	*b*
$HOCH_2^+$	174	*a*
$CH_3OCH_2^+$	158	*b*
$CH_3OCH_2^+$	167–173	*c*
$CH_3OC^+HOCH_3$	101–113	*c*
$(CH_3O)_3C^+$	66–74	*c*
$CH_3OC^+HCH_3$	146	*c*
$(CH_3O)_2C^+CH_3$	131	*c*
$CH_3OC^+(CH_3)_2$	99	*c*
$H_2NCH_2^+$	176	*b*
$(CH_3)_2NCH_2^+$	165	*a*
$HSCH_2^+$	212	*a*
$CH_3SCH_2^+$	199	*a*
HOC^+HOH	109	*b*
$CH_3CH_2^+$	224	*b*
FCH_2^+	233, 197	*a*, *c*
$ClCH_2^+$	228, 226	*a*, *c*
$BrCH_2^+$	220, 217	*a*, *c*
ICH_2^+	232, 221	*a*, *c*

[a] R. W. Taft, R. H. Martin, and F. W. Lampe, *J. Amer. Chem. Soc.*, **87**, 2490 (1965). [b] M. S. B. Munson and J. L. Franklin, *J. Phys. Chem.*, **68**, 3191 (1964). [c] R. H. Martin, F. W. Lampe, and R. W. Taft, *J. Amer. Chem. Soc.*, **88**, 1353 (1966).

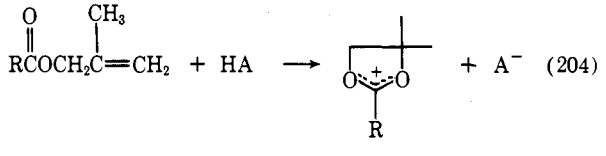
Table XXIII

Stabilization Energy (Relative to CH_3^+) of Substituted Methyl Cations in the Gas Phase[a]

Ion	$SE \pm 3$ kcal/mol	Ion	$SE \pm 3$ kcal/mol
$CH_3OCH_2^+$	66	$NCCH_2^+$	−10
$(CH_3O)_2CH^+$	85	FCH_2^+	27
$(CH_3O)_3C^+$	90	$ClCH_2^+$	30

[a] R. H. Martin, F. W. Lampe, and R. W. Taft, *J. Amer. Chem. Soc.*, **88**, 1353 (1966).

heterocycles in solution, and this area will not be covered here. Because there are few data on the thermodynamics of solution formation of heterocyclic cations, the coverage here is limited. The heats of formation of some five- and six-membered heterocycles containing one or two oxygen atoms have now been measured calorimetrically in sulfuric and fluorosulfonic acids[88,89] in a calorimeter designed by Arnett.[346] The heats of formation of the 1,3-dioxolan-2-ylium ions have been compared with heats of protonation in fluorosulfuric acid of a variety of different compounds. These data are shown in Table XXIV. The heterocyclic cations were formed by protonation and cyclization sequence developed by Pittman and McManus as shown in eq 204. This reaction is very fast



(204)

(346) E. M. Arnett, R. P. Quirk, and J. J. Burke, *J. Amer. Chem. Soc.*, 92, 1260 (1970); also see E. M. Arnett and J. W. Larsen in ref 26, p 441.

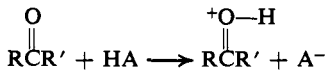
Table XXIV

Relative Heats of Protonation in Fluorosulfonic Acid at 25°

Compound	$\Delta\bar{H}_{s,CCl_4}$, kcal/mol	$\Delta H_{R^+,FSO_3H}$, kcal/mol
$Ph_2C{=}CH_2$	+0.1 ± 0.07	−14.7 ± 0.2[a]
$H_3C{-}COCH_3$	+0.79 ± 0.02	−19.1 ± 0.1[b]
CH_3COOEt	+0.1 ± 0.00	−17.4 ± 0.1[b]
PhCOCl	+0.72 ± 0.1	−6.0 ± 0.5[b]
Et_2O	−0.42 ± 0.01	−19.1 ± 0.7[c]
EtOH	+3.8[c]	−19.1
H_2O	+4.2	−16.4[c]
Et_3N	−0.64 ± 0.08	−49.2 ± 0.3[c]
$CH_3COOCH_2C(CH_3){=}CH_2$	+0.72 ± 0.03	−31.5 ± 0.4
$C_6H_5COOCH_2C(CH_3){=}CH_2$	+0.62 ± 0.11	−28.6 ± 0.2
p-$MeOC_6H_4COOCH_2C(CH_3){=}CH_2$	+0.67 ± 0.08	−32.6 ± 0.8

[a] E. M. Arnett and J. V. Carter, unpublished data. [b] E. M. Arnett, R. P. Quirk, and J. W. Larsen, *J. Amer. Chem. Soc.*, **92**, 3977 (1970). [c] Ethylene chloride was used as the standard state rather than carbon tetrachloride.

and gives no product other than the desired ion. These heats of cation formation may be compared directly to the heats of protonation, for example



The heats of cation formation correspond to the differences in the stability of the cation and its precursor and an unknown contribution due to the anion. Thus the differences between the heats of protonation in a series of compounds is the substituent effect on the stability difference between the precursor and its cation. The anion term remains constant in a given acid solvent and will cancel out.

As can be seen from the data in Table XXIV, the 1,3-dioxolan-2-ylium ions are very stable. Their heats of formation are about −30 kcal/mol, which is nearly twice that obtained by protonating esters such as ethyl acetate and more than twice that for the protonation of 1,1-diphenylethylene to give the very stable diphenylmethyl carbonium ion. For comparison, the heat of protonation of triethylamine is −49.2 kcal/mol.

The substituent effect on the stability of some 1,3-dioxolan-2-ylium ions is shown in Table XXV. The substituent effects observed are often different from effects normally observed in solvolysis reactions. Noteworthy in this respect, the replacing of a 2-methyl substituent by a phenyl group results in a larger (less exothermic) heat of formation. The same is true for a vinyl group.

This behavior was also observed in the rate constants for formation of this cation. As before, it is probably due to greater resonance interactions of the phenyl ring with the ester function in the ground state than with the corresponding atoms in the cation. Substitution of cyclopropyl for methyl has no effect on the heat of formation of 1,3-dioxolan-2-ylium ions from their ester precursors. In addition, a significant Baker–Nathan order was also observed. A correlation between heats of formation and the chemical shift of the ring protons exists with 2-aryl substituents, but not when the substituents are aliphatic. In solvolysis reactions, replacing a methyl group by a cyclopropyl, vinyl, or phenyl group is expected to result in an increase in the rate of reaction, whereas

Table XXV

Relative Heats of Formation of 2-Substituted Dioxolan-2-ylium Ions (I) in 99.5% Sulfuric Acid at 25°

R (at 2 position)	$\Delta\bar{H}_{s,CCl_4}$, kcal/mol	ΔH_{R^+}, kcal/mol
H	+0.99 ± 0.06	−20.1 ± 0.6
CH_3	+0.72 ± 0.03	−23.7 ± 0.2
Et	+0.67 ± 0.03	−23.0 ± 0.2
n-Pr	+0.26 ± 0.06	−22.8 ± 0.2
i-Pr	+0.07 ± 0.02	−23.2 ± 0.5[a]
t-Bu	+0.26 ± 0.02	−22.1 ± 0.6
$-CH_2=CH_2$	+0.45 ± 0.02	−19.2 ± 0.7
	+0.10 ± 0.01	−23.6 ± 0.3
C_6H_5NH	+6.40 ± 0.16	−25.5 ± 0.9
C_6H_5	+0.62 ± 0.11	−22.1 ± 0.3
$C_6H_5CH=CH$	+0.95 ± 0.07	−24.0 ± 0.2
p-BrC_6H_4	+0.44 ± 0.04[a]	−20.7 ± 0.1
p-$CH_3C_6H_4$	+0.28 ± 0.05	−21.9 ± 0.6
p-EtC_6H_4	+0.79 ± 0.04	−22.9 ± 0.1
p-$MeOC_6H_4$	+0.67 ± 0.08	−24.8 ± 0.3
p-ClC_6H_4	+0.41 ± 0.03[a]	−21.1 ± 0.2
m-ClC_6H_4	+0.38 ± 0.02	−20.1 ± 0.4
p-$NO_2C_6H_4$	+7.45 ± 0.36	*b*
m-$NO_2C_6H_4$	+1.43 ± 0.09	−21.7 ± 0.5
3,4,5-$(MeO)_3C_6H_2$	+1.07 ± 0.06	−26.4 ± 0.2
$(H_2C=C(CH_3)CH_2OOC)_2$-C_6H_4(*p*)	+9.27 ± 0.37	−38.1 ± 1.0
$(CH_2=C(CH_3)CH_2OOC)_2$-C_6H_4(*m*)	+7.48 ± 0.48	−37.6 ± 0.8

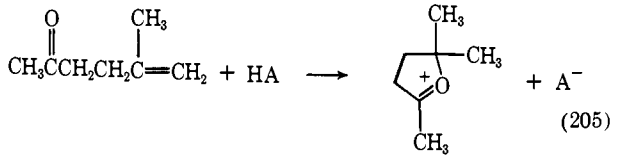
[a] Average of *e* measurements. [b] Exothermic drift. Extrapolation to infinite dilution yields a ΔH_{R^+} of 14 ± 2 kcal/mol.

the heat liberated on the conversion of the unsaturated ester to the 1,3-dioxolan-2-ylium ion is decreased or unchanged by these substituents.

In the case of vinyl groups, this is probably due to the resonance interactions in the starting ester being greater than in the cation. Apparently cyclopropyl stabilizes both the ester and cation to the same extent. This hypothesis could be tested by measuring the heats of combustion of the esters. Interpretation of the effect due to the phenyl is more difficult. One can balance the inductive electron withdrawal with the resonance stabilization to achieve the observed results. Alternatively, the phenyl group is quite large and is expected to have a destabilizing effect on the cation due to its larger size superimposed on whatever resonance stabilization it might provide. Also one can balance the resonance stabilization of the starting material with the stabilization of the product. This system does not permit a test between these alternatives, but a system which does is currently under investigation. It should be noted that the apparent destabilization by phenyl compared to methyl has been observed in a variety of systems.[347]

A rough correlation between the relative heats of formation of 4,4-dimethyl-1,3-dioxolan-2-ylium ions and nmr chemical shift values was reported for a series of 2-aryl derivatives.[89] The only compound not following the linear correlation was the *p*-nitro derivative. This was explained by invoking a strong interaction between the nitro group and the acid solvent. Using the kinetic data of Gash and Yuen[209] for acetolysis of *trans*-2-aroyloxycyclohexyl tosylates, Larsen[89] demonstrated there was a reasonable correlation between log *k* and the relative heats of formation for corresponding substituted 2-aryl-4,4-dimethyl-1,3-dioxolan-2-ylium ions.

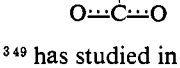
In addition to heats of dioxolan-2-ylium ion formation from esters, the heats of formation of oxolan-2-ylium ions from ketones were also measured.[89] These data are shown in Table XXVI. For both five- and six-membered ring cations, the



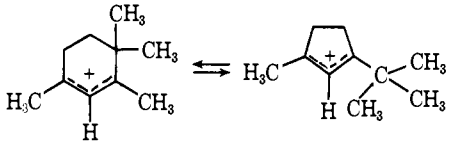
(205)

monooxo ion has a more exothermic heat of formation than does the corresponding dioxo ion. It was suggested that replacing a methylene group in the ketone by $-\ddot{O}-$ increased the stability of the precursor more than that of the ion. Thus, while in absolute terms the dioxo ions are probably more stable than their monooxo analogs, they have a smaller heat of formation owing to the greater stability of their precursors.

From the first two entries in Table XXVI it is obvious that the formation of the 1,3-dioxan-2-ylium ion is more exothermic than its five-membered counterpart. At first glance this situation is elegant confirmation of Eliel's statement that "the five-membered ring is easier to close but is [thermodynamically] less stable."[348] However, as Eliel points out, this situation is strongly effected by the substituents on the rings. This system is also complicated by the coplanarity of the



grouping. Sorensen[349] has studied in detail the rearrangement of several substituted cyclohexenyl cations to cyclopentenyl cations such as the system shown below for which $\Delta G = -1.40$ and $\Delta H = -1.45 \pm 0.5$ with the five-membered ring more stable. The oxonium ions are substituted quite differently from Sorensen's system, and a conformational analy-



sis predicted the six-membered 2,4,4-trimethyl-1,3-dioxan-2-ylium ion would be about 2.2 kcal/mol (*vs.* calorimeter value of 1.5 kcal/mol) more stable than the five-membered analog.[89]

Replacing the 2-hydrogen in the 4,4-dimethyldioxolan-2-ylium ion by a methyl group results in an increased stabilization of about 3.6 kcal/mol (Table XXV). It is also of interest that formation of the monooxonium ions from ketones is more exothermic than formation of the dioxonium ions by 2–4 kcal/mol. The ion with the charge spread over two oxygen atoms is expected to be thermodynamically more stable. We believe this apparent contradiction is due to a greater stabilization of the ground-state ester than of the ion when a methylene group is replaced by an oxygen.

The thermodynamic data in general support the conclu-

(347) J. W. Larsen, *J. Amer. Chem. Soc.*, 92, 5136 (1970).

(348) E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill, New York, N. Y., 1962, p 199.

(349) T. Sorensen, *J. Amer. Chem. Soc.*, 91, 6398 (1969).

Table XXVI

Relative Heats of Formation of a 1,3-Dioxonium Ion and Monooxonium Ions in 99.5% Sulfuric Acid at 25°

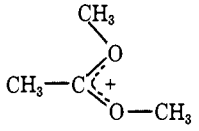
Precursor	$\Delta H_{s,CCl_4}$, *kcal/mol*	ΔH_{R^+}, *kcal/mol*	$\Delta\Delta H_{hydrog}$
$CH_3COOCH_2C(CH_3)=CH_2$	+0.72 ± 0.03	−23.7 ± 0.2	0
$CH_3COO(CH_2)_2C(CH_3)=CH_2$	−0.06 ± 0.02	−25.1 ± 0.1[a]	0
$CH_3COCH_2CH_2C(CH_3)=CH_2$	+0.46 ± 0.05	−27.7 ± 0.2	0
$CH_3COCH_2CH_2CH=C(CH_3)-CH_3$	+0.06 ± 0.07	−27.0 ± 0.4	−1.5
$CH_3COCH_2CH_2CH=CH_2$	+0.26 ± 0.03[b]	−26.3 ± 0.1[b]	+1.7

[a] The nmr of this cation was not free of other products. Average of the first two points used. Starting with the third point the heats became increasingly exothermic. [b] Average of three points.

sions derived from examination of the kinetics of cation formation. The thermodynamic studies have the advantage that the energy difference between two species of known structure is measured. Clearly, much more work in this area is desirable.

VII. Spectral Identification

Spectroscopic methods have proven to be indispensable in structure studies of acyclic heteronuclear substituted carbonium ions. Before discussing the cyclic ions, relevant studies of acyclic ions should be briefly considered. A detailed nmr, infrared, and ultraviolet spectroscopic study of acyclic alkoxymethyl cations has been reported.[350] Either as salts or in acid solution the spectral results are consistent with a coplanar structure for $(CH_3O)_3C^+$, $(CH_3O)_2C^+CH_3$, and $(CH_3O)_2CH^+$. For $(CH_3O)_3C^+$ the C_{3h} point group was indicated.[350] In $(CH_3O)_2C^+CH_3$ the energy of activation for rotation about the $^-O-C^+<$ bond was found to be 11±4 kcal/mol by variable-temperature nmr studies (T_c for CH_3O protons, 287°K).[350] Since at low temperatures the two methoxy groups were chemically nonequivalent, Ramsey and Taft concluded that **464** was the only important rotational isomer present. A larger rotational barrier was indicated for $(CH_3O)_2C^+H$.



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The infrared and ultraviolet spectra of these acyclic ions are particularly valuable for comparison with 1,3-dioxolan-2-ylium and related cations. In Table XXVII, the infrared frequencies and assignments for the trimethoxymethyl and triethoxymethyl cation fluoroborates are given. The assignments of the trimethoxymethyl cation absorptions in Table XXVII at 600 cm^{-1} to the ν_{22} and ν_{12} out-of-plane and in-plane bending modes were based on the analogies given in Table XXVIII. The strong band at 960 cm^{-1} is assigned to ν_{21}, the methyl carbon–oxygen stretch. For comparison the carbon–oxygen stretch is also found at 960 cm^{-1} in methyl carbonate. It would be expected that the C–O bond would have somewhat more double bond character in $(CH_3O)_2C^+CH_3$ or $(CH_3O)_2C^+-C_6H_4$-*p*-F than in $(CH_3O)_3C^+$ because only two oxygen atoms are able to conjugate with the charged carbon. This is borne out by the infrared frequencies of 1400 and 1390 cm^{-1} *vs.* 1380 cm^{-1}, respectively. Using $CH_3CO_2^-$ and CO_3^{2-} as models,

(350) B. G. Ramsey and R. W. Taft, *J. Amer. Chem. Soc.*, **88**, 3058 (1966).

Table XXVII

Infrared Frequencies for Trimethoxymethyl and Triethoxymethyl Cation Fluoroborates[a]

$(CH_3O)_3C^+BF_4^-$/*film*		$(EtO)_3C^+BF_4^-/CH_2Cl_2$ *and* CH_2CN	
Frequency, cm^{-1}	*Assignment for* C_{3h} *sym*	*Frequency,* cm^{-1}	*Assignment*
1710 (w)		1550 (s)	CH_2 deform
1675 (w)	BF_4^- $\nu_3 + \nu_4$ T_d sym	1450 (s)	CH_2 asym bend (deform)
1575 (s)	CH_3 asym bend (deform)	1435 (s)	
1560 (sh)		1380 (s)	CH_3 sym bend
1525 (sh)		1340 (s)	Asym stretch
1380 (s)	ν_{20} asym stretch	1030 (s)	BF_4^-
1030 (s)	ν_3 BF_4^- T_d sym	990 (ms)	Et–O stretch
960 (s)	ν_{21} CH_3–O stretch	890	CH_3CH_2
755 (ms)	ν_{12} out-of-plane bend	755 (ms)	Out-of-plane bend
600 (s)	ν_{22} in-plane bend	602 (s)	In-plane bend
525 + 537	ν_4 BF_4^- T_d sym	575 (s)	In-plane bend
		525 (s)	BF_4^-

[a] sh = shoulder, s = strong, ms = medium strong, w = weak.

Table XXVIII

Infrared Frequencies of Some Model Ions and Compounds[a]

Species	*Asym stretch*	*Out-of-plane bend*	*In-plane bend*
CO_3^-	1450–1440	880–860	700
NO_3^-	1380–1350	840–815	720
$(CH_3O)_3B$	1355	662	525
$(CH_3O)_3C^+$	1380	755	600

[a] Values in cm^{-1}.

it was calculated that alkoxymethyl cations have C=O π-bond orders in the range of 0.2–0.3.

The ultraviolet spectra of alkoxymethyl cations (either as BF_4^- salts or in H_2SO_4) exhibited no allowed transitions above 200 nm. This was expected because methyl borate has no transitions above 200 nm, and configuration interaction of the states ^+C-O and $C=O^+$ would be expected to cause a blue shift of the methoxymethyl cation absorption relative to methyl borate.

1,3-Dioxolan-2-ylium and 1,3-dioxan-2-ylium ions are constrained to a geometry which is trans,trans. The nmr spectrum of protonated formic acid shows the presence of two conformers: the *cis,trans*-**466**, which predominates over

Table XXIX

Nmr Spectra of 1,3-Dioxolan-2-ylium Cations[a]

Cation	Counterion	Solvent	Chemical shift			Ref
			C-2 substituent or C-2 H	C-4 H	C-5 H	
4-Formoxymethyl	$SbCl_6^-$	CD_3CN	9.40 (s)	6.22 (m)	5.60 (q), 5.40 (q)	102
2-Methyl	BF_4^-	100% FSO_3H	2.75 (s)		5.30 (s)	74
	BF_4^-	SO_2	Not reported		5.44 (s)	74
	BF_4^-	CD_3CN	2.67 (s)		5.21 (s)	82, 101
	$SbCl_6^-$	CD_3NO_2	2.97 (s)		5.58 (s)	101
	HF_2^-	HF	2.68 (s)		4.64 (m)	101
2-Ethyl	$SbCl_6^-$	CD_3NO_2	3.29 (q)		5.58 (s)	101
	$SbCl_6^-$	CD_3CN	3.12 (q)		5.42 (s)	101
2-*tert*-Butyl	BF_4^-	100% FSO_3H			5.30 (s)	74
	BF_4^-	SO_2			5.48 (s)	74
	$SbCl_6^-$	CD_3NO_2			5.59 (s)	101
	$SbCl_6^-$	CD_3CN			5.37 (s)	101
2-Cyclopropyl	BF_4^-	100% FSO_3H	2.47–2.08 (m)		5.17 (s)	74
	BF_4^-	SO_2	Not reported		5.38 (s)	74
2-Cyclobutyl	BF_4^-	100% FSO_3H	3.89–3.42 (q)		5.29 (s)	74
	BF_4^-	SO_2	Not reported		5.45 (s)	74
2-Vinyl	BF_4^-	100% FSO_3H	7.57–6.38 (m)[b]		5.35 (s)	74
2-(1-Propenyl)	BF_4^-	100% FSO_3H	6.53, 6.27 (d)		5.23 (s)	74
	BF_4^-	SO_2	Not reported		5.38 (s)	74
2-(2-Propenyl)	BF_4^-	100% FSO_3H			5.34 (s)	74
2-Styryl	BF_4^-	100% FSO_3H	6.98, 6.73 (d)		5.25 (s)	74
	BF_4^-	SO_2	Not reported		5.38 (s)	74
2-Phenyl	BF_4^-	100% FSO_3H			5.42 (s)	75
	BF_4^-	SO_2			5.57 (s)	75
	$SbCl_6^-$	CD_3CN			5.75 (s)	101
2-*p*-Anisyl	BF_4^-	100% FSO_3H			5.33 (s)	75
	BF_4^-	SO_2			5.48 (s)	75
	$SbCl_6^-$	CD_3NO_2			5.57 (s)	101
2-*p*-Tolyl	BF_4^-	100% FSO_3H			5.37 (s)	75
	BF_4^-	SO_2			5.53 (s)	75
	$SbCl_6^-$	CD_3NO_2			5.65 (s)	101
2-*m*-Tolyl	BF_4^-	100% FSO_3H			5.40 (s)	75
	BF_4^-	SO_2			5.56 (s)	75
2-*p*-Fluorophenyl	BF_4^-	100% FSO_3H			5.42 (s)	75
	BF_4^-	SO_2			5.52 (s)	75
2-*p*-Chlorophenyl	BF_4^-	100% FSO_3H			5.43 (s)	75
	BF_4^-	SO_2			5.60 (s)	75
2-*m*-Chlorophenyl	BF_4^-	100% FSO_3H			5.44 (s)	75
	BF_4^-	SO_2			5.65 (s)	75
2-*m*-Bromophenyl	BF_4^-	100% FSO_3H			5.47 (s)	75
	BF_4^-	SO_2			5.63 (s)	75
2-*m*-Fluorophenyl	BF_4^-	100% FSO_3H			5.40 (s)	75
	BF_4^-	SO_2			5.62 (s)	75
2-*m*-Nitrophenyl	BF_4^-	100% FSO_3H			5.58 (s)	75
	BF_4^-	SO_2			5.70 (s)	75
2-*p*-Nitrophenyl	BF_4^-	100% FSO_3H			5.59 (s)	75
	BF_4^-	SO_2			5.73 (s)	75
2-(2′,6′-Dimethoxyphenyl)	BF_4^-	CF_3CO_2H			4.77 (s)	68
2-(3′,4′,5′-Trimethoxyphenyl)	BF_4^-	100% FSO_3H			5.37 (s)	75
	BF_4^-	SO_2			5.53 (s)	75
2-(3′,4′-Dichlorophenyl)	BF_4^-	100% FSO_3H			5.47 (s)	75
	BF_4^-	SO_2			5.63 (s)	75
2-(3′-Trifluoromethylphenyl)	BF_4^-	100% FSO_3H			5.52 (s)	75
	BF_4^-	SO_2			5.68 (s)	75
2-(4′-Trifluoromethylphenyl)	BF_4^-	100% FSO_3H			5.52 (s)	75
	BF_4^-	SO_2			5.68 (s)	75
2-Hydroxy	FSO_3^-	100% FSO_3H	Not reported		5.26 (s)	74
2-*N*,*N*′-Diethylamino	BF_4^-	100% FSO_3H			4.98 (s)	74
2,4-Dimethyl	HSO_4^-	96% H_2SO_4	3.24 (s)	6.26 (m)	5.32 (t), 5.86 (t)	87
2,4,4-Trimethyl	HSO_4^-	96% H_2SO_4	3.21 (s)		5.44 (s)	87
2,4,4,5,5-Tetramethyl	$SbCl_6^-$	$SbF_5/FSO_3H/SO_2$	2.84 (s)			69
2,4,4,5,5-Pentamethyl	ClO_4^-	CD_3CN	2.70 (s)			90

Table XXIX (Continued)

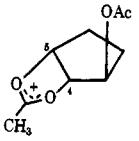
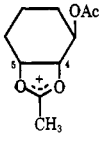
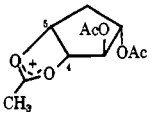
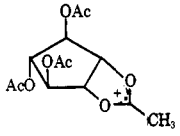
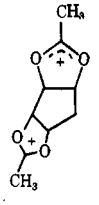
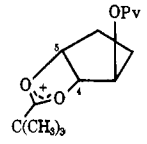
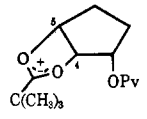
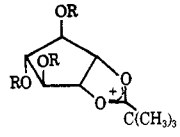
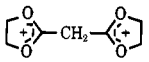
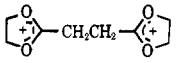
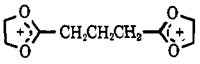
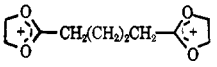
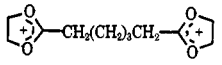
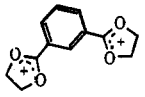
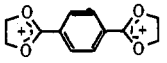
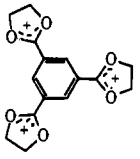
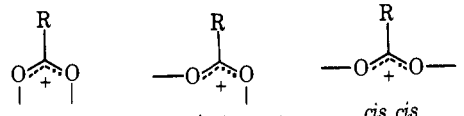
Cation	Counterion	Solvent	Chemical shift: C-2 substituent or C-2 H	Chemical shift: C-4 H	Chemical shift: C-5 H	Ref
2-Methyl-4-acetoxymethyl	$SbCl_6^-$	CD_3NO_2	3.05 (s)	6.24 (m)	5.64 (t), 5.43 (q)	98, 102
	$SbCl_6^-$	CD_3CN	2.90 (s)	6.00 (m)	5.42 (t), 5.21 (q)	102
	$SbCl_6^-$	C_6H_5CN	3.08 (s)	6.40 (m)	5.75 (t), 5.59 (t)	102
	$SbCl_6^-$	$C_6H_5NO_2$	3.34 (s)	Not reported	6.12 (t), 5.88 (t)	102
4-Chloromethyl-2-methyl	$SbCl_6^-$	CD_3NO_2	3.05 (s)	6.32 (m)	5.66 (q), 4.41 (q)	101
2-Methyl-4,5-*cis*-trimethylene	HF_2^-	HF	2.68 (s)	6.08 (m)		101
2-Methyl-4,5-*cis*-tetramethylene	BF_4^-	CD_3CN	2.72 (s)	5.70 (m)		82
	BF_4	Anhy HOAC	2.77 (s)	5.77 (m)		82
	$SbCl_6^-$	CD_3NO_2	2.95 (s)	5.99 (m)		101
	$SbCl_6^-$	CD_3CN	2.80 (s)	5.83 (m)		101
	$SbCl_6^-$	CD_3NO_2	3.02 (s)	6.02 (d)	6.40 (qui)	102
	$SbCl_6^-$	$C_6H_5NO_2$	3.32 (s)	6.42 (d)	6.80 (qui)	102
	HF_2^-	HF	2.77 (s)	5.96 (d)	6.25 (qui)	102
	$SbCl_6^-$	CD_3NO_2	3.05 (s)	6.30–5.80 (m)		102
	BF_4^-	CD_3CN	2.80 (s)	6.00–5.60 (m)		102
	BF_4^-	C_6H_5CN	2.97 (s)	6.30–5.90 (m)		102
	HF_2^-	HF	2.80 (s)	6.00–5.70 (m)		102
	BF_4^-	CD_3CN	2.84 (s)	5.94 (d)	6.30 (qui)	103
	$SbCl_6^-$	CD_3NO_2	2.87 (s)	Not reported		99
	HF_2^-	HF	2.90 (s)	6.20–5.60 (m)[e]		103
	BF_4^-	CD_3CN	2.87 (s)	6.02 (m)		103
	$2HF_2^-$	HF	2.84 (s)	6.47 (m)		101
2-Ethyl-4-propionoxymethyl	$SbCl_6^-$	CD_3NO_2	3.35 (s)	6.25 (m)	5.64 (q), 5.45 (q)	102
	$SbCl_6^-$	CD_3CN	3.18 (s)	6.00 (m)	5.40(t), 5.20 (q)	102
	$SbCl_6^-$	C_6H_5CN	3.40 (s)	6.45 (m)	5.82 (q), 5.58 (q)	102
2-*tert*-Butyl-4-pivaloxymethyl	$SbCl_6^-$	CD_3NO_2		6.32 (m)	5.68 (t), 5.45 (q)	102
	$SbCl_6^-$	CD_3CN		6.07 (m)	5.45 (t), 5.22 (q)	102
2-*tert*-Butyl-4,5-*cis*-trimethylene	$SbCl_6^-$	CD_3NO_2		6.33 (m)		101
	SbF_6^-	CD_3NO_2		6.23 (m)		101
	SbF_6^-	CD_3CN		6.17 (m)		102
	$SbCl_6^-$	CD_3NO_2		6.07 (d)	6.46 (qui)	102
Pv = Pivalate						
	$SbCl_6^-$	CD_3NO_2		6.23 (t)	6.30 (qui)	103
	HF_2^-	HF		6.00–5.40 (m)[e]		102

Table XXIX (Continued)

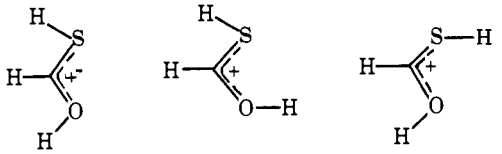
Cation	Counterion	Solvent	Chemical shift: C-2 substituent or C-2H	Chemical shift: C-4 H	Chemical shift: C-5 H	Ref
2-Phenyl-4-benzoxymethyl	$SbCl_6^-$	CD_3NO_2		6.50 (m)	5.86 (q), 5.65 (q)	102
	$SbCl_6^-$	$C_6H_5NO_2$		7.14 (m)	6.31 (q), 6.13 (q)	102
4-Chloromethyl-2-phenyl	$SbCl_6^-$	CD_3NO_2		6.45 (m)	5.81 (q), 5.59 (q)	101
2-*p*-Tolyl-4-*p*-toluoxymethyl	$SbCl_6^-$	CD_3CN		6.30 (m)	5.68 (q), 5.48 (q)	102
2-*p*-Anisyl-4-*p*-anisoxymethyl	$SbCl_6^-$	CD_3NO_2		6.40 (m)	5.80 (q), 5.56 (q)	102
2-Amino-4,4-dimethyl	HSO_4^-	96% H_2SO_4	8.72 (s)		5.26 (s)	87
	$2BF_4^-$	100% FSO_3H	Not observed		5.61 (s)	73
	$2BF_4^-$	100% FSO_3H	3.70 (s)		5.48 (s)	74
	$2BF_4^-$	100% FSO_3H	3.26 (t)		5.40 (s)	74
	$2BF_4^-$	100% FSO_3H	3.10 (m)		5.36 (s)	74
	$2BF_4^-$	100% FSO_3H	3.06 (m)		5.34 (s)	74
	$2BF_4^-$	100% FSO_3H			5.60 (s)	75
	$2BF_4^-$	100% FSO_3H			5.63 (s)	75
	$3BF_4^-$	100% FSO_3H			5.77 (s)	75
2-*p*-Anisyl-4,5-(5′α-cholestan-2′α,3′α)	$SbCl_6^-$	$CDCl_3$			5.77 (m)	96
2-*p*-Anisyl-4,5-(5′α-cholestan-2′β,3′β)	$SbCl_6^-$	$CDCl_3$			5.82 (m)	96
2-Phenyl-4,5-(9′β,10′α-decalin-2′β,3′α)	$SbCl_6^-$	CD_2Cl_2			5.89 (m)	96
2-Anisyl-4,5-(9′β,10′α-decalin-2′β,3′β)	$SbCl_6^-$	CD_2Cl_2			5.78 (m)	96

[a] Ppm downfield from either sodium 2,2-dimethyl-2-sila-5-pentansulfonate (liquid HF only) or TMS. s = singlet, d = doublet, t = triplet, q = quartet, qui = quintet, m = multiplet, b = broadened peak. [b] All vinyl protons. [c] A mixture of all ring protons.



trans,trans **465** *cis,trans* **466** *cis,cis* **467**

cis,cis-**467** by 2:1. The *trans,trans*-**465** is not observed.[351-353] In protonated acetic acid **466** predominates over **467** 95:5, and in all other protonated carboxylic acids studied, only **465** is observed.[354,355] On the other hand, protonated thioformic acid,[356] in 4:1 FSO_3H–SbF_5, exists as a mixture of three isomers, 60% *cis,trans*-**470**, 30% *cis,cis*-**468**, and 10% *cis,trans*-**469**.

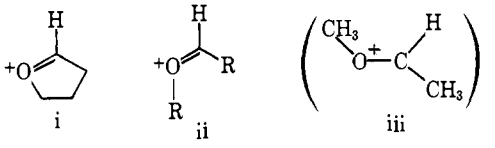


468 **469** **470**

Protonated esters and O-alkylated esters exhibit a constant behavior. The cis,trans geometry predominates in the formates to the extent of 70–90%, and in acetates and higher homologs only the cis,trans form is found.[357]

(351) G. A. Olah and A. M. White, *J. Amer. Chem. Soc.*, 89, 3591 (1967).
(352) H. Hogeveen, A. F. Bickel, C. W. Hilbers, E. L. Mackor, and C. MacLean, *Recl. Trav. Chim. Pays-Bas*, 86, 687 (1967).
(353) H. Hogeveen, A. F. Bickel, C. W. Hilbers, E. L. Mackor, and C. MacLean, *Chem. Commun.*, 898 (1966).
(354) M. Brookhart, G. C. Levy, and S. Winstein, *J. Amer. Chem. Soc.*, 89, 1735 (1967).
(355) G. A. Olah and A. M. White, *ibid.*, 89, 7072 (1967).
(356) G. A. Olah, A. T. Kee, and A. M. White, *J. Org. Chem.*, **34**, 1827 (1969).
(357) R. F. Borch, *J. Amer. Chem. Soc.*, 90, 5303 (1968).

With i, the geometry ii is required. This is not the most favorable geometry for the methoxymethyl carbonium ion iii and its higher homologs.[358]



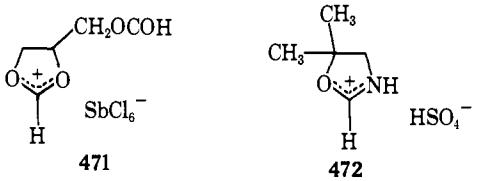
i ii iii

A. NMR SPECTROSCOPY

1. Five-Membered Rings, Two Heteroatoms

Nmr spectroscopy has been by far the most important spectroscopic technique used in the study of 1,3-dioxolan-2-ylium and related cations and many of the references include published spectra. The most complete study on the effect of substituents on chemical shift was done by Hart and Tomalia.[73-75] Using methods discussed in section IV, dioxolan-2-ylium ions were prepared and isolated as the stable tetrafluoroborates. Their nmr spectra were examined in SO_2 at $-20°$ and in FSO_3H at room temperature. Characteristic spectra were obtained with a sharp singlet for the equivalent ring methylene protons at δ 5.59–4.98 for a variety of substituents at C-2. Data for these cations along with those from several other studies are summarized in Table XXIX. Note that there is a downfield solvent shift of about 0.16 ppm in going from FSO_3H to SO_2. More will be said relative to solvent shifts later in this section. Compared to 1,3-dioxolanes, the ring protons in the corresponding cations are shifted downfield approximately 1.5–1.7 ppm in FSO_3H.[74]

Because 1,3-dioxolan-2-ylium ions with a hydrogen at C-2 are rare, nmr data for the chemical shift of the C-2 proton are sparse. Paulsen and Behre[102] found that the C-2 proton in the 4-substituted derivative **471** appeared at δ 9.40. This places that proton downfield by 0.5–1.0 ppm from the C-2 proton in a similarly substituted oxazolinium ion **472** even



471
9.40 (s)
in CD_3CN

472
8.87 (s)
in 96% H_2SO_4

after solvent shifts are considered. Protons on carbon atoms attached to the 2 position show considerably less deshielding than the C-4 and C-5 ring protons. As will be seen later in this section, deshielding is transmitted through aryl and alkyl groups substituted in the 2 position with the effect diminishing with chain length as expected.

Following the lead of Olah[359] and Taft,[360] Hart and Tomalia[75] did a quantitative correlation of the effects of *m*- and *p*-aryl substituents of 2-aryl groups on the chemical shift of the 1,3-dioxolan-2-ylium ring protons and found a linear correlation with Hammett σ values with a correlation coefficient of 0.966. A plot of their results is shown in Figure 4.

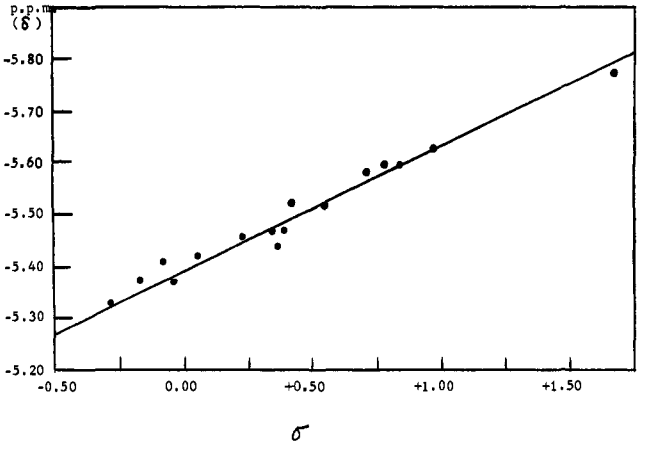
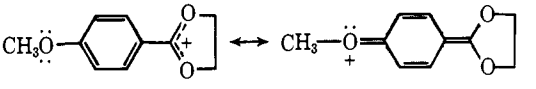


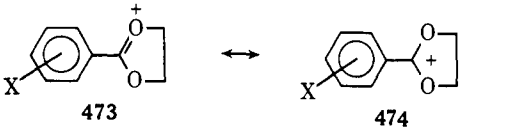
Figure 4. 1,3-Dioxolan-2-ylium ring proton chemical shift *vs.* Hammett σ (FSO_3H at 25°).

With σ^+ values a somewhat less satisfactory correlation (0.940) was obtained. Since δ appears to be directly related to the Hammett σ values, one expects to see the relative reactivity of the cations with nucleophiles in the same order.

Closer adherence to σ rather than to σ^+ values suggests[67] that resonance interactions between electron-supplying substituents and C-2 of the type shown are not strong. This further indicates[75] that the most important contributor to the resonance hybrid is **473** rather than **474**.



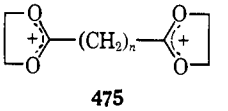
(206)



473 **474** (207)

Hart and Tomalia[73,75] also synthesized and reported nmr data on several dications and one trication. A Hammett correlation plot yielded meta and para substituent constants for the 1,3-dioxolan-2-ylium group. Interestingly, the +0.94 σ value for the para dication is the largest known.

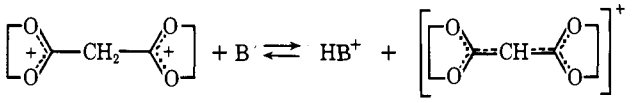
Based on nmr studies of a variety of substituents (see Table XXIX), a nitrogen substituted at C-2 most effectively delocalizes charge from the ring. Of alkyl groups, cyclopropyl is best. Some caution should be exercised in relating nmr shifts to cation stabilities, however, since heats of formation data reported in section VI are *relative to* the starting ester. Of the substituents studied, dications appear to delocalize less since they present special electronic problems. For example, consider the series of dications (**475**) with n = 0–5.



475

Attempts to prepare the compound with n = 0 were unsuccessful by normal routes,[74] indicating the potential instability of that situation. With n = 1 the central protons could not be observed, presumably due to the exchange with the solvent. This exchange was rationalized[74] to occur *via* the monocation because of the presumed strong acidity of the dication.

(358) G. A. Olah and J. Sommer, *J. Amer. Chem. Soc.*, 90, 4323 (1968).
(359) C. A. Cupas, M. B. Comisarow, and G. A. Olah, *ibid.*, **88**, 361 (1966).
(360) R. W. Taft and L. D. McKeever, *ibid.*, **87**, 2489 (1965).



The chemical shifts of the chain methylene protons in this dictation series are compiled in Table XXX. It can readily

Table XXX

Chemical Shifts of Chain Protons in α,α' Symmetrical Dication 475

No. of chain carbons	*Chemical shift, δ*
2	3.70 (s)
3	3.26 (t), 2.46 (q)
4	3.10 (m), 2.02 (m)
5	3.06 (m), 2.36–1.36 (m)

be seen from these data that the effect of the second cation center upon the α' protons rapidly decreases as the chain lengthens.

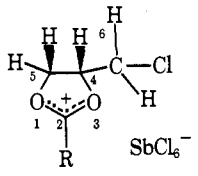
Hart and Tomalia[74] further treated the effect of a second cationic center upon the ring protons and found that a plot of the chemical shifts of the ring protons *vs.* the number of methylene groups could be made to fit where 5.30 is identical

$$\delta = 5.30 + [1.60/(n + 1)^2]$$

with both the resonance of the example where $n = \infty$ and to the 2-methyl monocation. A plot of the α-methylene proton chemical shifts as a function of n led to a good fit to the equation.

$$\delta = 2.94[1 + (1/n^2)]$$

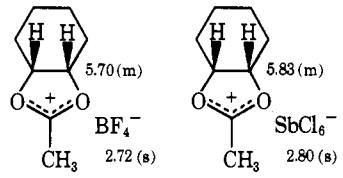
An excellent detailed analysis of nmr spectra of some 1,3-dioxolan-2-ylium salts has recently been reported by Paulsen and Behre.[101] Examples of the coupling constants in unsymmetrical ions are illustrated below with values for two 4-chloromethyl ions (**476**).



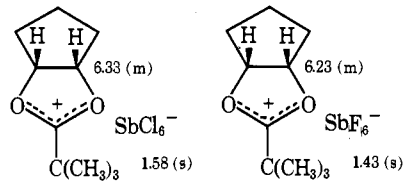
476

	R = CH_3	R = C_6H_5
$J_{4,5}$	8.0 Hz	8.0 Hz
$J_{4,5'}$	9.0	8.4
$J_{5,5'}$	10.0	10.2
$J_{4,6}$	2.8	3.2
$J_{4,6'}$	3.6	3.8
$J_{6,6'}$	14.0	14.0

As mentioned earlier, a solvent shift was observed initially in these systems by Hart and Tomalia.[74,75] The magnitude can vary greatly as the solvent is changed. Before this shift is discussed in detail, the effect of the counterion in nonacetic solvents must be noted. There are only two examples from Table XXIX which can be compared. While the data for cation **477** are from different laboratories,[82,101] the chemical shifts of **478** were from the same article.[101] Thus, one is led to propose that, for these cations, some tight ion pair exists in solvents such as acetonitrile and nitromethane and that the counterion affects the chemical shift.



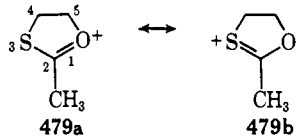
477



478

The effects of solvents on the chemical shifts are even more significant than the counterion effect. Although a quantitative treatment cannot be made, the data qualitatively suggest that the solvent may cause a downfield shift in the order $FSO_3H <$ $HF \sim CD_3CN < SO_2 < CD_3NO_2 < C_6H_5CN < C_6H_5NO_2$.

Let us now discuss the effect of varying one of the ring heteroatoms on the chemical shifts of the ring protons of the cations. *A priori*, one expects that the ring protons at C-4 of **479** should be more shielded by sulfur than by oxygen. Other



479a **479b**

than the relative size of the atoms, a factor in the difference in the two values is likely the greater contribution of resonance structure **479a** in the oxathiolan-2-ylium ion.

At present time only circumstantial evidence is available concerning the nature of the bonding and charge density in 1,3-dioxolan-2-ylium and most related cations. McManus, Lee, and Emerson[361] have found that long-range coupling between the C-2 methyl and C-4 protons occurs in simple oxazolinium **480** and thiazolinium **481** ions. A similar long-range coupling through the same five bonds, attributable to a σ–π interaction, occurs in the free bases[183,297] and in the

480 **481**

isoelectronic olefins.[362,363] This suggests that, in these two simple cases, the structure is better represented by having the charge predominantly on nitrogen[362,363] since any other arrangement would not satisfy the requirements of the interpretation of the data. Despite these results, a significant charge could still exist on oxygen since the bond lengths in the ion are shortened, allowing a greater overlap between the oxygen and C-2 position.

With the latter information, the nmr data of McManus, Carroll, and Pittman[176] may be interpreted to yield chemical

(361) S. P. McManus, K. Y. Lee, and M. T. Emerson, unpublished results.
(362) S. Sternhill, *Pure Appl. Chem.*, 14, 15 (1964).
(363) M. Barfield and B. Chakrabarti, *Chem. Rev.*, 69, 757 (1969).

Table XXXI

Nmr Spectral Data of Oxazolinium Cations in H_2SO_4[a]

Cation	*C-2H*	*C-2 substituent α-C-H*	*C-4H*	*C-5H*	*NH*
2-Methyl		2.9 (s)	4.62 (t)	5.53 (t)	9.94 (b)
2-Propyl		3.20 (t)	4.64 (t)	5.56 (t)	9.68 (b)
2,5-Dimethyl		2.95 (s)	4.41 (m)	5.56 (t)	9.44 (b)
5-Methyl	8.87 (s)		4.47 (s)		Not obsd
2,4,4-Trimethyl		2.90 (s)		5.17 (s)	10.01 (b)
5,5-Dimethyl	8.81 (s)		4.37 (s, b)		10.22 (s, b)
2,5,5-Trimethyl		2.90 (s)	4.34 (s)		9.95 (s)
2-Phenyl[b]			4.48 (t)	5.42 (t)	10.10 (b)
5-Methyl-2-phenyl			4.72 (t), 4.20 (t)	5.91 (m)	9.98 (b)
5-Methyl-2-*p*-nitrophenyl			5.05 (t), 4.64 (t)	6.30 (m)	9.80 (b)
5-Methyl-2-*p*-tolyl			4.45 (b)	5.58 (m)	9.48 (b)
5-Methyl-2-*p*-fluorophenyl			4.50 (b)	5.61 (m)	9.63
5,5-Dimethyl-2-phenyl			4.30 (s)		9.72
5,5-Dimethyl-2-*p*-nitrophenyl			4.59 (s)		10.68 (b)
2-Amino-5-methyl		Not obsd	4.19 (b)	5.50 (m)	Not obsd
2-Methoxy-5-methyl			3.66 (m)	4.86 (m)	Not obsd
2-Ethoxy-5-methyl			3.64 (m)	4.79 (m)	Not obsd
2,5-Dimethyl-5-phenyl		3.01 (s)	4.67 (s)		9.75

[a] Reference 176; s = singlet, t = triplet, m = multiple, b = broadened; all measurements are in ppm relative to TMS as a standard (internal capillary). [b] Reference 178.

shift values for the C-5 protons in thiazolinium ions and oxazolinium ions which are related to classical iminium and oxonium ions. The values for the thiazolinium ions might be expected to compare quite favorably to C-5 protons in oxathiolan-2-ylium ions. Table XXXI contains a compilation of nmr data for several different oxazolinium cations. Table XXXII contains similar data for some thiazolinium cations.

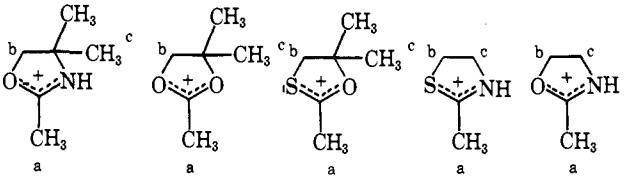
Table XXXII

Nmr Spectral Data of Thiazolinium Cations in H_2SO_4[a]

Cation	*C-2 substituent α-C-H*	*C-4H*	*C-5H*	*NH*
2-Methyl	3.14 (s)	4.91 (t)	4.28 (t)	Not obsd
2-Mercapto	Not obsd	4.93 (t)	4.42 (t)	9.95
2-Amino	Not obsd	4.59 (t)	4.17 (t)	Not obsd
2-Amino-5-methyl	8.3 (b)	5.43 (m)	4.20 (m)	Not obsd
2-Anilino-5-methyl	9.37	4.19 (b), 5.40 (b)	5.40 (b)	Not obsd
2-Anilino-5,5-dimethyl	9.50	4.17 (s)		Not obsd

[a] Reference 176; s = singlet, t = triplet, m = multiplet, b = broadened; all values are in ppm downfield from TMS (internal capillary).

Listed below are comparable systems (all in 90–96% H_2SO_4 solution) each containing two heteroatoms. While the *a priori* predictions on sulfur *vs.* oxygen shielding are confirmed, nothing concerning the contribution of sulfur or oxygen toward stabilization of the cationic center can be said unless the chemical shifts are compared with those of the neutral heterocyclic precursors. Tomalia, *et al.*,[181] used the term $\Delta\delta$ to show the effect of deshielding on the chemical shift in oxazolinium ions. The $\Delta\delta$ values for the 2-methyloxazolinium (**480**) and 2-methylthiazolinium (**481**) cations relative to the free bases in CCl_4[183] are shown below. It should also be



482 **483** **484** **485** **486**

Ion no.	Chemical shift, δ[87,176] a	b	c
482	2.90 (s)	5.17 (s)	2.03 (s)
483	3.21 (s)	5.44 (s)	2.29 (s)
484	3.38 (s)	4.38 (s)	2.37 (s)
485	3.14 (s)	4.28 (t, J = 9.1)	4.91 (t, J = 9.1)
486	2.90 (s)	5.53 (t, J = 9.9)	4.62 (t, J = 9.9)

Cation	$\Delta\delta$ a	b	c
480	0.93	1.22	0.85
481	0.99	1.04	0.79

pointed out that the methyl protons in the *tert*-butyl cation appear at about 4.1 ppm[364] which is considerably downfield from the 2-methyl group in either cation. Taken together, these data tend to indicate charge delocalization to both heteroatoms although the participation by oxygen may be slightly greater than that by sulfur.

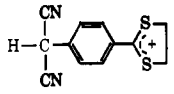
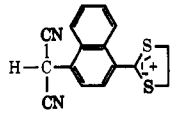
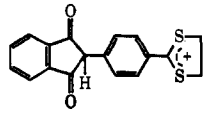
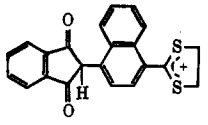
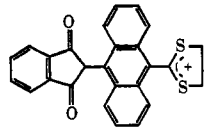
Two items deserve further comment. First, in the simple oxazolinium ions, the protons on carbon adjacent to oxygen are always downfield of those on carbon adjacent to nitrogen. The reverse is true in thiazolinium ions. Some examples where the two types of protons became mixed have been described. Secondly, the five-membered ring systems appear to be planar, and in concentrated acid the ring protons appear as sharp triplets[176] due to equality of J_{cis} and J_{trans}.

The magnitude of the coupling constants for ring protons in oxazolinium ions is about 9.8–10 Hz, an increase of about 1.0–1.5 as compared to the parent oxazolines. In thiazolin-

(364) G. A. Olah, *Science*, 168, 1298 (1970).

Table XXXIII

Nmr Spectral Data of Some 1,3-Dithiolan-2-ylium Cations[a]

Cation	Solvent	$H_{aliphatic}$	H_{tert}	$H_{aromatic}$
	H_2SO_4	4.2 (s)		7.7 (m)
	H_2SO_4	4.6 (s)	5.8 (s)	8.2 (m)
	H_2SO_4	4.5 (s)	6.2 (s)	7.9 (m)
	CF_3CO_2H	4.5 (s)	4.9 (s)	7.8 (b)
	CF_3CO_2H	4.7 (s)	5.7 (s)	8.0 (b)
	CF_3CO_2H	5.0 (b)	6.5 (s)	8.0 (b)

[a] Shifts are relative to TMS as internal (CF_3CO_2H) or external (H_2SO_4) standard. Some compounds may exist predominantly in the quinone methide form. s = singlet, m = multiplet, b = broadened signal.

ium ions the coupling constants range from 8.0 to 9.1 Hz with the lower value for the 2-mercapto derivative. While 2-mercaptothiazoline shows a coupling constant similar to that of the cation, most others show an increase of about 1.0 Hz upon going to the cation.

Finally, we will treat dithiolan-2-ylium cations. Since 2-alkyl-substituted ions are not very common, a lack of data prevents us from including this class of ions with the others in the direct comparison above. Generalities, treated above, can be further studied by use of the data of Gompper, *et al.*[113] (see Table XXXIII).) Note, for example, that the aliphatic ring protons in the 2-phenyl cation (first entry) appear at 4.2 ppm. This puts those protons 1.2–1.3 ppm upfield of protons in the identically substituted dioxolan-2-ylium cation.[75] Data for some 2-(*N,N*-dimethylamino)-1,3-dithiolan-2-ylium salts are included in the uv section.

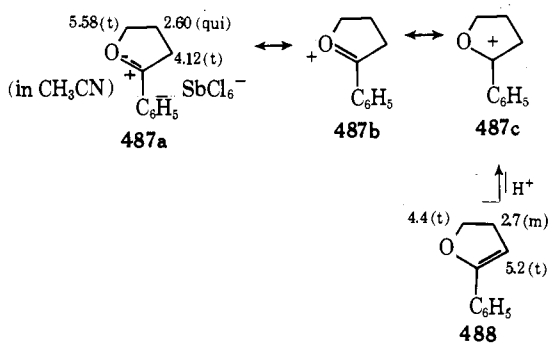
2. 1,3-Dioxan-2-ylium Cations

1,3-Dioxan-2-ylium ions have not been studied by nmr in any detail. One set of data, that from the recent work of Paulsen and Behre,[101] is presented here in tabular form (see Table XXXIV). Note the similarity of chemical shifts between these ions and the 1,3-dioxolan-2-ylium cations. The central methylene group protons exhibit some deshielding as is expected.

3. Oxolan-2-ylium Cations

Oxolan-2-ylium salts isolated in the solvotic studies[58,59] or in acid-catalyzed ketone cyclization studies[60–62] have been well characterized by nmr spectroscopy. These data are presented in Table XXXV. Nmr was also very useful in studying the H–D exchange characteristics of the protons in these systems and others as discussed earlier.[60,63]

Ward and Sherman[59] compared the chemical shifts of the various methylene protons of **487** with those of the parent dihydrofuran **488**. Since proton exchange[60,63] in oxolan-2-



(208)

ylium ions occurs solely *via* the dihydrofuran if an aryl group is substituted at C-2, then the model chosen is reasonable. With this model, the $\Delta\delta$'s for the C-3 and C-5 protons are 1.08 and 1.18. In trifluoroacetic acid the shifts were greater and the C-5 protons were shifted to a greater extent (than the C-3 protons) leading Ward and Sherman[59] to suggest that the charge density was greatest on oxygen; *i.e.*, structure **487b** is preponderate. This observation was supported by earlier work on protonated ketones by Olah, *et al.*, by the Hammett treatment of Hart and Tomalia,[75] and by Pedersen's nmr studies.[83]

A comparison of the values reported for the same ions in

Table XXXIV

Nmr Spectra of Some 1,3-Dioxan-2-ylium Cations[a]

Cation	Counterion	Solvent	C-2 substituent α-C-H or C-2H	C-4 and C-6H	C-5H
2-Methyl	$SbCl_6^-$	CD_3NO_2	2.77 (s)	5.15 (t)	2.74 (qui)
	HF_2^-	HF	2.57 (s)	4.95 (t)	2.50 (qui)
2-*tert*-Butyl	$SbCl_6^-$	CD_3NO_2		5.23 (t)	2.74 (qui)
2-Phenyl	$SbCl_6^-$	CD_3NO_2		5.33 (t)	2.82 (qui)
2-*p*-Tolyl	$SbCl_6^-$	CD_3NO_2		5.32 (t)	2.72 (qui)
2-*p*-Anisyl	$SbCl_6^-$	CD_3NO_2		5.27 (t)	2.77 (qui)
2-Methyl-*cis*-4,6-trimethylene	$SbCl_6^-$	CD_3NO_2	2.68 (s)	5.90 (m)	2.80–2.40 (m)[b]
2-*tert*-Butyl-*cis*-4,6-trimethylene	$SbCl_6^-$	CD_3NO_2		5.97 (m)	2.80–2.40 (m)[b]
	$SbCl_6^-$	CD_3CN		5.82 (m)	2.80–2.40 (m)[b]
2-Methyl-*cis*-4,6-tetramethylene	$SbCl_6^-$	CD_3NO_2	2.85 (s)	5.70 (m)	2.70–1.80 (m)[b]
2-Methyl-5,5-bisacetoxymethyl	HF_2^-	HF	2.64 (s)	4.95 (s)	

[a] Reference 101; values are in ppm downfield from TMS except in HF where sodium 2,2-dimethyl-2-sila-5-pentanesulfonate is used as the internal standard. [b] Includes bicyclic ring methylene protons.

Table XXXV

Nmr Spectra of Oxolan-2-ylium Cations[a]

Cation	Counter-ion	Solvent	C-2 substituent α-C-H	C-3H	C-4H	C-5H	Ref
2-Methyl	HSO_4^-	90% H_2SO_4	3.48 (s)	4.28 (t)	3.03 (qui)	6.13 (t)	63
	HSO_4^-	95% H_2SO_4	3.10	3.90	2.66	5.77	61
2,3-Dimethyl	HSO_4^-	90% H_2SO_4	3.48 (s)	4.37 (m)	3.24 (t), 2.73 (t)	6.04 (t)	63
2,5-Dimethyl	HSO_4^-	96% H_2SO_4	3.47 (s)	4.30 (t)	3.27 (t), 2.69 (t)	6.58 (m)	60
	SbF_6	HF–SbF_5 (9:1)	3.02 (s)	3.87 (t)	2.9–2.1 (m)	6.17 (m)	61
	HSO_4^-	95% H_2SO_4	3.04 (s)	3.90 (t)	2.27 (t), 2.86 (t)	6.20 (m)	61
2,3,5-Trimethyl	HSO_4^-	90% H_2SO_4	3.43 (s)	4.29 (m)	2.9–2.1 (m)	6.29 (m)	63
2-Methyl-5-ethyl	HF_2^-	HF	3.00	3.83	2.9–2.1	5.96	61
	HSO_4^-	95% H_2SO_4	3.03	3.87	2.9–2.1	5.96	61
2,5,5-Trimethyl	HSO_4^-	90% H_2SO_4	3.44 (s)	4.38 (t)	2.91 (t)		63
	HSO_4^-	95% H_2SO_4	2.99 (s)	3.93 (t)	2.48 (t)		61
	SbF_6	HF–SbF_5 (9:1)	2.98 (s)	3.93 (t)	2.52 (t)		61
2,5-Dimethyl-5-ethyl	SbF_6^-	HF–SbF_5 (9:1)	2.99 (s)[b]	3.94 (t)	2.50 (m)		61
2-Methyl-5-phenyl	HSO_4^-	90% H_2SO_4	3.40 (s)	4.31 (t)	3.06 (t), 2.47 (t)	7.03 (t)	63
2-*tert*-Butyl-4,5,5-trimethyl	BF_4^-	SO_2		3.27 (m)	2.25 (m)		62
2-Cyclopropyl	HSO_4^-	90% H_2SO_4	3.07 (m)	4.36 (t)	Not well resolved[c]	6.22 (t)	63
2-Phenyl	HSO_4^-	90% H_2SO_4		4.50 (t)	3.03 (qui)	6.00 (t)	63
	$SbCl_6^-$	CH_3CN		4.12 (t)	2.60 (qui)	5.58 (t)	59
2-Phenyl-4-5,5-trimethyl	BF_4^-	CF_3CO_2H		3.75 (m)	2.50 (m)		62
2,5-Diphenyl	HSO_4^-	90% H_2SO_4		4.49 (t)	3.19 (t), 2.92 (t)	6.91 (t)	63

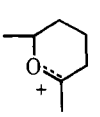
[a] All values are in ppm downfield from TMS; note that the values from ref 61 were measured relative to $(CH_3)_4N^+$ and corrected based on $\delta = 3.2$ for that ion. [b] Shows some coupling (t, $J = 1$ Hz) with the C-3 protons. [c] The cyclopropyl ions interfere with this assignment.

concentrated H_2SO_4 by Pittman and McManus[60,63] and by Brouwer[61] reveals a significant difference in the measured chemical shift values. A small change is expected with acid concentration. Another reason for the difference is the error in the correction in using the $(CH_3)_4N^+$ as an internal standard[61] as opposed to the use of an internal TMS capillary.[60,63]

Like other five-membered ring cations discussed here and the 2,3-dihydrofuran system, the nmr spectra are usually simplified as a result of the equivalence of the cis and trans vicinal coupling constants between the 3,4 and the 4,5 positions. Pittman and McManus determined the coupling constants for the C-3, C-4, and C-5 positions to range between 7.1 and 7.8 Hz.

4. *Oxan-2-ylium Cations*

As with most other six-membered ring heterocyclic cations, there is only a limited amount of data available due to the relative instability of the six-membered ring cations. Ward and Sherman[59] were able to observe the 2-phenyloxan-2-ylium ion as an intermediate in the solvolysis of 5-(*p*-bromobenzenesulfonoxy)valerophenone in trifluoroacetic acid even though ring opening by trifluoroacetate ion was rapid. They found the C-3, C-4, C-5, and C-6 protons at δ 3.9 (broadened triplet), 2.2 (broad multiplet), and 5.4 (broadened triplet), respectively. Brouwer[61] obtained acceptable nmr data for **489** and **490** although both rearranged to more stable cations as



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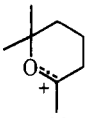

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discussed in section IV. Brouwer's data are presented in Table XXXVI. Compared to oxolan-2-ylium ions the protons on

Table XXXVI

Nmr Spectral Data for Oxan-2-ylium Cations[a]

Cation	*Solvent*	*CH_3 at C-2*	*C-3H*	*C-4, 5H*	*C-6H*	*CH_3 at C-6*
2,6-Dimethyl	HF	2.86	3.4	2.1–2.2	5.4	1.82
	95% H_2SO_4	2.91	3.40	2.1–2.2	5.40	1.81
2,6,6-Trimethyl	HF	2.83	3.38	2.1–2.2	...	1.80

[a] Ppm downfield from TMS using $(CH_3)_4N^+$ as an internal reference.

carbon adjacent to oxygen in oxan-2-ylium ions are upfield by 0.5–0.7 ppm, and the C-3 protons are upfield by about 0.4 ppm.

B. INFRARED SPECTROSCOPY

Unlike nmr spectroscopy, the use of ir techniques in the structure proof of 1,3-dioxolan-2-ylium salts has been limited. Because of this and since isolation of the salt is usually required before analysis, only a modest treatment will be given here.

Magnuson, Hirt, and Lauer[90] reported absorption bands for 2,4,4,5,5-pentamethyl-1,3-dioxolan-2-ylium perchlorate at 1536 (s) and 1511 (s) cm^{-1}. Absorption in that region has been assigned to the stretching modes of the O–C–O system by King and Allbutt.[96] The latter investigators further assigned absorption peaks at 1520 (s) and 1460 (s) cm^{-1} in the 2-phenyl salts and at 1460 (s) and 1435 (m) cm^{-1} in the 2-*p*-anisyl salts to the same stretching modes. They argued that conjugation in the latter compounds should cause the observed shift to lower energy. None of these ions abosorb in the region between 2000 and 1610 cm^{-1}.

For the 2-phenyloxolan-2-ylium hexachloroantimonate Ward and Sherman[59] reported ir bands at 1595, 1510, 1440, 1390, and 1290 cm^{-1}. None of the bands was assigned and the relative intensities were not reported. The primary purpose of the measurement in that study, however, was the verification that no free carbonyl band existed.

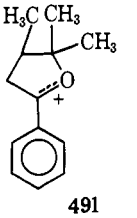
Oxazolinium and thiazolinium salts have been isolated by the thousands. The ability to isolate the free bases, however, has caused more interest to be placed on the ir studies of the free bases.[365–367]

According to Bellamy,[368] in salts of pyridine, indolene, and Schiff's bases the group C=NH^+ absorbs at 2500–2325 cm^{-1}. If other nearby heteroatoms are absent, second absorptions at 2200 and 1800 cm^{-1} appear. In a wide variety of 1-pyrrolines, 2-oxazolines, 2-thiazolines, 5,6-dihydro-1,3-oxazines, or thiazines, the C=N stretch occurs between 1664 and 1608 cm^{-1} with the majority of them near 1650 cm^{-1}.[365,369] Tomalia[181] assigns a 1700-cm^{-1} absorption of 2-dimethylamino-2-oxazolinium tetrafluoroborate to the NC^+O function.

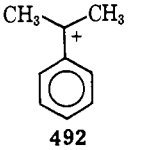
C. ULTRAVIOLET SPECTROSCOPY

A recent treatment of electronic spectra of carbonium ions has appeared.[370] That review did not discuss heteronuclear substituted cations of the type treated here. The alkoxymethyl cations, for example, exhibit no absorption above 200 nm as expected.[350] In much of the data now available, one must carefully avoid confusing substituent effects from the true electronic structural properties of the ions. Beringer and Galton[68] reported that the uv spectrum of 2-(2′,6′-dimethoxyphenyl)-1,3-dioxolan-2-ylium tetrafluoroborate was identical with that of β-bromoethyl 2,6-dimethoxybenzoate, from which the cation was prepared. The absorption maxima for the salt in acetonitrile were at 217 and 281 nm (ϵ_{max} 8600 and 2510, respectively). Pittman and Garrigan[371] substantiated the above inference that no significant uv absorption due to the dioxolan-2-ylium ring exists by finding no absorption above 220 nm for the 4,4,5,5-tetramethyl-1,3-dioxolan-2-ylium ion in H_2SO_4.

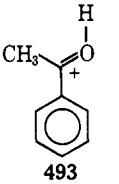
In view of the above, no uv absorption above 200 nm is expected for oxolan-2-ylium ions. Dimroth and Mach[62] did not report any uv data for 2-*tert*-butyl-4,5,5-trimethyloxolan-2-ylium cation, but they reported that a methanol solution of the corresponding 2-phenyl analog **491** has λ_{max} at 390 nm (ε 735). For comparison the 2-phenyl-2-propyl cation (**492**) has λ_{max} at 390 and 326 (ε 1,400 and 11,000, respectively).[372] Another model might be that of an appropriately substituted protonated ketone. Campbell and Edwards[373] found that protonated aliphatic ketones do not show absorption maxima above 200 nm. Protonated acetophenone **493**,



491



492



493

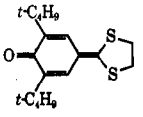
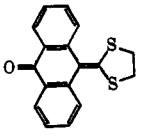
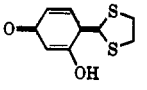
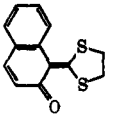
which is a reasonable model for **491**, shows λ_{max} 335 and 296 (ε 2,140 and 18,600).[374] Thus one might conclude from these data that the charge density in both protonated ketones and oxolan-2-ylium ions is greater at oxygen.

Gompper[113] and Nakai[117] have independently contributed considerably toward defining the nature and stability of 1,3-dithiolan-2-ylium salts. Gompper has investigated the very interesting class of compounds capable of reasonance between the heterocyclic cation form **494b** and the quinone methide

(365) A. I. Meyers, *J. Org. Chem.*, 26, 218 (1961).
(366) Z. Eckstein, K. Majewski, and P. Gluzinski, *Rocz. Chem.*, 36, 73 (1962).
(367) Z. Eckstein, P. Glazinski, W. Hofman, and T. Urbański, *J. Chem. Soc.*, 489 (1961).
(368) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," 2nd ed, Methuen, London, 1958, p 260.
(369) A. I. Meyers, *J. Org. Chem.*, 24, 1233 (1959).
(370) G. A. Olah, C. U. Pittman, Jr., and M. C. R. Symons in ref 26, pp 153–222.
(371) C. U. Pittman, Jr., and B. Garrigan, unpublished results.
(372) J. A. Grace and M. C. R. Symons, *J. Chem. Soc.*, 958 (1958).
(373) H. J. Campbell and J. T. Edwards, *Can. J. Chem.*, 38, 2109 (1960).
(374) J. Rosenbaum, M. Rosenbaun, and M. C. R. Symons, *Mol. Phys.*, 3, 205 (1960).

Table XXXVII

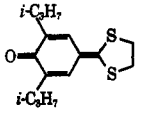
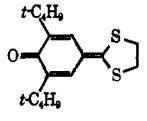
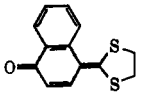
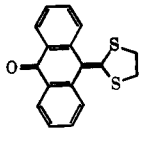
Uv Spectra of 494 in Formamide–Ethyl Acetate[a]

Compound	—100% formamide— λ_{max}	Log ϵ	Formamide–ethyl acetate (9:1) λ_{max}	Log ϵ	—Ethyl acetate— λ_{max}	Log ϵ
	427 413	4.57 4.48	425 412	4.52 4.50	409 400	4.52 4.53
	425 308	3.99 4.00			408 3.7	4.05 3.95
	463 365	3.53 4.21			433 350	3.46 3.89
	450 430	4.03 4.05	450 428	4.02 4.05	446 423	3.92 4.03

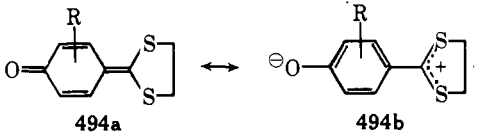
[a] Reference 375; λ_{max} in nm.

Table XXXVIII

Solvent Dependence of the Uv Spectra of 494a[a]

Compound	λ_{max}, nm (log ϵ) — % Dioxane in dioxane–formamide mixture — 100%	80%	50%	20%
	411 (4.52)	423 (4.53)	432 (4.53)	435 (4.53)
	403 (4.53)	410 (4.53)	422 (4.53)	428 (4.53)
	434 (4.10)	445 (4.09)	452 (4.09)	459 (4.08)
	406 (4.04)	415 (4.05)	421 (4.02)	425 (4.00)

[a] Reference 375.

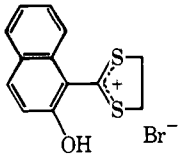


494a ↔ 494b (209)

494a. Other studies, such as those of Wizinger and Dürr,[111] were covered in section IV, but since the heterocyclic carbonium ions are capable of being aromatic (*i.e.*, benzo derivatives), their uv spectra will not be treated here.

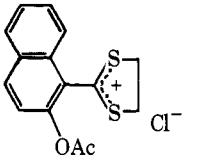
Gompper, Kutter, and Schmidt[115] have prepared and recorded the uv spectra of several 2-(1-naphthyl)-1,3-dithiolan-2-ylium salts. The similarity of the uv maxima of these ions to the maxima of the quinone methide **497** is more than coincidental. Gompper, Schmidt, and Kutter[375] discussed in detail the electronic structure of quinone methides such as **494**. By measuring the uv in various solvents or solvent mixtures (see Tables XXXVII and XXXVIII), it was determined that **494** shows postive solvatochromism resulting from resonance. Dipole moment measurements (Table XXXIX) allowed Gompper[375] to estimate the percentage of **494b** in the ground-state structure. From the dipole measurements,

(375) R. Gompper, R. R. Schmidt, and E. Kutter, *Justus Liebigs Ann. Chem.*, 684, 37 (1965).



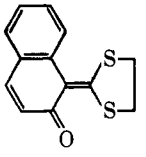
495

λ_{max}, nm(log ϵ), CH_3CN
446 (3.98), 427 (4.00), 300 (4.13)



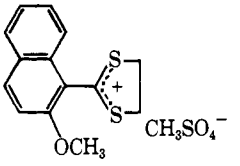
496

λ_{max}, nm(log ϵ), CH_3CN
442 (4.02), 423 (4.09), 299 (4.24)



497

λ_{max}, nm(log ϵ), CH_3OH
450 (4.06), 428 (4.08), 301 (4.14)

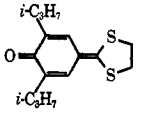
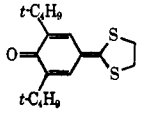
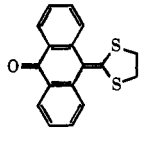


498

λ_{max}, nm(log ϵ), CH_3CN
464 (4.19), 376 (3.89), 309 (3.71)

Table XXXIX

Dipole Moment Measurements of 494 at 20° in Benzene Solution[a]

Compound	*Dipole moment, D*	*% of* **494b** *present in ground-state equilibrium mixture*
	6.31	15–17
	6.36	15–17
	4.80	10–11

[a] Reference 375.

a value of 30.8 D was calculated for the basic structure **494b**, and **494a** was estimated to have a dipole moment of 1.5–2.0 D.

Nakai, Ueno, and Okawara[117] found a definite trend in the electronic spectra of 2-(*N,N*-dimethylamino) derivatives of varying ring sizes. Their data are shown in Table XL. Note that there is a strong shift of absorption maxima toward lower energy as the ring size increases. A similar trend has been observed in the electronic spectra of cyclic alkenyl carbonium ions.[370] In that case the interpretation included the suggestion that 1,3 π overlap will be progressively more significant as the bond angle $[C{=}{=}C{=}{=}C]^+$, thus the ring size, decreases. Nakai, *et al.*,[117] noted for the triheteronuclear substituted ions they studied, that the spectral trend suggests that α-heteroatoms stabilize the ground state more than the excited state. Thus, as the ring size decreases, the ground state is more stabilized presumably because of a more developed 1,3 overlap in the $[S{=}{=}C{=}{=}S]^+$ system.

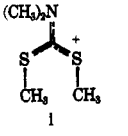
The ring size effect also is prominent in the nmr spectra of the ions in Table XL. A change in ring size affects the chemical shift of the *S*-methylene protons in the ring more than those of the *N*-methyl protons, but both are definitely affected. The higher contribution from the sulfonium ion structure in the lower ring sizes causes a greater deshielding of the *S*-methylene protons as is predicted.

Table XL

Effect of Ring Size on the Spectral Properties of Dithiolan-2-ylium Salts[a]

Ring size	λ_{max},[b] *nm*	*Nmr, δ, ppm[c]* $-SCH_2-$	$-NCH_3$	CCH_2C
5	249	4.06 (s)	3.58 (s)	
6	262	4.43 (t)	3.55 (s)	2.27 (t)
7	275	3.47 (m)	3.61 (s)	2.10 (m)
d	276	2.85 (s)[e]	3.70 (s)	

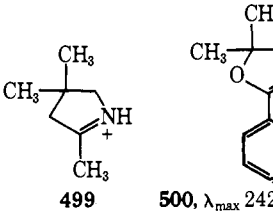
[a] Reference 117; all are perchlorate salts. [b] Accurate molar extinction coefficients could not be obtained owing to the partial hydrolysis occurring during the measurements; values, however, ranged between 0.70 and 1.42 × 10^4. [c] The solvent is unknown; measurements are in ppm downfield from TMS as an internal standard; s = singlet, t = triplet, m = multiplet. [d] Compound is i as



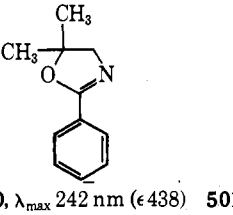
1

shown. [e] The S-CH_3 protons.

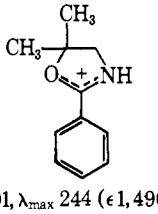
For the cyclic iminium cation **499**, Bonnett[376] has reported no maxima above 210 nm, while others[377] found that some iminium chromophores had modest absorptions near 220 nm. Pittman, *et al.*,[378] found that some oxazolinium ions in H_2SO_4 absorbed at about the same wavelength as the free bases (*i.e.*, **500** and **501**), although there was generally a hyperchromic effect upon protonation. The 2,4,4,6-tetramethyl-5,6-dihydro-1,3-oxazinium cation contained an absorption at 316 nm (ϵ 140) not present in the free base. The thiazolinium ion **502** has λ_{max} 445 nm[379] as opposed to a λ_{max} 275 nm for an analogous triene **503**.[380]



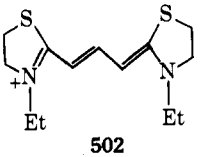
499



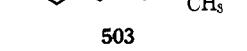
500, λ_{max} 242 nm (ϵ 438)



501, λ_{max} 244 (ϵ 1,490)



502



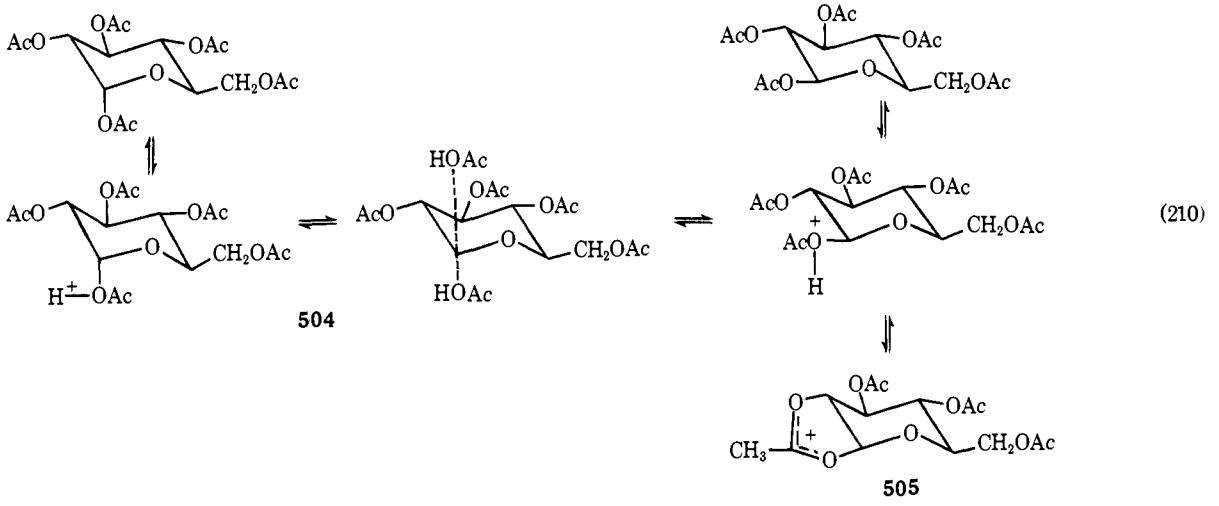
503

(376) R. Bonnett, *J. Chem. Soc.*, 2313 (1965).
(377) G. Optiz, H. Hellmann, and H. W. Schubert, *Justus Liebigs Ann. Chem.*, **623**, 117 (1959).
(378) C. U. Pittman, Jr., and coworkers, unpublished results.
(379) L. G. S. Brooker, F. L. White, and R. H. Sprague, *J. Amer. Chem. Soc.*, **73**, 1087 (1951).
(380) I. Fleming and D. H. Williams, "Spectroscopic Methods in Organic Chemistry," McGraw-Hill, New York, N. Y., 1966, p 19.

VIII. Occurrence in Carbohydrates

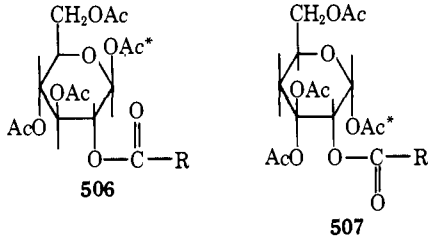
A. DIOXOLAN-2-YLIUM IONS

The early work of Lemieux and Isbell and of Tipson[381] demonstrated the intervention of 1,3-dioxolan-2-ylium and related cations in carbohydrate reactions. Now a large number of carbohydrate reactions have been found in which these ions play an important role. An early example was reported by Lemieux.[381a] In the H_2SO_4-catalyzed anomerization of glucose pentaacetates in acetic acid, ionization proceeds simultaneously with and without neighboring group participation. In the α anomer the rates of anomerization and acetate-exchange are identical, but in the β anomer exchange of acetate is about 15 times faster than anomerization. Thus, the β anomer must have a path to undergo acetate exchange without anomerization, while it must also have a common transition state (**504**) with the α anomer for the $\alpha \rightleftharpoons \beta$ interconversion.



(210)

This high reactivity of β-D-glucopyranose pentaacetate compared with that of its α anomer has been demonstrated under a wide range of conditions using both Lewis acid and proton acid catalysts.[53,55,382-385] Lemieux[381a] studied the effects of varying the C-2 substituent on the dissociation of C-1 acetoxy group. The anomeric $ClCH_2COO$-, Cl_2CHCOO-, and Cl_3CCOO- derivatives of the 1,3,4,6-tetra-*O*-acetyl-D-glucopyranoses (**506** and **507**) were examined. Anomerizations were performed in 0.5 *M* H_2SO_4 in 1:1 HOAc–acetic anhydride media. With increasing chlorine substitution, the rate data show that there is a decrease in participation.



In addition to the rate decrease, the rate ratio of **506**:**507** decreases for **a**, **b**, and **d**. Thus while inductive effects are manifest in the dissociations of both **506** and **507**, those of **506** also feel anchimeric assistance (see Table XLI).

Table XLI

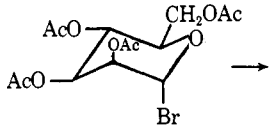
Rates of Dissociation of C-1 Acetoxy Group of D-Glucose Derivatives as Measured by Exchange at 25°

R	*2-O-Acyl deriv*	*Rate, $k \times 10^4$ min^{-1}*
CH_3	**506a**	4600
CH_3	**507a**	55.5
CH_2Cl	**506b**	498
CH_2Cl	**507b**	18.8
$CHCl_2$	**506c**	46.0
CCl_3	**506d**	12.0
CCl_3	**507d**	1.1

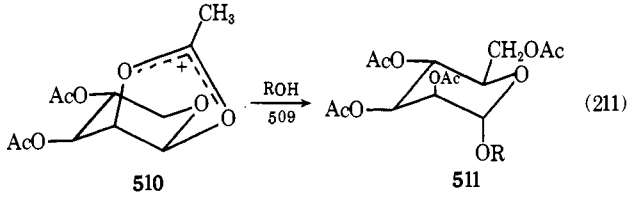
In section V.B the stereochemistry of formation and reaction with nucleophiles of 1,3-dioxolan-2-ylium and 1,3-dioxan-2-ylium ions was extensively treated. The principles outlined in that section form the foundation for examining carbohydrate reactions proceeding through these intermediates. The reactions treated throughout this section bear witness to this fact. Many interesting reactions and rearrangements proceed only because of the intervention of 1,3-dioxolan-2-ylium ions. Gorin and Perlin[386] showed that the reaction of tetra-*O*-acetyl-α-D-mannopyranosyl bromide (**508**) with 1,2,3,4-tetra-*O*-acetyl-β-D-glucose (**509**) formed α-linked disaccharide **511** with retention of configuration. Only through the intervention of 1,3-dioxolan-2-ylium ion **510** is this reaction readily explained. The preferred trans diaxial opening of **510** agrees with the preference for this diaxial opening discussed in section V.B (eq 143 and 144) where strong nonbonded 1,3 diaxial interactions do not occur.

Two interesting rearrangements were reported by Buchanan and Schwarz. The interconversion of methyl 2,3-anhydro-α-D-mannoside and 3,4-anhydro-α-D-altroside, and that of their 6-*O*-triphenylmethyl ethers, has been studied.[387] For example, a neighboring trans-*O*-acetyl group at the 2 position (**512**) greatly increases the rate of the epoxide ring opening and causes the opening to be stereospecific. Again the diaxial

(381) R. S. Tipson, *J. Biol. Chem.*, 130, 55 (1939).
(381a) R. U. Lemieux, C. Brice, and G. Huber, *Can. J. Chem.*, 33, 134 (1955); see B. Capon and W. G. Overend, *Advan. Carbohyd. Chem.*, 15, 42 (1960), for a more detailed mechanistic discussion.
(382) R. U. Lemieux and C. Brice, *Can. J. Chem.*, 30, 295 (1952).
(383) E. M. Montgomery, N. K. Richtmyer, and C. S. Hudson, *J. Amer. Chem. Soc.*, 64, 690 (1942).
(384) K. C. Tsou and A. M. Seligman, *ibid.*, 75, 1042 (1953).
(385) R. U. Lemieux and G. Huber, *Can. J. Chem.*, 33, 128 (1955).
(386) P. A. Gorin and A. S. Perlin, *ibid.*, 37, 1930 (1959).
(387) J. G. Buchanan and J. C. P. Schwarz, *J. Chem. Soc.*, 4770 (1962).

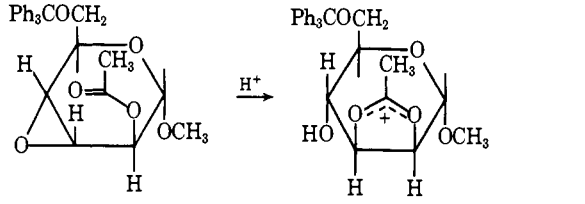


508



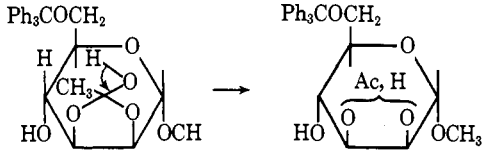
(211)

510 511



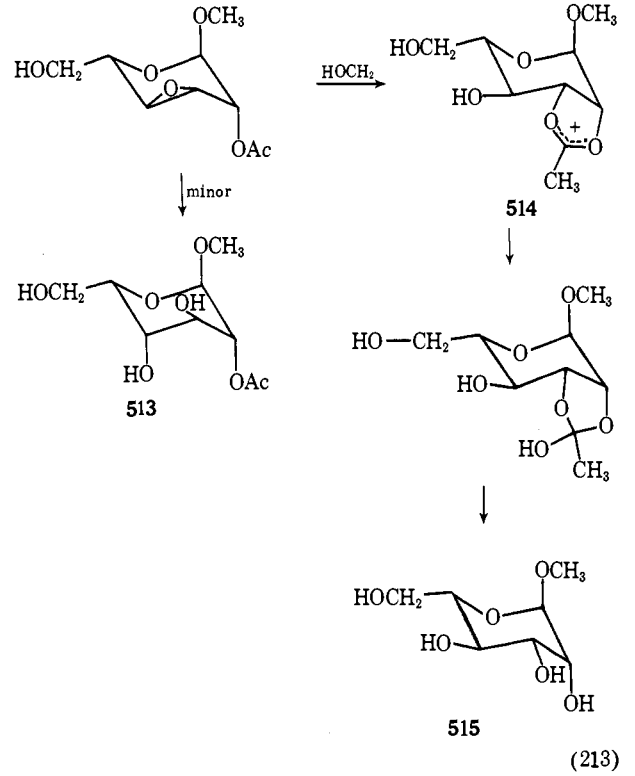
(212)

512



opening is demonstrated in analogy with previous work from the same laboratory cited in eq 152 and 153 of section V.B.

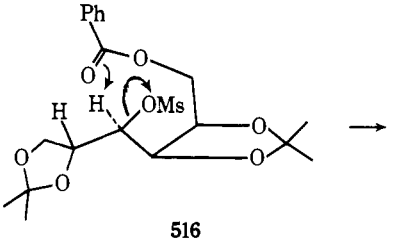
Epoxide ring opening in methyl 2-*O*-acetyl-3,4-anhydro-α-D-altroside in aqueous acetic acid gave mannose derivative **515** almost entirely.[387] Again, neighboring group participation, *via* ion **514**, must be invoked because, without it, idose derivative **513** would be the expected product. It is most likely



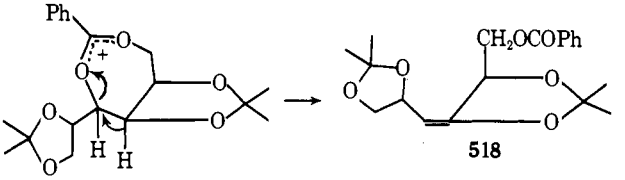
513 514 515

(213)

that the conversion of 6-*O*-benzoyl-1,2:4,5-di-*O*-isopropylidene-3-*O*-methanesulfonyl-D-mannitol (**516**) into enol ether **518** takes place through the seven-membered 1,3-dioxepan-2-ylium ion **517** because neighboring group benzyloxy group



516

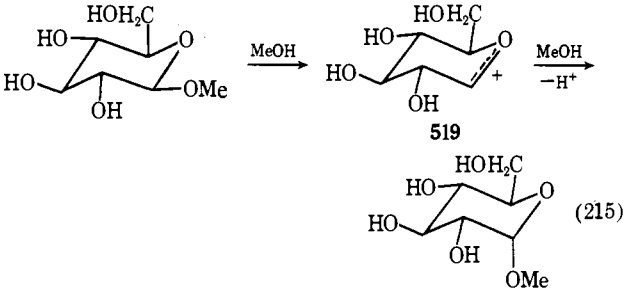


517 518

(214)

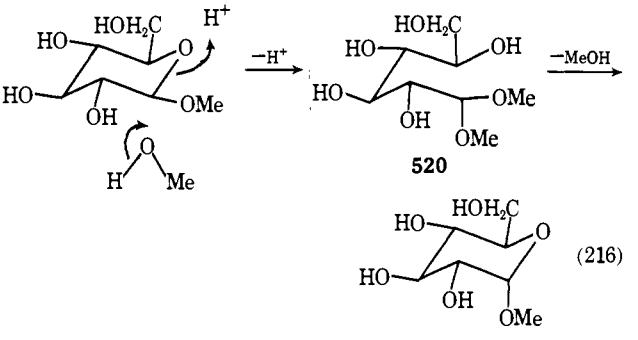
participation results in a geometry suitable for elimination.[388]

The acid-catalyzed anomerization of the methyl glucopyranosides in CD_3OD proceeds with complete exchange of the methoxyl group with solvent.[389-392] This result is consistent with either the intervention of an oxolan-2-ylium cation **519** (eq 215) or the acid-catalyzed ring opening followed by reclosure with loss of methanol (eq 216). Since the acetal



519

(215)



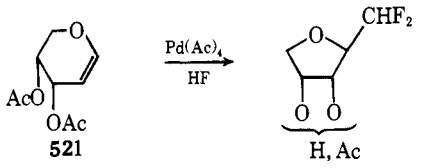
520

(216)

520 was independently shown to form furanosides and not pyranosides under the reaction conditions, the second mechanism can be ruled out. The first mechanism is also consistent with the entropies of activation (+5 to +8 eu) which have been measured.

The treatment of diacetate **521** with lead tetracetate–HF

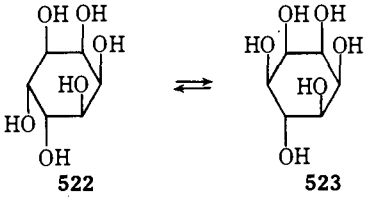
(388) M. A. Bukhari, A. B. Foster, J. M. Webber, and J. Lehmann, *Carbohyd. Res.*, 1, 485 (1966).
(389) B. Capon and D. Thacker, *J. Chem. Soc. B*, 1010 (1967).
(390) B. Capon, *Chem. Commun.*, 21 (1967).
(391) J. Swiderski and A. Temeriusg, *Carbohyd. Res.*, 3, 225 (1966).
(392) G. Wagner and H. Frenzel, *Pharmazie*, 8, 415 (1967).



521 (217)

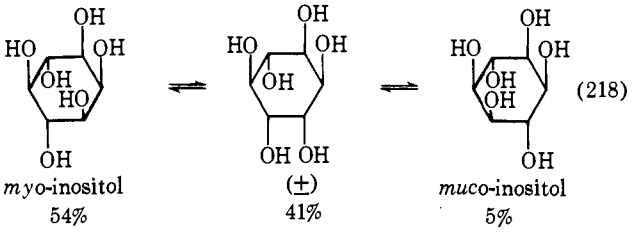
resulted in the monoacetate of 2,5-anhydro-1-deoxy-1,1-difluoro-D-ribitol. This reaction is most easily explained invoking an intermediate 1,3-dioxolan-2-ylium ion.

Once it had been demonstrated that *allo*-inositol (**522**) could be partially converted into *epi*-inositol (**523**) by *p*-toluene-



522 **523**

sulfonic acid in 95% acetic acid,[393] a study of the equilibrations of inositols, inositol methyl ethers, cyclohexanepentanols, and cyclohexanetriols in acetic acid–sulfuric acid was conducted.[394,395] A large number of cyclitol equilibrations were worked out. A few representative examples are summarized in eq 218–220 below. All the equilibrations could



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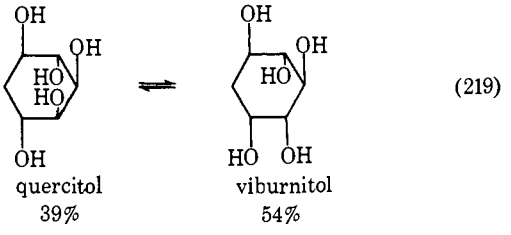
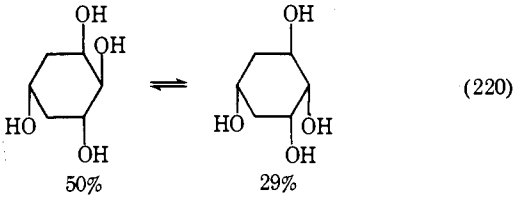
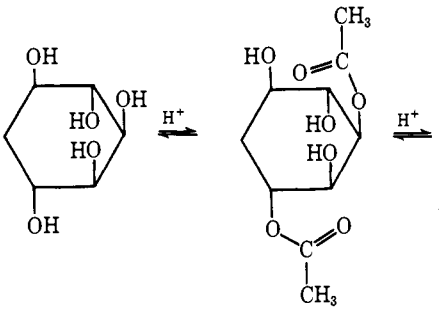


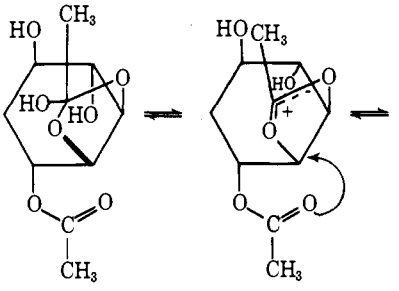
(219)

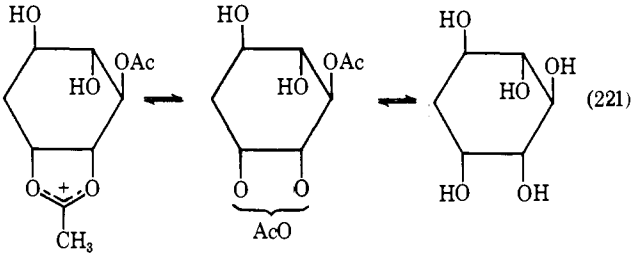


(220)

be explained by invoking acetylation or partial acetylation of the cyclitol followed by rearrangements involving bridged 1,3-dioxolan-2-ylium ions. The following aspects of these reactions are then explained: (1) why the reactions are reversible; (2) why cis and trans hydroxyl groups are necessary on adjacent carbon atoms; (3) the lack of equilibration in the absence of acetic acid. For example, the mechanism of the

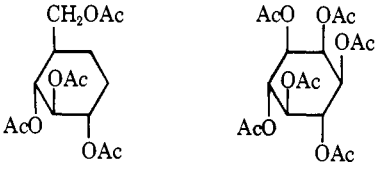






(221)

interconversion of quercitol and viburnitol can be represented as shown in eq 221. A monoacetate can be converted to a cyclic 1,3-dioxolan-2-ylium ion when the oxygen atoms in the cyclohexane system are cis related. The presence of another acetoxy group trans and adjacent to this bridged ion permits nucleophilic opening of the bridged ion with the formation of a second bridged ion and results in inversion of configuration at the site of nucleophilic opening. The failure to find any inversion products after treatment of 1,5-anhydro-D-glucitol tetracetate (**524**) with HF[396] emphasizes the need for a contiguous cis–trans triacetoxy sequence. On the other hand, the treatment of *myo*-inositol hexaacetate (**525**) in HF



524 **525**

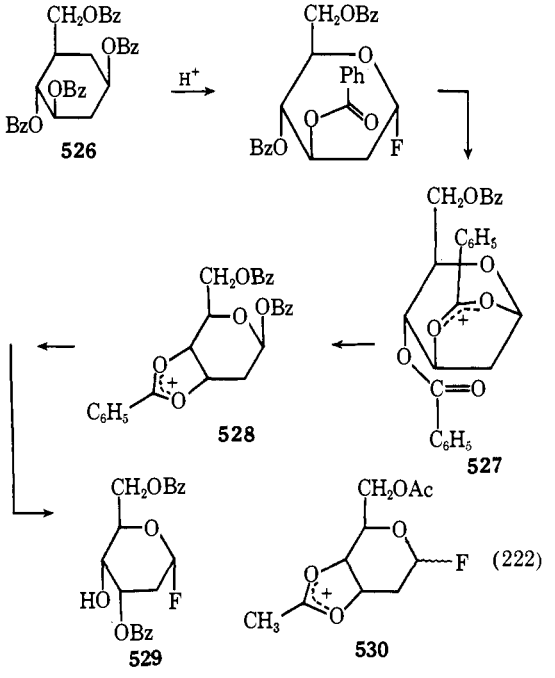
at 18° for 9 hr gave *muco*-inositol as the major product.[397] This product arose from inversion at both C-1 and C-3 of **525**. Many other interesting examples of intermediate 1,3-dioxolan-2-ylium ions in cyclitol and glycitols rearrangements, such as the conversion of the racemic methyl ester of

(393) M. E. Pitman, M.S. Thesis, University of Tasmania, 1957; see ref 394.
(394) S. J. Angyal, P. A. J. Gorin, and M. E. Pitman, *J. Chem. Soc.*, 1807 (1965).
(395) P. A. J. Gorin, *Can. J. Chem.*, 41, 2417 (1963).
(396) E. J. Hedgley and H. G. Fletcher, Jr., *J. Amer. Chem. Soc.*, **85**, 1615 (1963).
(397) E. J. Hedgley and H. G. Fletcher, Jr., *ibid.*, **84**, 3726 (1962).

triacetyl-4-epishikimic acid to both racemic methyl shikimate and racemic 4-epishikimate,[398] exist.[399-402]

In liquid HF, glycitols and cyclitols are rather stable, but reactions of their acylated derivatives, as seen in a few examples above, are far more complex involving Walden inversions, ring openings and closing, ring contractions, and other rearrangements. A rigorous review of this area will not be attempted here because comprehensive discussions of the literature through 1968 by Lenard[1] and through 1969 by Paulsen[403] have appeared. These reviews cover liquid HF reactions of diacetoxycyclohexanes, acetylated cyclitols, glycitols, 1,4- and 1,5-anhydroglycitols, and monosaccharides.

Acylated mono- and disaccharides give their acylated glycosyl fluorides on treatment with HF, and in many of these examples Walden inversions occur through 1,3-dioxolan-2-ylium ions.[404-407] In the rearrangement of tetra-*O*-benzoyl-β-D-arabinohexopyranose (**526**) to 3,6-di-*O*-benzoyl-2-deoxy-α-D-ribohexopyranosyl fluoride (**529**) (in 62% yield), it would appear that the 1,3-dioxan-2-ylium ion **527** is involved.[407] If this is the case, the inversion would then occur by intramolecular cyclization of the C-4 benzoyl group at C-3 as shown in **528**. In the all acetyl analog, ion **530** is a stable end

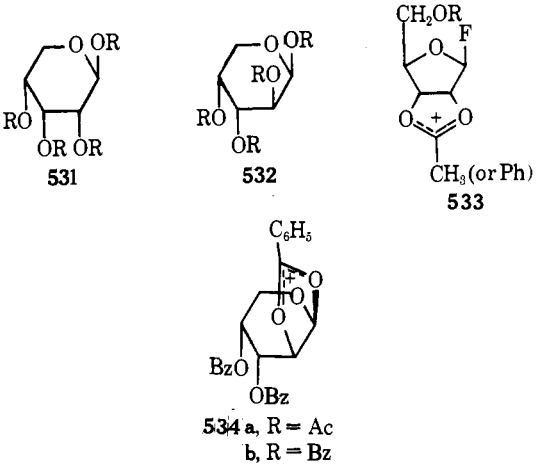


(222)

product in HF, but, as with **529**, the intermediate ions were not definitively identified.

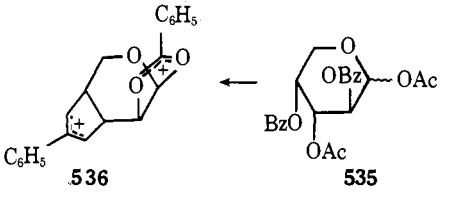
As was emphasized in section V.B, the acyl groups must be trans in order to participate (*i.e.*, **527** → **528**). Furthermore, as King and Allbutt[97] showed (eq 147–149) in rigidly anchored systems, the hydrolysis of 1,3-dioxolan-2-ylium ions proceeds *via* path a to an ortho acid which decomposes to give a cis hydroxy ester with the ester function almost exclusively axial. This path is followed in the conversion of **528** to **529**.

Recently, Pedersen has applied nmr studies of monosaccharides in strong acids to elucidate the mechanism by which they rearrange.[403,408,409] For example, tetra-*O*-acetyl-β-D-ribopyranose (**531a**), tetra-*O*-acetyl-β-D-arabino-pyranose (**532a**), and the benzoyl analogs **531** and **532b** all form ion **533** when allowed to stand in HF.[409] In addition, ion **534** has



been identified as an intermediate in the rearrangement of tetrabenzoates **531b** and **532b** to **533** and also as an intermediate when tri-*O*-benzoyl-β-D-ribopyranosyl fluoride is dissolved in HF.

Pedersen[409] has also identified the bis-2-phenyl-1,3-dioxolan-2-ylium (**536**) as a product formed in strong acid media from mixed diacetate-dibenzoate **535**. Interestingly, ion **536** is not formed from **532b**.

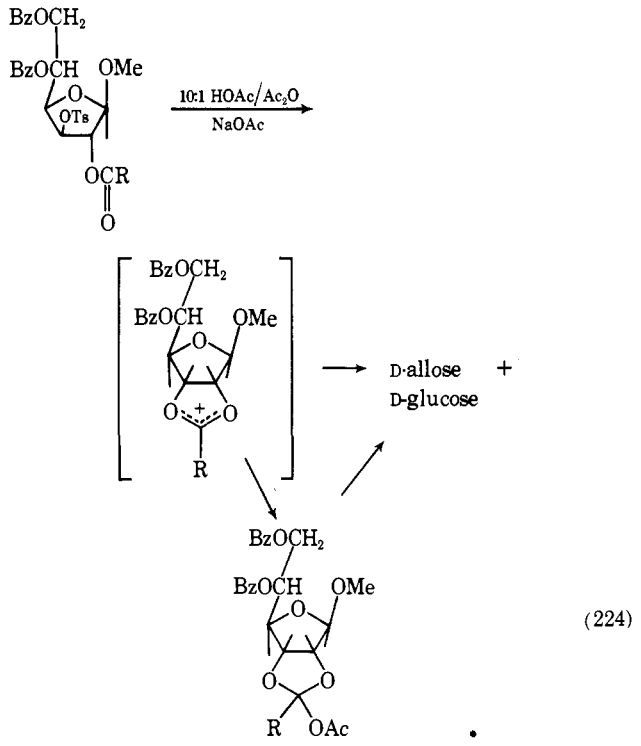


(223)

In one of the first reports of the application of neighboring acetoxy group participation in modifying sugars, Short[410] described solvolysis of several mixed esters of D-glucose to D-allose derivatives (eq 224). It is interesting that the predominant product was D-allose (sometimes in excess of 70% yield), which results from cis ring opening. Since steric factors would slow trans attack by the acetate ion, the fomation of an ortho diacetate best accounts for this result.

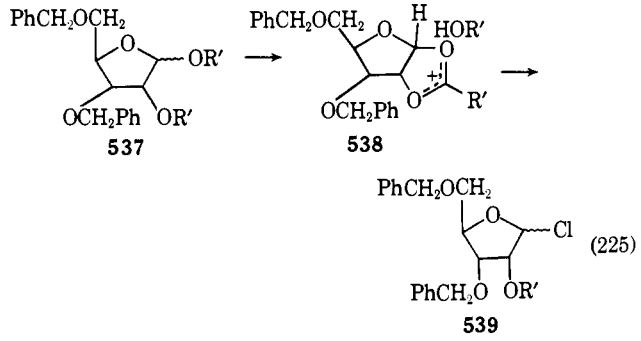
Several other examples of 1,3-dioxolan-2-ylium ion intervention in monosaccharides are known. In the preparation of 3,5-di-*O*-benzyl-2-*O*-*p*-phenylazobenzoyl-D-ribofuranosyl chloride (**539**) and its benzoyl analog, the reaction proceeds through the intermediate ion **538**,[411] as shown in eq 225.

(398) R. Grew and S. Kersten, *Chem. Ber.*, **100**, 2546 (1967).
(399) E. J. Hedgley and H. G. Fletcher, Jr., *J. Amer. Chem. Soc.*, **86**, 1583 (1964).
(400) E. J. Hedgley and H. G. Fletcher, Jr., *ibid.*, **86**, 1576 (1964).
(401) E. J. Hedgley and H. G. Fletcher, Jr., *ibid.*, **85**, 1615 (1963).
(402) C. Pedersen, *Acta Chem. Scand.*, **17**, 1269 (1963).
(403) H. Paulsen, H. Behre, and C. P. Herold, *Fortschr. Chem. Forsch.*, **14**, 472 (1970).
(404) F. Micheel and A. Klemer, *Advan. Carbohyd. Chem.*, 16, 85 (1961).
(404) F. Micheel and A. Klemer, *Advan. Carbohyd. Chem.*, 16, 85 (1961).
(405) L. D. Hall and J. F. Manville, *Can. J. Chem.*, **45**, 1299 (1967).
(406) C. Pedersen and H. G. Fletcher, Jr., *J. Amer. Chem. Soc.*, **82**, 941 (1960).
(407) I. Lundt and C. Pedersen, *Acta Chem. Scand.*, **21**, 1239 (1967).
(408) N. Gregersen and C. Pedersen, *ibid.*, **22**, 1307 (1968).
(409) C. Pedersen, *ibid.*, **22**, 1888 (1968).
(410) W. A. Short, *Diss. Abstr.*, **22**, 2202 (1962).
(411) M. Haga, R. K. Ness, and H. G. Fletcher, *J. Org. Chem.*, **33**, 1810 (1968).



(224)

R = CH_3, C_6H_5, p-$CH_3OC_6H_4$



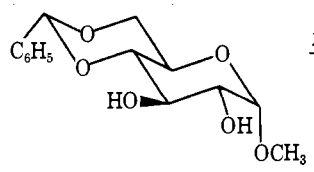
(225)

a, R' = $C_6H_5N{=}NC_6H_4(p)CO-$; b, R' = C_6H_5C-

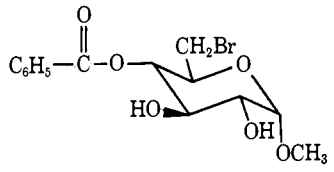
In a series of furanosyl chlorides it was shown that acyl groups not contiguous to C-1 (*i.e.*, at either C-5 or C-3) exerted a net stabilizing effect on the C-1 halogen bond.[412] The slower rates of solvolyses of these compounds argue against 1,3-dioxan-2-ylium ion intervention in these systems. A similar series[413] of D-glucopyranosyl bromides, having a C-2 benzyl group, were progressively substituted with *p*-nitrobenzoyl groups (*vs.* benzoyl groups) and the solvolysis rates in this series also dropped.

Hanessian and coworkers have pioneered the reaction of *N*-bromosuccinimide (NBS) with many carbohydrate derivatives and discovered that many of the reactions proceeded through cyclic 1,3-dioxan-2-ylium ions.[414-417] These reactions are of importance in selective carbohydrate synthesis. For example, the treatment of methyl 4,6-*O*-benzylidenehexopyranosides with NBS in refluxing carbon tetrachloride affords, with few exceptions, methyl 4-*O*-benzoyl-6-bromo-6-deoxyhexopyranosides as the major products. Selectively, C-4 benzoylated 6-substituted hexopyranose derivatives are amenable to a variety of further transformations.

In the case of methyl 4,6-*O*-benzylidene-α-D-glucopyranoside (**540**) the major product, isolated in 60% yield, was methyl 4-*O*-benzoyl-6-bromo-6-deoxy-α-D-glucopyranoside (**541**). The β-anomeric glycoside **542** gave its corresponding β-D-glucopyranoside **543** in 67% yield.

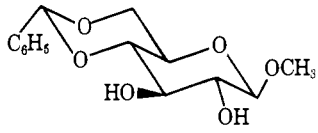


540

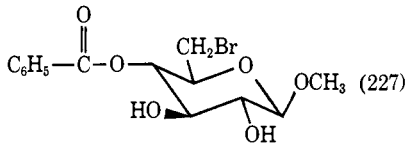


(226)

541

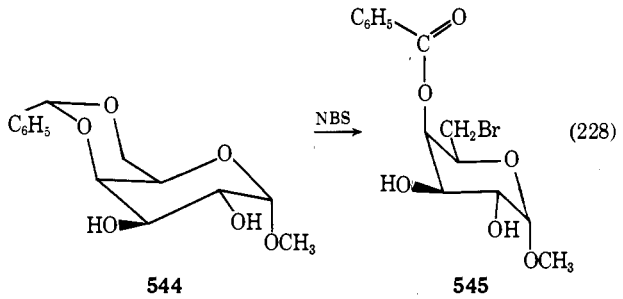


542



(227)

543

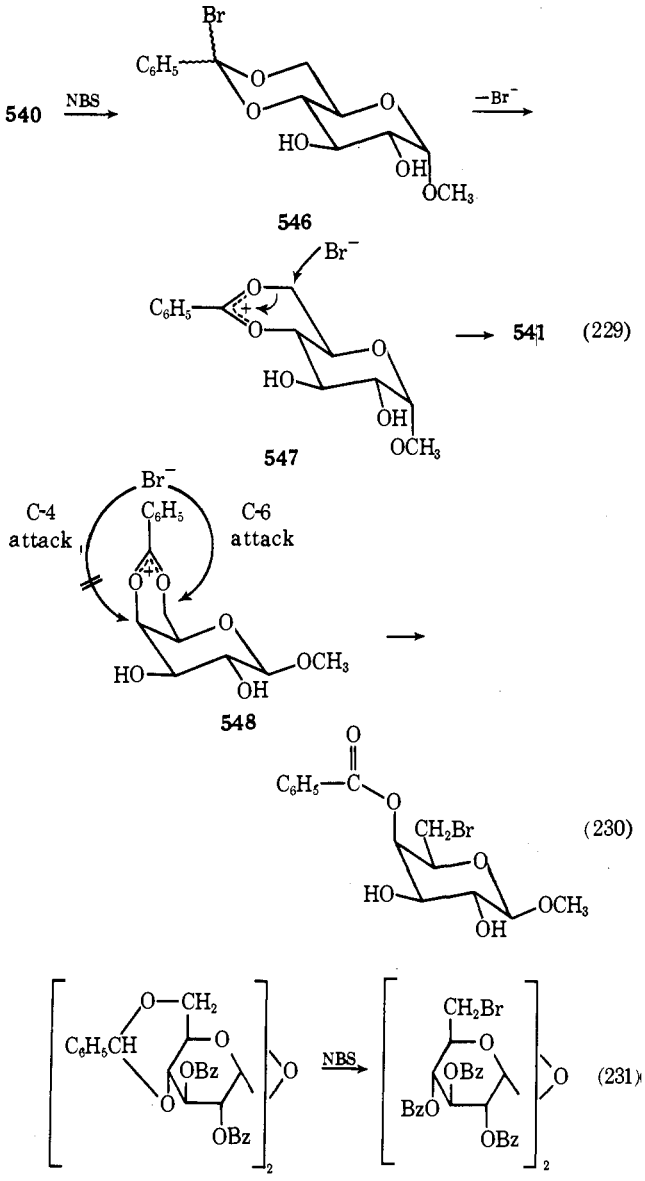


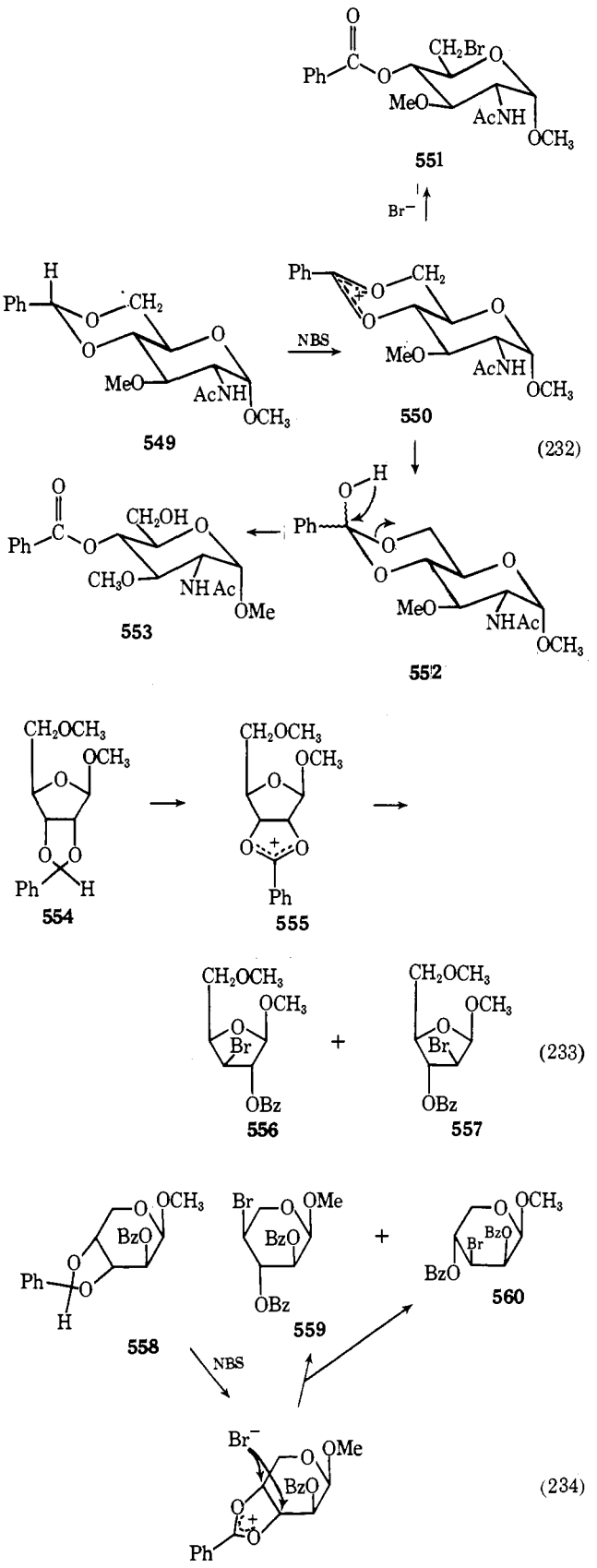
(228)

544 **545**

4,5-*O*-Benzylidene-α-D-galactopyranoside (**544**) on treatment with NBS gave the corresponding 6-bromo-4-benzoate **545** in over 90% yield. The mechanism involves bromination at the 2 position of the 1,3-dioxane ring (**540** → **546**) followed by loss of bromide to give an intermediate 1,3-dioxan-2-ylium ion **547** which opens by nucleophilic attack on C-6 (**547** → **541**). In the β-D-galactopyranoside series, the intermediate 1,3-dioxan-2-ylium ion **548** is opened by bromide attack at C-6, but no product derived from C-4 opening has been found. This reaction has also been adapted to *O*-benzylidene acetals of disaccharides (see, for example, eq 231) and to the benzylidene acetals of amino sugar glycosides.[416] When

(412) C. P. J. Glaudemans and H. G. Fletcher, Jr., *J. Amer. Chem. Soc.*, 87, 4636 (1965).
(413) T. Ishikawa and H. G. Fletcher, Jr., *J. Org. Chem.*, **34**, 563 (1969).
(414) S. Hanessian, *Carbohyd. Res.*, 2, 86 (1966).
(415) S. Hanessian and N. R. Plessas, *J. Org. Chem.*, **34**, 1035 (1969).
(416) S. Hanessian and N. R. Plessas, *ibid.*, **34**, 1045 (1969).
(417) S. Hanessian and N. R. Plessas, *ibid.*, **34**, 1053 (1969).



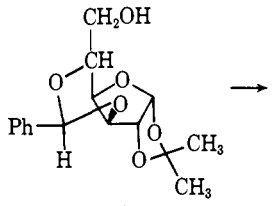


methyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-3-*O*-methyl-α-D-glucopyranoside (**549**) was treated with NBS in the presence of small amounts of water, the intermediate 1,3-dioxan-2-ylium ion **550** gave the 6-bromo-6-deoxy **551** derivative by Br^- attack at C-6, but competitive attack by hydroxyl ion on ion **550** followed by stereoselective collapse of the resulting ortho ester **552** gave the 6-hydroxy derivative **553**.[416] Jones and coworkers used this NBS reaction to introduce the potential 6-deoxy group in their synthesis of the branched-chain sugar arcanose.[418] Hanessian and Plessas[417] have further extended the use of this reaction to methyl 2,3-*O*-benzylidene-5-*O*-methyl-β-D-ribofuranoside (**554**) to give about equal amounts of the 3-bromo-3-deoxy-β-D-arabinofuranoside (**556**) and the 2-bromo-2-deoxy-β-D-xylofuranoside (**557**) through ion **555**. This application to the production of trans-oriented bromobenzoates is important in view of the limited number of methods available for such inversions in furanoid derivatives. In addition, methyl-2-*O*-benzoyl-3,4-*O*-benzylidene-β-D-arabinopyranoside (**558**) reacted with NBS to give **559** and **560** in a ratio of 1:2.

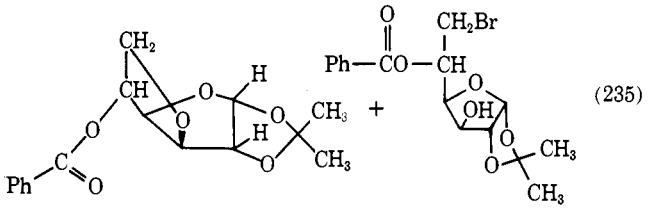
A third type of *O*-benzylidene sugar is comprised of a select group where the acetyl ring joins two secondary hydroxy groups, one situated in a ring and the other on an acyclic carbon. For example, 3,5-*O*-benzylidene-1,2-*O*-isopropylidene-D-glucofuranose (**561**) was chosen as a model to demon-

(418) B. Howarth, W. A. Szarek, and J. K. N. Jones, *Chem. Commun.*, 62 (1968).

strate its reaction with NBS. Two products were formed (neither were expected ring-opened products). They were 3,6-anhydro-5-*O*-benzoyl-1,2-*O*-isopropylidene-D-glucofuranose (**562**) (smaller fraction) and 5-*O*-benzoyl-6-bromo-6-deoxy-1,2-*O*-isopropylidene-D-glucofuranose (**563**). Since none of the



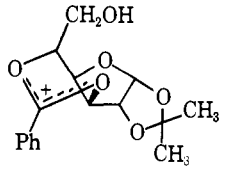
561



(235)

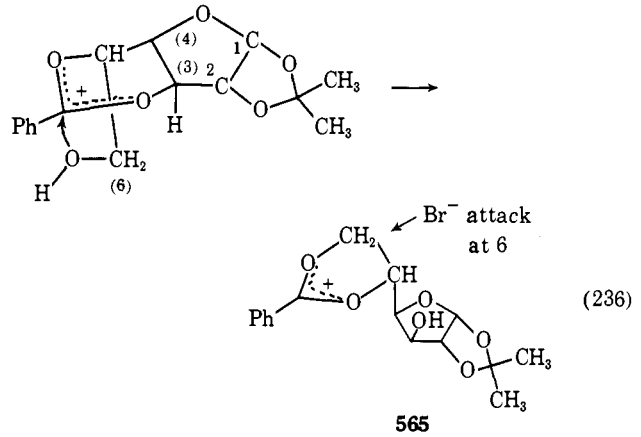
562 **563**

expected 3(5)-bromodeoxy-5(3)-benzoate derivatives, which would result from an attack on the initially formed benzoxonium ion **564**, were formed, it is clear products **562** and **563** are



564

formed by the rearrangement of **564**. Inspection of molecular models reveals that the C-6 hydroxyl group is in a favorable position for intramolecular attack (eq 236) to give rearranged



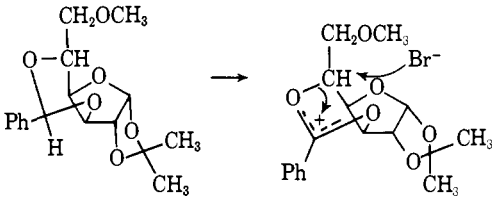
(236)

565

benzoxonium ion **565** which also contains a 1,3-dioxolan-2-ylium ion ring.

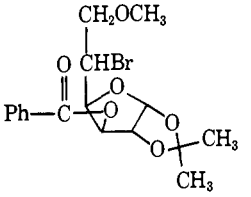
The carbons of this ring include secondary carbon 5 and primary carbon 6, and bromide ion selectively attacks the less hindered primary carbon 6 to give **563**. Compound **562** is produced by intramolecular nucleophilic attack by the 3-hydroxyl group at C-6 to open the dioxolenium ring.

The presence of a hydroxyl group at C-6 in **561** has a profound influence on the nature of the products formed in the NBS reaction. This can be further illustrated by examining the reaction of the 6-*O*-methyl derivative of **561** (**566**). The reaction of **566** produced a single product, identified as 3-*O*-benzoyl-5-bromo-5-deoxy-1,2-*O*-isopropylidene-6-*O*-methyl-L-idofuranose (**567**). In this case, a 1,3-dioxan-2-ylium ion, **566a**, analogous to ion **564** is formed. Since no 6-OH group is



566 **566a**

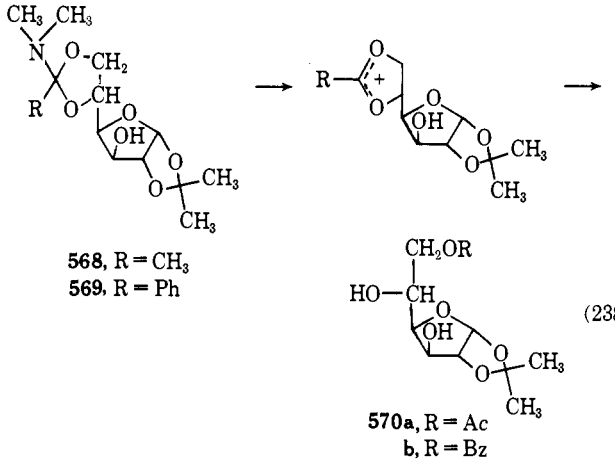
(237)



567

present, the intramolecular route of attack (which had previously converted **564** to ion **565**) cannot operate, and product **567** is formed by selective attack of Br^- at C-5.

1,3-Dioxolan-2-ylium ions have been invoked in the hydrolysis of the 5,6-acetals **568** and **569** of 1,2-*O*-isopropylidene-α-D-glucofuranose in aqueous HOAc at pH 4 to give 6-*O*-acetyl-1,2-*O*-isopropylidene-α-D-glucofuranose (**570a**) and its corresponding benzoate (**570b**). The overall reaction se-



568, R = CH_3
569, R = Ph

(238)

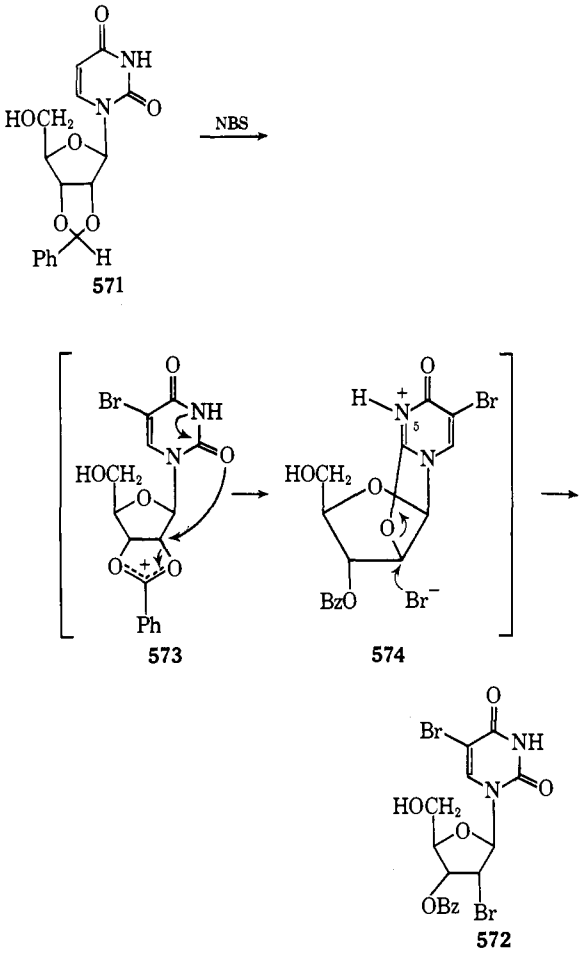
570a, R = Ac
b, R = Bz

quence represents an efficient, though indirect, procedure for preferential esterification of primary hydroxyl groups in acyclic diols.[419]

Successful application of the NBS ring opening of *O*-benzylidene acetals has recently been extended to afford nucleoside derivatives,[420] and it provides a preparative route to selectively substituted halo and deoxy nucleosides from which a variety of significant transformations can be effected. These

(419) S. Hanessian and E. Moralioglu, *Tetrahedron Lett.*, 813 (1971).
(420) M. M. Ponpipon and S. Hanessian, *Carbohyd. Res.*, 17, 248 (1971).

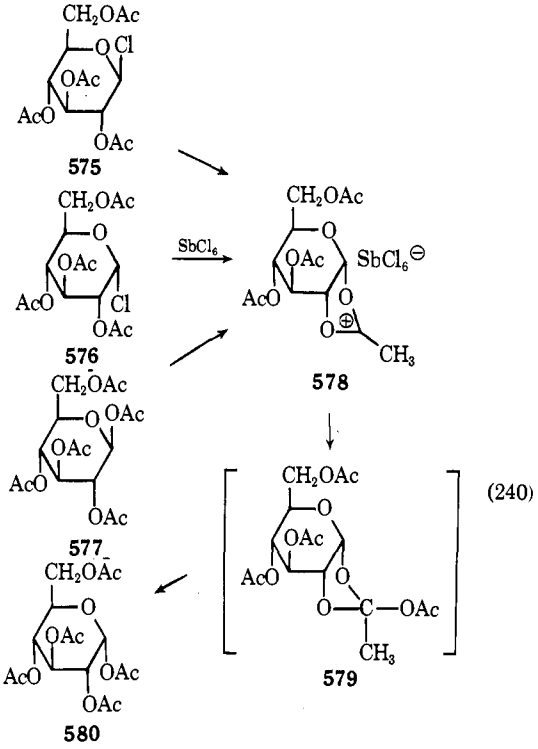
reactions proceed *via* 2-phenyldioxolan-2-ylium ions. For example, the reaction of 2′,3′-*O*-benzylideneuridine (**571**) with NBS in 1,1,2,2-tetrachloroethane and CCl_4 gave 56% of 3′-*O*-benzoyl-2′,5-dibromo-2′-deoxyuridine (**572**). This reaction proceeds through 2′-(2-phenyldioxolan-2-ylium) ion **573** followed by intramolecular participation to give the protonated 2,2′-anhydro intermediate **574**. **574** undergoes stereoselective attack by bromide ion to give the observed product.



(239)

Several stable 1,3-dioxolan-2-ylium salts of acetylated hexoses and pentoses have now been prepared and isolated.[421,422] Dioxolan-2-ylium ion **578** has been prepared by treating pyranosyl chlorides **575** and **576** or the β-pentaacetate **577** with $SbCl_5$ in methylene chloride.[421] Treatment of ion **578** with acetic anhydride gives penta-*O*-acetyl-α-D-glucopyranose (**580**). The 2-trichloroacetoxy analog of **577** (**581**) on treatment with $SbCl_5$ does not give a 1,3-dioxolan-2-ylium ion. Apparently the strong $-I$ effect of the three chlorine atoms reduces the oxygen's nucleophilicity to the point where the cyclic ion does not form. Instead the oxan-2-ylium ion **582** is formed and work-up yields chloride **583** stereoselectively. The hexachloroantimonate salts **585** and **588** have also been prepared, and on treatment with acetic anhydride both give the corresponding cis 1,2-acetates.

Two interesting rearrangements involving sequential 1,3-dioxolan-2-ylium ion interconversions have been elucidated



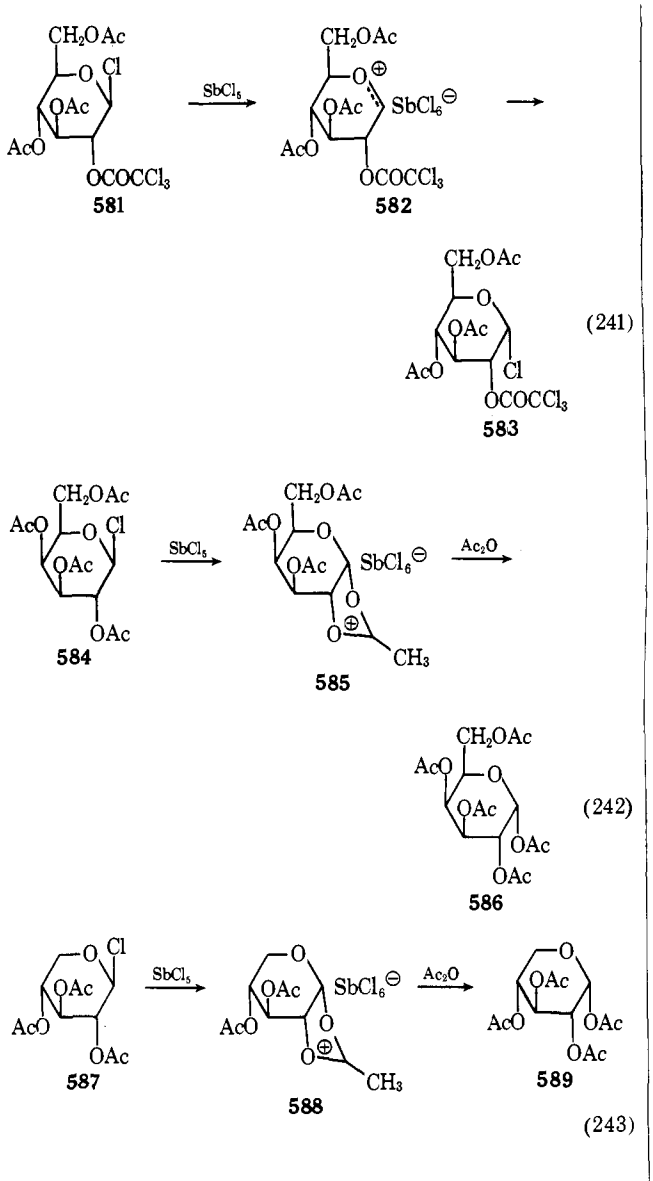
(240)

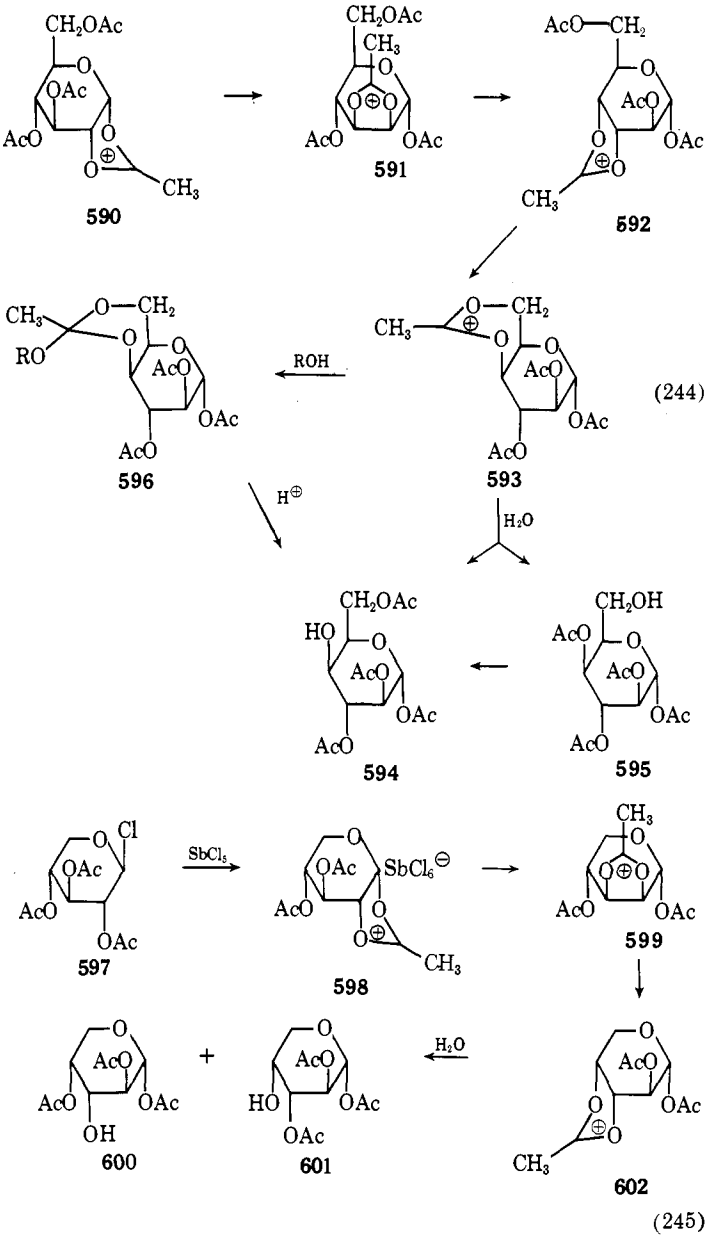
by Paulsen.[422] In the first, ion **590** is converted to 1,2,3,6-tetra-*O*-acetyl-α-D-idopyranose (**594**) and its 1,2,3,4-tetra-*O*-acetyl analog **595** in aqueous sodium acetate. This requires three separate 1,3-dioxolan-2-ylium cation intermediates, **591**, **592**, and **593**. Anhydrous alcohols give ortho ester **596** which opens very rapidly to **594** in dilute acids. Treating 2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl chloride (**597**) with $SbCl_5$ gives salt **598** which must rearrange through ion **599** to **602** because the proucts of aqueous sodium acetate hydrolysis are 1,2,3- and 1,2,4-tri-*O*-acetyl-α-D-arabinopyranose, **601** and **600**, respectively. These examples illustrate the unique chemistry, which is rich in synthetic potential, available on using the concepts of heteroatom-stabilized carbonium ions in carbohydrates.

B. OXAZOLINIUM IONS

The anchimeric assistance of acylamino groups in nucleophilic displacements on neighboring carbon atoms has also been used to synthetic advantage. A good example is provided by the chemistry of 2-deoxyaldoses.[423-425] One might predict that in 2-acylamino-2-deoxyaldose derivatives, the 2-acylamino group may facilitate the departure of a trans-oriented substituent at C-1 while a cis substituent would be uneffected. Since an acylamino group provides more anchimeric assistance than acyloxy groups, this route is especially attractive. It is now known that several 2-acetamido-1-*O*-acyl-2-deoxy-β-D-gluco- (and -galacto-) pyranose derivatives undergo both methanolysis and hydrolysis involving amido group participation with its resulting oxazolinium ion formation. For example, 2-acetamido-1-*O*-acetyl-3,4,6-tri-*O*-benzyl-2-deoxy-β-D-glucopyranose (**603**) (or its 1-*O*-benzoyl analog) are converted in methanol to the cis-fused oxazolinium ion

(421) H. Paulsen, W. P. Trautwein, F. G. Espinosa, and K. Heyns, *Tetrahedron Lett.*, 4131 (1966).
422) H. Paulsen, W. P. Trautwein, F. G. Espinosa, and K. Heyns, *ibid.*, 4137 (1966).
(423) N. Pravdić, T. D. Inch, and H. G. Fletcher, Jr., *J. Org. Chem.*, 32, 1815 (1967).
(424) T. D. Inch and H. G. Fletcher, *ibid.*, 31, 1810 (1966).
(425) T. D. Inch and H. G. Fletcher, *ibid.*, 31, 1815 (1966).





604 which undergoes nucleophilic ring opening to give methyl 2-acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-β-D-glycopyranoside (**605**). The same reactions have been performed in the β-D-galactopyranose series (**606** → **608**).[424,426]

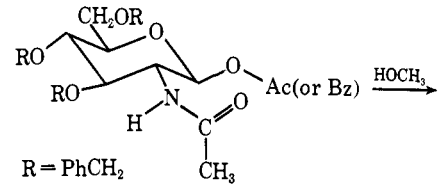
Fletcher and Salo demonstrated the scope of this 2-acylamido participation in their study of the reaction of 2-acylamido-2-deoxyaldoses with $ZnCl_2$–benzyl alcohol in butyl acetate at 125°.[427] Under these conditions, 2-acetamido-1,3,4,-6-tetra-*O*-acetyl-2-deoxy-β-D-glucopyranose (**609**) is rapidly converted to benzyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranoside (**611**) in high yield. The α anomer reacts far more slowly and gives **611** as well as the anomeric α-benzyl glycoside **612**.

In a similar fashion, the trans glycoside, methyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glycopyranoside (**613a**), is readily cleaved to a mixture of **611** and **612**, but its cis anomer **613b** is not attacked under these conditions. To compare the 2-acylamino group with a neighboring 2-*O*-acetyl group, methyl β-D-glucopyranoside tetracetate (**614**) was subjected to these same conditions and was found to be stable. This emphasizes the greater anchimeric driving force of the 2-acylamino group. The extension of 2-acylamido participation to selective cleavage of β-linked disaccharides was also discussed.[427]

In all these reactions neighboring group participation, with its concurrent oxazolinium ion formation, is indicated by (1) the much more rapid rate of hydrolysis (solvolyses) of the trans 1,2 derivatives, (2) the fact that the 2-acetamido-1-*O*-acyl (or -1-*O*-methyl) derivatives react in a stereospecific manner to yield trans 1,2-products, and (3) the fact that the oxazolinium ions have, in a few cases, been trapped and their corresponding 2-oxazolines isolated. These reactions have now been extended to transglycosylation reactions of methylated 2-acetamido-2-deoxy-β-D-glucopyranosides.[428]

Monosaccharides containing oxazoline rings also undergo reactions through oxazolinium ions.[429] Oxazolines that are derived from 2-acylamino-2-deoxyaldoses in which C-1 and C-2 of the sugar moiety are part of the oxazoline ring have now

(426) R. Harrison and H. G. Fletcher, Jr., *J. Org. Chem.*, 30, 2317 (1965).
(427) W. L. Salo and H. G. Fletcher, Jr., *ibid.*, 33, 3585 (1968).
(428) W. L. Salo and H. G. Fletcher, Jr., *ibid.*, 34, 3026 (1969).
(429) W. L. Salo and H. G. Fletcher, Jr., *ibid.*, 34, 3189 (1969).



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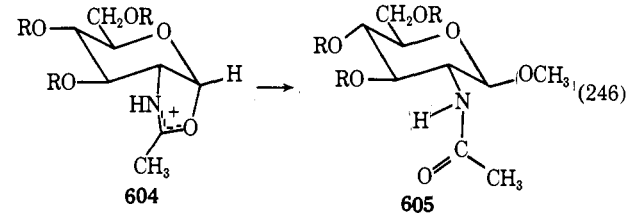
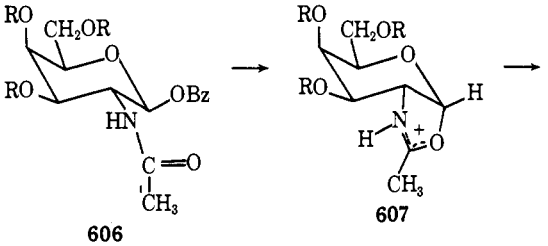
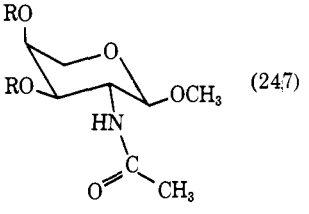


604 605

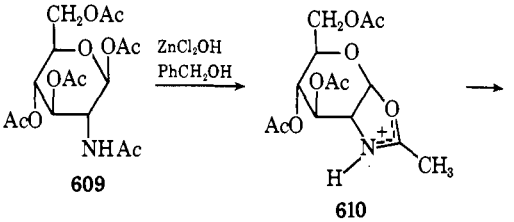


606 607

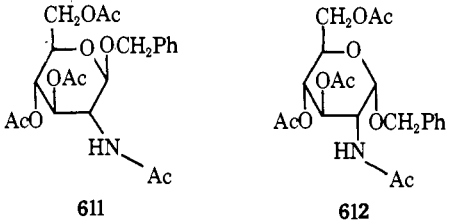


608

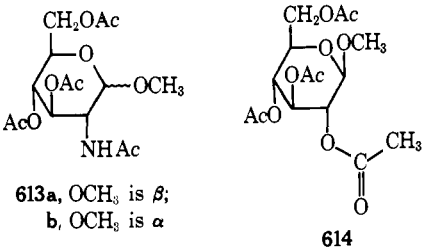
R = PhCO or H



609 610

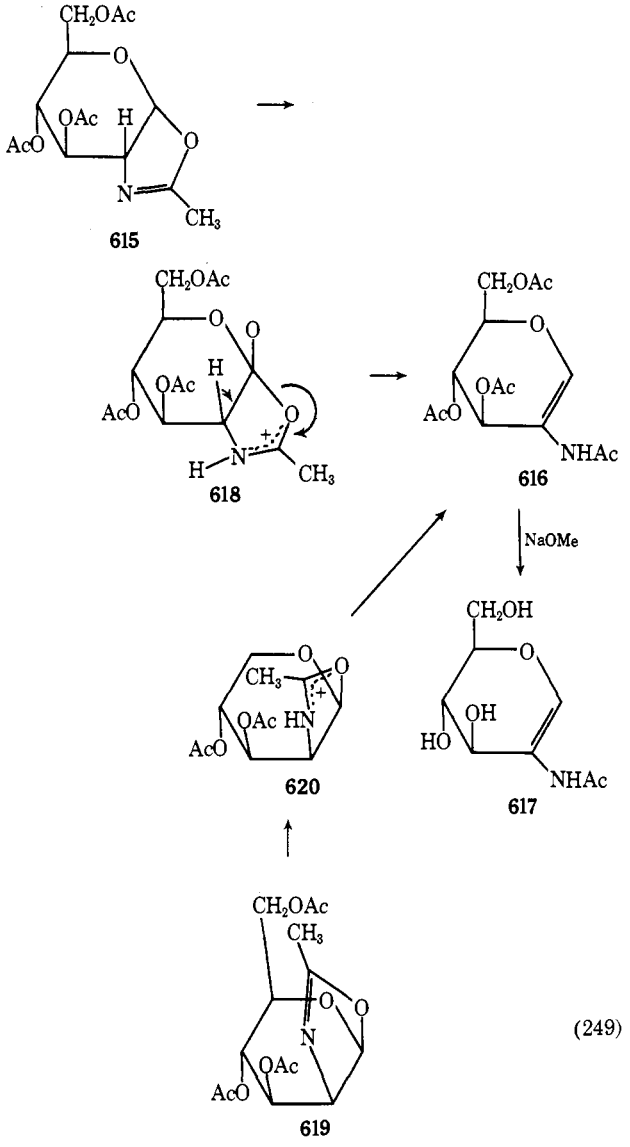


611 612



613a, OCH_3 is β; b, OCH_3 is α 614

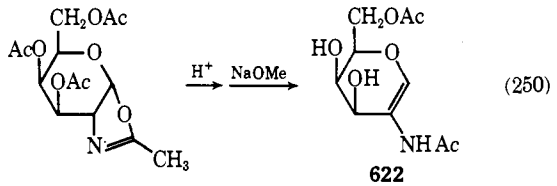
been prepared by a variety of methods.[429-434] Salo and Fletcher[429] showed that acetylated oxazoline **615** from 2-acetamido-2-deoxy-D-glucose readily isomerizes at 100° in tetramethylurea solution containing *p*-toluenesulfonic acid to give **616** which on sodium methoxide hydrolysis gave 2-acetamido-D-glucal (**617**). The acetylated oxazoline **619** derived from 2-acetamido-2-deoxy-D-mannose also gave **616**. The oxazolinium ions **618** and **620** were intermediates. The unique



615 618 616 620 617 619

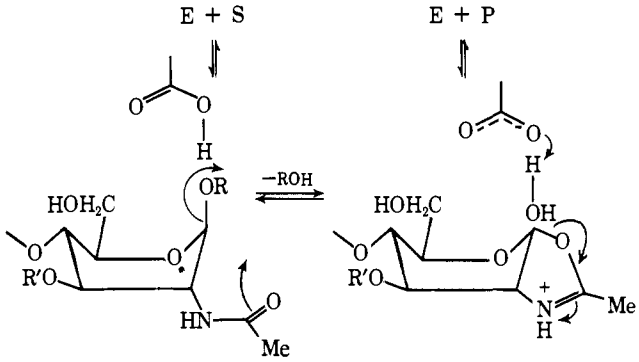
rearrangement of these two oxazolinium ions, in which a proton is lost from the 4 position of the heterocycle and the C-5 oxygen bond cleaves, probably arises from the fusion to the sugar system. The rearrangement appears to offer a practical synthesis of some general applicability. For example, galactopyranooxazoline (**621**) under these conditions gives 2-acetamido-D-galactal (**622**).

(430) F. Micheel and H. Kochling, *Chem. Ber.*, **90**, 1597 (1957); 93, 2372 (1960).
(431) S. Konstas, I. Photaki, and L. Zervas, *ibid.*, **92**, 1288 (1959).
(432) M. L. Wolfrom and M. W. Winkley, *J. Org. Chem.*, **31**, 3711 (1966).
(433) T. Osawa, *Chem. Pharm. Bull.*, **8**, 597 (1960).
(434) A. Y. Khorlin, M. L. Shul'man, S. E. Zurabyan, I. M. Privalova, and Y. L. Kopaevich, *Izv. Akad. Nauk. SSSR, Ser. Khim.*, 227 (1968).



621 622 (250)

The mechanism of the hydrolysis of aryl di-*N*-acetyl-β-chitobiosides catalyzed by lysozyme has been studied.[435-437] Based on the detailed X-ray diffraction study of lysozyme and its complex with tri-*N*-acetylchitotriose[438,439] and kinetic studies,[435,436] one possible mechanism involved neighboring amide group participation where the pyranose ring of the substrate was in the boat conformation as shown below. To



determine if the 2-acetamido group of substrates could provide this anchimeric assistance in the hydrolytic cleavage of the β-glycoside bond,[440-442] thus facilitating the enzymatic catalysis, Piszkiewicz and Bruice[443] studied the model substrates *o*- and *p*-nitrophenyl glucopyranosides and *o*- and *p*-nitrophenyl 2-acetamido-2-deoxyglucopyranosides. These compounds were considered to be legitimate models since chemically and structurally similar *p*-nitrophenyl 2-acetamido-2-deoxy-β-D-glucopyranosides have exhibited activity as substrates for lysozyme.[444,445] It was found that the hydrolysis of both *o*- and *p*-nitrophenyl 2-acetamido-2-deoxy-glucopyranosides and their corresponding glucosides is spontaneous where trans 1,2 stereochemistry is present. The α anomers (cis 1,2 stereochemistry) exhibit only specific acid- or base-catalyzed hydrolysis. The spontaneous rates for the β anomers were attributed to stereospecific participation by acetamido and hydroxyl groups, and 2-acetamido participation is about 10^3 times more effective than hydroxyl participation. Detailed kinetic studies indicated that 2-acetamido participation occurred in neutral hydrolyses (ArO as the leaving group), but it probably is not operative in the acid-catalyzed hydrolyses with ArOH leaving.

IX. Conclusions

A large number of 1,3-dioxolan-2-ylium and related cations have now been synthesized, isolated, and studied. An even larger number have been used knowingly or unknowingly as reaction intermediates in syntheses. From the studies of the ions, a wealth of qualitative, as well as some important quantitative data has been generated. From this base of information, significant quantitative studies, which promise to yield important new and useful knowledge, have emerged. An already significant number of applications of these ions in synthesis, particularly in the carbohydrate field, has appeared.

In spite of the large number of studies, several distinct areas of investigation and application remain for future workers. Insufficient thermochemical and other data, which allow one to quantitatively access how and to what extent each heteroatom stabilizes a given structural class of cations, are available. Comprehensive theoretical studies on heteronuclear-substituted carbonium ions are also lacking. For example, no extended Hückel, INDO, or MINDO calculations, let alone *ab initio* studies, have been reported. Thus, a ripe area of research exists in this area which one of us (C. U. P.) is now following.

As far as chemical studies go, there remains a wide variety of variables which have as yet not been explored. For example, no studies of halogenated derivatives have been reported. A more far-reaching study would involve the replacement of the cationic carbon with other atoms such as nitrogen, phosphorus, silicon, or perhaps sulfur. There remain some areas of a more practical nature which deserve study. These include systematic competitive experiments to yield the relative rates at which a series of heterocyclic cations react with a given series of nucleophiles. Definitive studies are needed to elucidate the reasons for the physiological activity of a given class of substituted heterocyclic ions or compounds. Also, there remains a great potential for the ions as polymer intermediates and in finished polymers.

Regardless of the above possibilities, probably the most important area awaiting exploitation is the use of stable ambident heterocyclic carbonium ions as alkylating agents. To date, nothing comparable to the general use of the trimethyloxonium ion as a methylating agent[7] has yet developed for heterocyclic carbonium ions, although Kochetkov has contributed significant pioneering work in the synthesis of glycosides and oligosaccharides from ortho ester derivatives (see ref 446). However, these ions are stable; they are easily synthesized from a variety of reagents; they can be derivatized in an almost infinite variety of ways; and their reactivity can be enormously varied by choice of heteroatoms and substituents. Thus, the chemist has at his disposal a varied class of alkylating agents of great potential that have not been specifically exploited. Furthermore, from studies of their ambident reactivity it is already possible to design the alkylating agent to react in a predictable way with a nucleophilic site in a substrate molecule. Since the salts of so many of these ions are exceptionally stable, they can be made and easily stored in a

(435) G. Lowe, G. Sheppard, M. L. Sinnott, and A. Williams, *Biochem J.*, **104**, 893 (1967).
(436) G. Lowe, *Proc. Roy. Soc., Ser. B.*, **167**, 431 (1967).
(437) G. Lowe and G. Sheppard, *Chem. Commun.*, 529 (1968).
(438) C. C. F. Blake, G. A. Mair, A. C. T. North, D. C. Phillips, and V. R. Sarma, *Proc. Roy. Soc., Ser. B*, **167**, 365, 378 (1967).
(439) D. C. Phillips, *Proc. Nat. Acad. Sci. U. S.*, **57**, 484 (1967).
(440) N. Sharon, T. Osawa, H. M. Flowers, and R. W. Jeanloz, *J. Biol. Chem.*, **241**, 223 (1966).
(441) J. A. Rupley and V. Gates, *Proc. Nat. Acad. Sci. U. S.*, **57**, 496 (1967).
(442) M. Wenzel, H. P. Lenk, and E. Schutte, *Z. Physiol. Chem.*, **327** 13 (1962).
(443) D. Piszkiewicz and T. C. Bruice, *J. Amer. Chem. Soc.*, **89**, 6237 (1967).
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(445) T. Osawa and Y. Nakazawa, *Biochim. Biophys. Acta*, **130**, 56 (1966).
(446) T. D. Inch, G. J. Lewis, and N. E. Williams, *Carbohyd. Res.*, **16**, 17 (1971).

dry environment or in sealed tubes. It is then logical to expect that in the not too distant future, many of these salts will become commercially available. We believe that heterocyclic carbonium ion salts will eventually be incorporated into the synthetic chemists' arsenal of convenient and specific reagents.

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