SOLVOLYTIC DISPLACEMENT REACTIONS AT SATURATED CARBON ATOMS

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CONTENTS

I. INTRODUCTION

Nucleophilic displacement reactions in organic chemistry have long been described by the symbols S_N1 and S_N2 introduced by Hughes, Ingold, and Patel (364). These symbols have been used indiscriminately both for experimental properties of reactions and for particular reaction mechanisms. Experimental observations are facts which, if correct, are invariant with time. Reaction mechanisms are derived concepts which can and frequently do change as new facts are observed. The use of the same symbols for both types of properties is a possible source of confusion. In this review the S_N1 and S_N2 labels have been used exclusively as symbols for particular reaction mechanisms (Sections IV,B and III,B, respectively).

The title, "Solvolytic Displacement Reactions," is meant to relate to an ill-defined set of reactions of alkyl and substituted alkyl halides, sulfonates, and certain other esters. Many but not all of the examples involve direct reaction with the solvent as a reagent. In this set of reactions are many which show first-order kinetics. The reactions have in common a consistent interpretation in terms of an electron-deficient carbon intermediate.

Closely related to this set of reactions is the well-known one-step or direct displacement reaction. Some discussion of the so-called S_N2 reaction is inevitable, and many of the methods and concepts later required for an understanding of solvolytic displacement reactions are introduced in this discussion.

The earliest ideas relating to displacement reactions have been reviewed elsewhere (348, 522) and will not be repeated here. The important concept of S_N1 and S_N2 mechanisms as developed by Hughes and Ingold and their collaborators has been presented many times (351, 352, 353, 354, 378) but is repeated in this review. A number of American authors have recently advanced more or less restricted interpretations which are based on new and vigorous researches and which differ in important respects from the concepts of Hughes and Ingold. Although these recent offerings have much in common, semantic differences have generally prevented a complete unification. The present review includes an attempted integration of these views which is based on a consistent set of postulates. The development of the postulates is presented in terms of the widely accepted transition state theory. Interpretations of structural effects are based on molecular orbital and valence-bond (resonance) concepts, which are frequently presented conjointly.

II. The Generalized Displacement Reaction

The generalized displacement reaction may be defined as a reaction in which a bond between two atoms is replaced by a bond between one of these atoms and a third:

$$X + R—Y \rightarrow Y + R—X$$
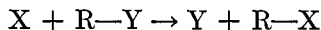
Although a great many chemical reactions fall under this generalization, the class of reactions to be considered here is that in which groups X and Y are Lewis bases (having a pair of unshared electrons) and in which the central atom is a saturated (tetrahedral) carbon. The solvolytic reactions reviewed in Section IV include those reactions in which the Lewis base, X, is a solvent molecule.

III. The Direct Displacement Reaction

A. KINETICS AND STEREOCHEMISTRY

Experimental observations resulting from the application of kinetic and stereochemical procedures have contributed substantially to an understanding of the course and mechanism of the displacement reaction as a function of structure. A great many displacement reactions of the non-solvolytic type have been found to follow second-order kinetics, in which the rate of reaction is proportional to the concentration of each of the reactants (461). When such second-order displacements are carried out on an asymmetric carbon atom, it is generally found for monofunctional and for some polyfunctional compounds that an inversion of configuration has accompanied each act of displacement. This now familiar phenomenon has been demonstrated for the reactions of alkyl halides with halide ion (372, 373, 590, 594a), hydroxide and ethoxide ion (359, 366), acetate ion (585), and dimethyl sulfide (570), as well as for the reactions of alkyl sulfonates with various salts and bases (344, 390, 432, 504, 505, 591). The phenomenon has been observed also in the reactions of quaternary ammonium salts with hydroxide (520) and with acetate (581) ions. Among the many examples of displacement accompanied by configurational inversion at the

reacting center in polyfunctional compounds are the reactions of α-halo acids and esters with halide ion (169, 495, 497, 698) and the ring-opening reactions of ethylene oxides (290).

B. MECHANISM

The second-order kinetics and configurational inversion were qualitatively accounted for in a satisfying manner by Lewis (427; cf. also 412), who suggested that a new bond is formed to the central carbon atom as the old bond is broken, with the action occurring simultaneously at opposite ends of the carbon tetrahedron. This concept was given quantum-mechanical expression by London (433), although formulated for the similar displacements of radicals.

1. The transition state theory

Lewis' concept gained its fullest expression with the development of the transition state theory (275). Consider the case in which the entering group is attacking at the rear of the bond to be broken, i.e., that case in which the three reacting atoms lie in a straight line. The progress of the reaction may be regarded as a function of the two bond distances, r_{XC} and r_{YC}. Since the reaction is occurring in a condensed phase in which the molecular collision frequency is exceedingly high, the system may, furthermore, be considered as being always in equilibrium; therefore, for each conceivable value of r_{XC} and r_{YC} a standard free energy can, in principle, be defined by allowing all other variables such as other bond distances and angles, the position and configuration of solvent molecules, etc., to adopt such values as will make this free energy a minimum. The resulting function is given diagrammatically in figure 1, in which the curved lines represent the loci of points having the same free energy. The increasing thicknesses of the lines represent approximately increasing values of the free energy.
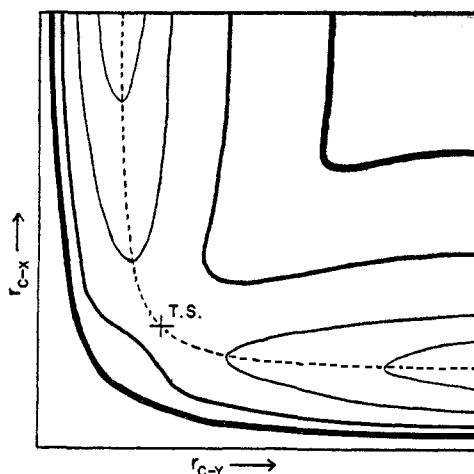
FIG. 1. Free energy diagram for a direct displacement reaction. Increase in the thickness of the contour line represents an increase in the free energy value.
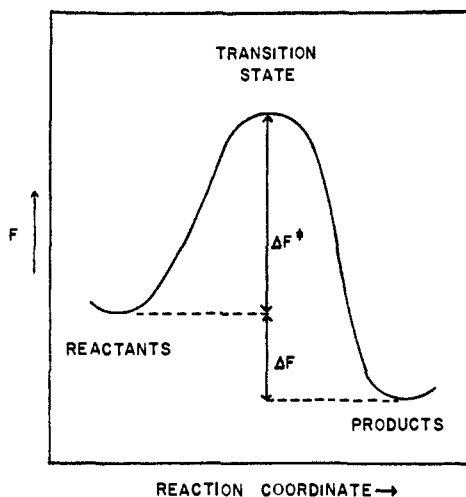
FIG. 2. Free energy profile of a direct displacement reaction along the "reaction coordinate."

The general representation is that of two valleys meeting at a saddle point.[1] The dotted line in figure 1 indicates the reaction path of lowest free energy. If the free energy is plotted as a function of a distance parameter along this path (the "reaction coordinate"), the curve in figure 2 is obtained.

In order to achieve reaction the system must overcome a free energy maximum, $\Delta F^{\ddagger}$, the free energy of activation (figure 2), which is associated with a particular configuration, the transition state (T.S. in figure 1). From the postulates of the absolute rate theory (275) the rate constant for the reaction in solution is given by equation 1 in which κ, the "transmission coefficient," is usually taken as unity for the reactions being considered, $\mathbf{k}$ is Boltzmann's constant, and h is Planck's constant.

$$\text{Rate constant} = \kappa \frac{\mathbf{k}T}{h} e^{-\Delta F^{\ddagger}/RT} \tag{1}$$

In terms of the transition state theory the mechanism of a particular displacement reaction would be completely specified by defining the complete free energy surface. However, since $\Delta F^{\ddagger}$ is the minimum consistent with reaction, all other reaction paths must require greater available work; inasmuch as the rate is an exponential function of the free energy, other paths frequently need not be considered. A reaction mechanism may then be defined in terms of the structure of the transition state configuration and its thermodynamic properties.

[1] The usual treatment (42, 100, 275, 522) is given in terms of potential energy, which is a less practical property in condensed media. The present treatment is probably no less rigorous and has greater utility.

2. Structure of the transition state

The structure of the transition state may be regarded as a resonance hybrid of structures I, II, and III (670). The hybrid structure may be written as IV, in which the dotted lines represent partial covalent bonds with the charge dis-

$$
X-\overset{|}{\underset{|}{C}}\diagup \quad \overset{-}{:}Y \quad \leftrightarrow \quad \overset{-}{X}: \quad \overset{|}{\underset{|}{C^+}}\diagup \quad \overset{-}{:}Y \quad \leftrightarrow \quad \overset{-}{X}: \quad \overset{|}{\underset{|}{C}}\diagup-Y
$$

$$
\text{I} \qquad\qquad\qquad \text{II} \qquad\qquad\qquad \text{III}
$$

$$
\overset{\delta(-)}{X}\cdots\cdots\overset{|}{\underset{|\ \delta(+)}{C}}\diagup\cdots\cdots\overset{\delta(-)}{Y}
$$

$$
\text{IV}
$$
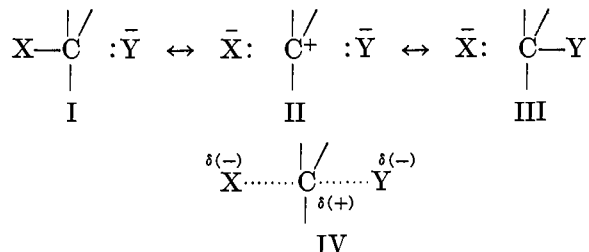
tribution as indicated. Alternatively, the transition state may be examined from a molecular orbital viewpoint and the structure written as in figure 3. To arrive at this structure, a rehybridization of the four original sp^3 orbitals of the central
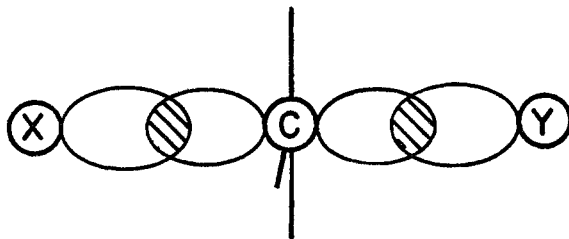
FIG. 3. An orbital representation of the transition state of a direct displacement reaction.

carbon must take place. The three bonds not undergoing reaction are coplanar and are made up of three sp^2 orbitals of the central carbon. The remaining p orbital, perpendicular to the plane of the other three orbitals, and an orbital of both the entering and the leaving group combine in the manner shown in figure 3 to form a set of molecular orbitals. In the usual LCAO approximation three molecular orbitals will be formed, two of which, a bonding and a nonbonding orbital, will contain the total of four electrons available.[2] Since atoms X and Y are generally effectively more electronegative than carbon, the central carbon atom will be partially electron-deficient.

The overall mechanism just outlined is often referred to as the Walden inversion (100, 640), the bimolecular or direct displacement mechanism, or, rather commonly, the S_N2 (bimolecular nucleophilic substitution) mechanism

[2] For an account of the molecular orbital method, see C. A. Coulson (164). Diagrams such as figure 3, which are used frequently throughout this review, are representations of the manner in which pertinent *atomic orbitals* combine to form molecular orbitals. They are not representations of the resulting molecular orbitals. Alternatively, the figures could be called atomic orbital diagrams.

(364). The mechanism is consistent with a variety of experimental observations; for example, the inertness towards displacement of bridgehead halides such as apocamphyl chloride (V) is readily explained, since the rear is protected and since configurational inversion is impossible (11, 46).

$$
\begin{array}{c}
CCl \\
H_2C \qquad CH_2 \\
H_3CCCH_3 \\
H_2C \qquad CH_2 \\
CH \\
V
\end{array}
$$
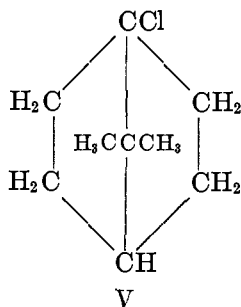
3. Possible existence of an intermediate

Calculations for the reaction of hydrogen atoms with hydrogen molecules have resulted in a potential energy curve as given in figure 4, in which the configuration H····H····H lies not at a maximum of energy but in a trough (246). The implied stabilization of the symmetrical H_3 structure may be nothing more than an artifact of the approximations made; nevertheless, one must consider the possibility that the configuration described as a transition state on page 577 is actually an intermediate (605, 670). In such a case there would be two transition states, one on each side of the free energy minimum representing the intermediate. If the two transition states correspond to different standard free energies, the higher will determine the rate of reaction. The structure of such a transition state could be represented by the molecular orbital diagram in figure 5. In this representation, the three non-reacting orbitals of the central carbon will be
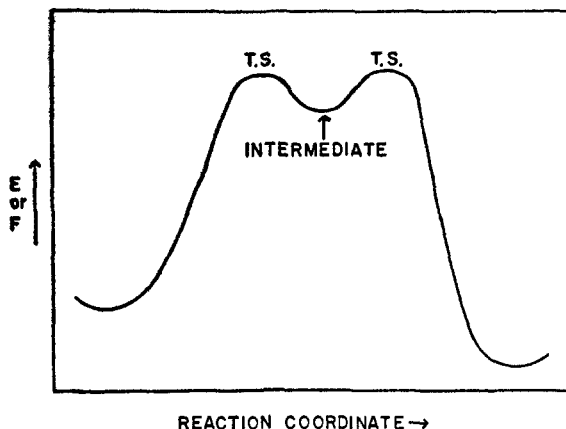
FIG. 4. Energy or free energy curve for a reaction with an unstable intermediate.
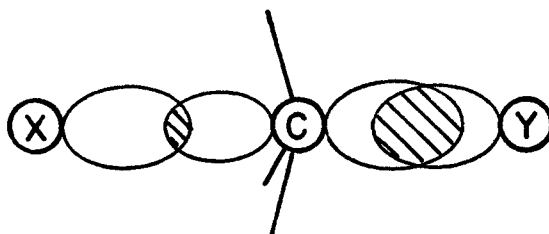
FIG. 5. Orbital representation of the transition state of a direct displacement reaction with an unstable intermediate.

hybrid orbitals intermediate between sp^3 and sp^2. The "reaction orbital" is intermediate between sp^3 and p. At least in some cases, a symmetrical structure such as that in figure 3 might reasonably be expected to possess greater stability than a structure like that in figure 5.

An intermediate in direct displacement reactions has never been detected. Indeed, if the dip in the free energy curve is no greater than of the order of RT ($\sim$600 cal./mole), the average translational energy of molecular systems in a fluid phase, the existence of a trough could not possibly be detected. If the difference in energy between the transition states and the intermediate is this small, however, the respective structures are undoubtedly very similar (303). In most cases figure 3 is a valid *approximation* to the structure of the transition state and most conclusions derived on the basis of this structure will be valid. Important exceptions will be noted.

C. RELATIVE RATES

1. Energy and entropy of activation

The application of the Arrhenius equation

$$k = Ae^{-E^{\ddagger}/RT} \tag{2}$$

to the rate constants obtained for a displacement reaction at different temperatures yields two parameters, A, from the temperature-independent factor, and $E^{\ddagger}$, the "activation energy," from the temperature-dependent factor. According to the absolute rate theory, the free energy of activation may be divided into an enthalpy of activation, $\Delta H^{\ddagger}$, and an entropy of activation, $\Delta S^{\ddagger}$, by equation 3 (275). The two sets of parameters for reactions in solution are related by

$$\Delta F^{\ddagger} = \Delta H^{\ddagger} - T\Delta S^{\ddagger} \tag{3}$$

equations 4 and 5 or 6, although the following distinction is important: A and $E^{\ddagger}$ are empirical constants which are taken to fit experimental data over a rather limited temperature range; $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ are theoretical quantities which are temperature-dependent in principle; hence, equations 4, 5, and 6 cannot be

strictly correct. In equation 6 the time unit is the second and the entropy unit is calories per degree.

$$\Delta H^{\ddagger} = E^{\ddagger} - RT \tag{4}$$

$$A = \frac{ekT}{h} e^{\Delta S^{\ddagger}/R} \tag{5}$$

$$\Delta S^{\ddagger} = 4.576 \log \frac{A}{T} - 49.203 \tag{6}$$

Although the enthalpy (or energy) and entropy of activation are related by equation 3 (and 4) and by the condition that $\Delta F^{\ddagger}$ be a minimum, to a first approximation, the activation energy is often associated with bonding forces and the entropy of activation with the freedom of atomic motions.

2. Concept of relative rates

When the reactivities of two systems are being compared, the question arises as to which experimentally determinable quantities are the most theoretically significant in the interpretation of reaction rate data. Because of the minimization condition, the free energy of activation may be regarded as most fundamental. The logarithm of a rate constant relative to that of a standard system (k_0) at the same temperature is directly proportional to the corresponding difference in free energies of activation. The minimization condition and equation 7 justify the use of relative rates rather than energies and entropies of activation when considering differences in reactivity.

$$\Delta F^{\ddagger} - \Delta F_0^{\ddagger} = 2.303RT \log k/k_0 \tag{7}$$

A practical justification for the utilization of relative rates is found in a consideration of experimental errors. Rate data accurate to 10 or 15 per cent are not uncommon and correspond to errors in $\Delta F^{\ddagger}$ of <0.1 kcal./mole. On the other hand, energies of activation are rarely better than ± 1 kcal./mole (514; for another reason, see reference 357).

One basis for criticism of the use of relative rates is inherent in the fact that they are temperature-dependent if the activation energies for the two reactions considered are not identical. While true, the criticism is frequently not important in practice; for example, if a relative rate is 1.0 at 25°C., a 1 kcal. difference in activation energies will make the relative rate 1.4 at 100°C.; for a difference of 3 kcal., the relative rate at 100°C. will change by only threefold. Where the activation energies differ by 5 or more kcal. the reaction rates *in practice* frequently differ by several orders of magnitude, so that even a large change with temperature would not affect any derived conclusions. Nevertheless, the temperature variation means that *small differences in relative rates with changes in structure should not be considered as usefully significant.* A possible exception might be made for cases in which a given structural change causes a small *but consistent* change in relative rate in a variety of systems.

In direct displacement reactions, structural variations may be considered

in the attacking base, in the carbon system undergoing reaction, in the leaving group, and in the solvent. Each of these components will be discussed in turn, with other variables held constant. The effect of one structural variation is not independent of the other variables; nevertheless, the magnitude of the dependency is often small compared to the effect of the structural variation being considered. It is shown in succeeding sections that the same structural variation in pairs of different systems often results in the same order of magnitude of the relative rate ratio.

3. *Structural effects in the attacking base*

The relative ability of a molecule or ion to act as a displacing base on carbon is called its *nucleophilic* ability. Important factors in determining *nucleophilicity* are the solvation energy of the base, the strength of its bond with a carbon $2p$ orbital, its steric effect, and, since a change in charge state is involved in the S_N2 reaction, the electronegativity and polarizability of the reacting atom. A measure of this nucleophilicity is obtained by examining the relative rates of displacement in a constant system in which only the attacking base is varied. Unfortunately, despite the very many kinetic investigations of displacement reactions, relatively few data are available for this purpose. Some of the useful experimental results are given in table 1. From these data a list of relative nucleophilic abilities has been compiled in table 2. The slowest reactant, nitrate ion, was chosen as the standard.

Swain and Scott (609) have defined a nucleophilic constant as the logarithm of the rate of reaction of a nucleophile with methyl bromide in water relative to the rate of the reaction of methyl bromide with water itself. The choice of the solvent as the standard may be a poor one, since the reaction of methyl bromide with water is not necessarily an S_N2 reaction. The nucleophilic constants of Swain and Scott are given in table 3. Between the groups which appear in both table 2 and table 3, the correlation is fair.

Among the cases in which attachment to a particular atom is compared, there is a rough correlation between basicity and nucleophilicity; for example, both properties decrease along the following series: $C_2H_5O^- > C_6H_5O^- > H_2O$; $C_4H_9S^- > C_6H_5S^- > $ thiourea; $(C_2H_5)_3N > C_6H_5N(CH_3)_2 > $ pyridine. Within a more limited range of structural variation there is rather good correlation between the two properties. This result indicates that electron access to the reacting center is important in facilitating reaction. Good linear correlations between nucleophilicity and basicity exist in displacements by *m*- and *p*-substituted phenols (99, 281, 289) and anilines (191, 245, 330, 403). In these cases the structural variation occurs sufficiently far from the reacting center that the only real change has been in the ability of the reacting base to supply electrons at the transition state.

When the attacking atom is changed all correlation vanishes. Sodium butyl-mercaptide is about as basic as sodium phenoxide but is 10^3 times as nucleophilic. Phenoxide ion and bromide ion are of comparable nucleophilicity but differ by $\sim10^{17}$ in basicity. There are a number of such examples. Even when the

TABLE 1

Relative displacement rates of attacking bases

$$RX + B \rightarrow RB + X$$

RX	Solvent	Temperature	Pyridine	$(CH_3)_3N$	$(C_2H_5)_3N$	Quinoline	Quinuclidine	Dimethylaniline	References
		°C.							
CH_3I	Benzene	25	1	1730	144	0.26			(654)
CH_3I	Nitrobenzene	25	1		96		5500	0.26	(115, 231, 404)
C_2H_5I	Nitrobenzene	25	1	.	11		2800		(114, 115)

RX	Solvent	Temperature	C_6H_5ONa	Sodium Eugenoxide	Dimethylaniline	C_2H_5ONa	Sodium Guaiacoxide	Sodium Salt of 1-Phenyl-3-thiourazole	I^-	Sodium α-Naphthoxide	References
		°C.									
CH_3I	Ethanol	25	1	3.9	0.29	5.0	2.1				(325, 444, 458, 508, 543, 556, 696)
C_2H_5I	Ethanol	25	1	4.3		2.1	1.9	157	5.8		(142, 325, 441, 444, 458, 556, 696)
C_3H_7I	Ethanol	40	1	1.9	0.037	1.8	1.2		8.9	1.9	(170, 325, 441, 444, 458, 508, 556, 696)

RX	Solvent	Temperature	C_2H_5ONa	Pyridine	Quinoline	Br^-	Cl^-	Dimethylaniline	References
		°C.							
C_3H_7Br	Ethanol	55	1	0.0091		0.26			(148, 206, 456)
C_4H_9Br	90% Aqueous acetone	40				1	0.14		(418, 582)
Allyl bromide	Ethanol	40	1	0.052	0.0076	0.54		0.13	(159, 471, 624)

RX	Solvent	Temperature	C_6H_5ONa	C_6H_5SNa	C_4H_9SNa	C_2H_5ONa	$(CH_3)_3N$	CH_3COO^-	NO_3^-	References
		°C.								
C_4H_9Br	Ethanol	25	1	1260	1830					(515)
			Sodium Salt of 1-Phenyl-3-thiourazole (X)		$S_2O_3^{--}$					
C_2H_5Br	50% Aqueous ethanol	25	1		0.49					(2, 186)
C_3H_7Br	50% Aqueous ethanol	25	1		0.37					(2, 186)
C_2H_5I	Ethanol	50				1	0.028	0.02	0.001	(228a)

TABLE 2

Average relative displacement rates of attacking bases

Nucleophile	Relative Rate	Log Relative Rate	Nucleophile	Relative Rate	Log Relative Rate
$C_4H_9S^-$	680,000	5.8	Br^-	500	2.7
$C_6H_5S^-$	470,000	5.7	Phenoxide ion	400	2.6
3-Phenyl-1-thiourazolate ion (X)	75,000	4.9	Cl^-	80	1.9
I^-	3,700	3.6	$N(CH_3)_3$[b]	30	1.5
$S_2O_3^{--}$[a]	3,200	3.5	CH_3COO^-	20	1.3
Eugenoxide ion	1,200	3.1	Dimethylaniline[b]	20	1.3
Ethoxide ion	1,000	3.0	Pyridine[b]	20	1.3
α-Naphthoxide ion	1,000	3.0	Quinoline[b]	8	0.9
Guaiacoxide ion	600	2.8	NO_3^-	1	0.0

[a] This value holds for 50 per cent aqueous ethanol.

[b] Because these are neutral molecules being compared with ions, the solvent will greatly change the relative rates (see page 603). Values given are for ethanol.

TABLE 3

Nucleophilic constants of Swain and Scott

Nucleophile	Nucleophilic Constants of Swain and Scott (322, 609)	Nucleophile	Nucleophilic Constants of Swain and Scott (322, 609)
$S_2O_3^{--}$	6.4	Thiourea	4.1
HS^-	5.1	N_3^-	4.0
CN^-	5.1	Br^-	3.9
I^-	5.0	Pyridine	3.6
SCN^-	4.8	Cl^-	3.0
Aniline	4.5	CH_3COO^-	2.7
OH^-	4.2	Water	0.0

atoms compared are rather similar there is no correlation. Bromide ion is less basic but more nucleophilic than chloride ion. The explanation may be that nucleophilicity is measured by the free energy difference between a species when free and when bonded to a carbon $2p$ orbital; basicity is measured by the free energy difference between a species when free and when bonded to a hydrogen $1s$ orbital. With the larger atoms the extent of orbital overlap may well be more important when bonded with the larger, more diffuse p orbital.

4. Structural effects in the substrate

A number of published rate studies have had as their aim the elucidation of the effect of structure on rate. Much of the data is of limited usefulness because the amount of concurrent elimination which may have occurred together with displacement was not evaluated. The available data were scrutinized in an effort to obtain at least a qualitative idea of the effect on the direct displacement rate of structural variation in the central carbon system. The rates of a number of simple systems relative to the corresponding ethyl system as a standard are listed in table 4. Those data were omitted in which the complication of concurrent elimination seemed likely. An effort was made to determine the relative rates in the neighborhood of 50°C.

A change in the reaction system can cause a change in the relative rate of a

TABLE 4

Relative reactivities of simple alkyl halides

Reaction	Solvent	Temperature	CH₃	C₂H₅	n-C₃H₇	C₄H₉	i-C₃H₇	i-C₄H₉	Allyl	Benzyl	Neopentyl	References
		°C.										
RCl + I⁻	Acetone	60	93	1.0	0.37	0.52	0.0076		33	93		(157)
RBr + I⁻ [a]	Acetone	25	145	1.0	0.82		0.0078	0.036			0.000012	(260)
RBr + I⁻	Acetone	25	30	1.0					100		0.000015	(219, 364, 463)
RI + I⁻ [a]	Acetone	25		1.0			0.0088				0.000018	(197)
RI + I⁻	Ethanol	50		1.0	0.66	0.38	0.037	0.051	33	78		(441, 448, 554, 587)
RBr + Br⁻ [a]	Acetone	25	76	1.0	0.65		0.011	0.033			0.000015	(196)
RBr + Br⁻	Aqueous acetone (90%)	50			(1)[b]	(1.1)[b]	(0.066)[b]	(0.076)[b]				(230, 418)
RI + Br⁻ [a]	Acetone	25	18	1.0	0.71		0.025	0.021				(261)
RBr + Cl⁻ [a]	Acetone	25	61	1.0	0.65		0.013	0.15			0.000026	(358)
RI + Cl⁻ [a]	Acetone	25	11.1	1.0	0.58		0.032	0.038			0.000014	(358a)
RBr + C₂H₅O⁻	Ethanol	55	23	1.0	0.32	0.23		0.034	11		0.0000048	(159, 206, 218, 362)
RBr + S₂O₃⁻⁻	Aqueous ethanol (50%)	50	67	1.0	0.48		0.039	0.025				(186, 226)
RI + pyridine	Benzene	50	12.9	1.0	0.33		0.045					(654)
RI + (CH₃)₃N	Benzene	50	67	1.0	0.24							(654)
RI + (C₂H₅)₃N	Nitrobenzene	50	129	1.0			0.011					(115, 405)
RI + quinuclidine	Nitrobenzene	50	30	1.0			0.022					(115)
RI + pyridine	Nitrobenzene	50	14.2	1.0			0.061					(114)
RI + C₅H₅N(CH₃)₂	Ethanol	40	15.3	1.0	0.32				115			(508)
RBr + pyridine	Ethanol	55.6			(1)[b]				(70)[b]	(286)[b]		(148)
RBr + pyridine	Methanol	35		1.0	0.44				36	135		(501)
RBr + thiourea	Methanol	35		1.0	0.65				77	198		(501)

[a] These values were published too late for inclusion in table 5. The averages in table 5, however, are not significantly altered by inclusion of these new results.

[b] Rate relative to *n*-propyl.

TABLE 5

*Average relative rates of alkyl systems**

Radical	Relative Rate	Log Relative Rate	Radical	Relative Rate	Log Relative Rate
Methyl	30	1.5	Isobutyl	0.03	−1.5
Ethyl	1.0	0.0	Allyl	40	1.6
Propyl	0.4	−0.4	Benzyl	120	2.1
Butyl	0.4	−0.4	Neopentyl	10^{-5}	−5.0
Isopropyl	0.025	−1.6			

* The data in this table were derived from table 4.

given substrate by as much as tenfold. Nevertheless, the order of reactivity seems to be fairly constant for different substrates; for example, methyl compounds are *always* more reactive than the corresponding ethyl derivatives. As a rough semiquantitative measure of relative reactivity, the geometric averages of the relative rates for each substrate are listed in table 5. Rather than a simple relative rate ratio, equation 8 has recently been proposed to correlate reactivity (331a, 615a).

$$\log \frac{k}{k_0} = r\alpha \tag{8}$$

In this equation α is a structure constant dependent on the nature of the alkyl group and r is a reaction constant dependent on the particular reaction system. The use of simple relative rates as adopted in this review (because of the scarcity of pertinent data) is equivalent to the case of equation 8 with $r = 1$ for all S_N2 reactions.

(a) Effect of conjugation

The effect of conjugation of the reacting center with a double bond or with a benzene ring is pronounced; the rate enhancement is rather large. This enhancement may be attributed to stabilization of the transition state by π-bond overlap
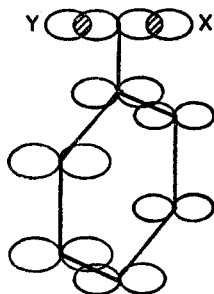
FIG. 6   FIG. 7

FIG. 6. Orbital representation of the transition state of a direct displacement reaction with a benzyl halide.
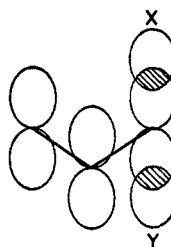
FIG. 7. Orbital representation of the transition state of a direct displacement reaction on an allyl halide.

as in figures 6 and 7 or, equivalently, as in structures VI and VII. (The dotted lines in VI and VII refer to p_σ or p_π bonds.) In valence-bond terminology the effect is ascribed to lowering of the energy of the transition-state resonance hybrid by the introduction of structures of the type of VIII and IX.
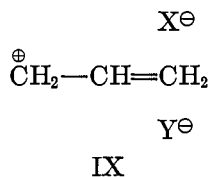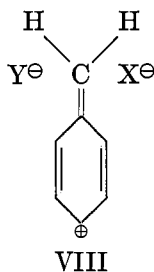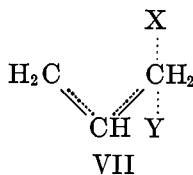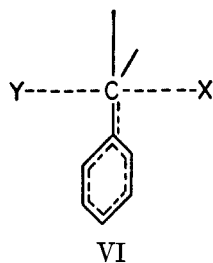
(b) Alkyl series: α-methyl substitution

i. Relative rates

Increasing alkyl substitution on the reacting carbon results in a substantial decrease in displacement rate; e.g., relative rates for direct displacement for the series methyl, ethyl, isopropyl are approximately 1200:40:1 (table 5). A controversy has developed over the explanation of this result. On the one hand, because of the electron-repelling inductive effect of methyl groups, the rate sequence " ... is attributable to the diminished positive charge on the carbon atom which attracts the approaching base." (336) This explanation has its basis in an assumed *polar effect* (198, 289, 378). On the other hand, the explanation has been offered that the greater effective bulk of increasing alkyl substitution sterically opposes the close approach of a nucleophilic reagent. This explanation is based on *steric hindrance* (115, 233, 235, 380, 449, 521). The suggestion has also been made that the two effects are of comparable importance (198, 222).

The argument based on transition state theory is the following: the structure of the transition state in direct displacement reactions was represented as possessing a partially electron-deficient central carbon atom (page 577). In the ground state, the carbon atom will have a partial positive charge due to ionic character in the C—X bond. If the amount of positive charge on the central carbon atom in the transition state is greater than in the ground state, substituents which can stabilize the positive charge by resonance or by an electron-donating inductive effect will cause a rate acceleration. Conversely, if the

amount of positive charge on the central carbon is less in the transition state, inductively electron-donating groups will cause a decrease in the rate. In principle, the rate changes wrought by different substituents should allow an inference concerning the changes in charge density at the reacting carbon. In practice, unfortunately, the experimental results frequently lead to opposing conclusions. Furthermore, much of the older data is invalid because the reactions measured were eliminations rather than substitutions (332).

In succeeding sections the experimental results obtained for different systems will be discussed in more detail. For the present, however, it would seem for the simple alkyl systems that the experimental facts are better in accord with the hypothesis that the central carbon atom has a slightly greater positive charge at the transition state than in the ground state. This direction agrees with an analogy to solvolytic reactions (pages 638, 678) but is opposite that assumed by Hughes and Ingold and coworkers (198, 222, 378), by Green and Kenyon (289), and by Hinshelwood, Laidler, and Timm (336) (*cf.* pages 595, 673). If this hypothesis is correct, the observed decreases in rates for the series methyl, ethyl, isopropyl must be due to an overriding steric hindrance.

ii. Tertiary systems

It has long been known that tertiary alkyl halides are rather unreactive towards some displacement reactions (695), but until recently it has not been possible to estimate their relative rate in direct displacement reactions. The rate measurements of Acree and Shadinger (2) did not give good second-order rate constants for the reaction of *tert*-butyl iodide with the sodium salt of 1-phenyl-3-thiourazole (X) in 50 per cent aqueous alcohol; this reaction was doubtless complicated by concurrent solvolysis. Conant and Hussey (157) found that *tert*-butyl chloride is more reactive than isopropyl chloride towards potassium iodide in acetone, but this result is contradicted by more recent work (440, 521).

$$\begin{array}{c} C_6H_5N\text{------}N \\ | \quad\quad \| \\ O\text{==}C \quad\quad CS^{\ominus} \quad Na^{\oplus} \\ \diagdown \quad \diagup \\ NH \\ X \end{array}$$
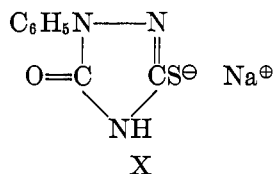
The small amount of water which Conant and Hussey's acetone contained (491) may have caused simultaneous solvolysis of the tertiary halide. The halide-exchange rate constants reported for tertiary halides by McKay (441) and by LeRoux, Lu, Sugden, and Thomsen (417) were determined with only one or two kinetic points each and there is no assurance that these reactions were of second order. Indeed, the rate of exchange of *tert*-butyl iodide with iodide ion in liquid sulfur dioxide has been reported to be independent of the iodide-ion concentration (630).

Recent work, however, has given quantitative measures of the reactivity of *tert*-butyl halides in direct displacement reactions. LeRoux and Swart (419) have found that the kinetics of the reaction of bromide ion with *tert*-butyl

bromide in acetone solution has both a first-order and a second-order component. The second-order rate constant has 0.14 the value for isopropyl bromide at 40°C. (419).

De la Mare, Hughes, Ingold, and Mackie (196, 197, 358) also found evidence for mixed first-order and second-order kinetics in the reactions of *tert*-butyl halides with halide ion in acetone. The rate of the second-order displacement was found to be 0.07–0.34 times as rapid as the corresponding reactions of isopropyl halides. Consequently, the rate sequence in direct displacement reactions for the simple alkyl systems is: methyl > ethyl > isopropyl > *tert*-butyl. In marked contrast to the relative unreactivity of tertiary halides in direct displacement reactions is their high reactivity in solvolytic reactions (Part IV).

The reactions of tertiary halides are frequently complicated by predominant elimination. Olefin is the only product of the reaction of tertiary halides with tertiary amines (453) and with alcoholic potassium acetate (455), although other halides yield predominantly the corresponding quaternary ammonium salts and alkyl acetates, respectively. In cases in which concurrent solvolysis is possible, further striking differences are sometimes encountered; for example, primary and secondary alkyl halides on reaction with alcoholic sodium phenoxide yield the corresponding alkyl phenyl ether, although tertiary halides yield the corresponding *p*-alkylphenol (426, 555).

iii. Heteroatom substituents not on the reacting center

Halogen atoms at a distance from the reacting center would be expected to influence the reactivity of a system by their electron-attracting inductive effect. The most unambiguous experimental results are probably those of Hine and Brader (332), who measured the rates of reaction of β-haloethyl bromides with thiophenoxide ion in methanol and demonstrated that the reaction observed was that of displacement. Compared to the sterically similar compound *n*-propyl bromide, the displacement rates were *decreased* by a factor of five (table 6). The inference from this result is that the positive charge on the central carbon atom is greater in the transition state than in the ground state for these compounds.

The rest of the experimental data pertain to the reactions with potassium iodide in acetone. In this reaction β-oxygen substituents cause a 2- to 8-fold decrease in rate (table 6). However, in the γ-position such substituents generally cause an increase in the rate. This increase is still substantial when the substituent is in the δ-position.

There are several apparent inconsistencies with the hypothesis that the rate effects of heteroatom substituents in this reaction are due wholly to inductive effects transmitted to the reacting center. The reactivities of β-arylethyl chlorides give an acceptable Hammett correlation with $\rho = 0.590 \pm 0.118$ (381); i.e., electron-attracting groups lead to higher rates. The effect of substituents is not diminished when the phenyl group is one atom farther removed from the reacting center, as in aryl β-chloroethyl sulfides ($\rho = 0.626 \pm 0.097$) (381). If the rate variations were due to inductive effects, the value of ρ would be expected

TABLE 6

Displacement reaction rate effects of heteroatom substituents

Compound	$C_6H_5S^-$, CH_3OH, 20°C. (332)	Potassium Iodide, Acetone				
		25°C. (632)	50°C. (396, 397, 158)	75°C. (18a) $ArCH_2CH_2Cl$	55°C. (18) $ArSCH_2CH_2Cl$	75°C. (18) $ArSO_2CH_2CH_2Cl$
C_2H_5Br	1.47					
C_3H_7Br	0.96					
C_4H_9Br	1.00	1.00				
$FCH_2CH_2Br^{(a)}$	0.185					
$ClCH_2CH_2Br^{(a)}$	0.212					
$BrCH_2CH_2Br^{(b)}$	0.187					
$CH_3OCH_2CH_2Br$		0.13				
$C_4H_9OCH_2CH_2Br$		0.11				
C_4H_9Cl			1.00			
$CH_3SCH_2CH_2Cl$			1.5			
$CH_3SCH_2CH_2CH_2Cl$			2.5			
$C_6H_5SCH_2CH_2Cl$			0.56			
$C_6H_5SCH_2CH_2CH_2Cl$			2.7			
$C_6H_5OCH_2CH_2Cl$			0.30			
$C_6H_5OCH_2CH_2CH_2Cl$			1.7			
$C_6H_5OCH_2CH_2CH_2CH_2Cl$			1.4			
α-$C_{10}H_7OCH_2CH_2Cl$			0.33			
α-$C_{10}H_7OCH_2CH_2CH_2Cl$			2.0			
β-$C_{10}H_7OCH_2CH_2Cl$			0.33			
β-$C_{10}H_7OCH_2CH_2CH_2Cl$			2.0			
$C_6H_5COOCH_2CH_2Cl$			0.45			
$C_6H_5COOCH_2CH_2CH_2Cl$			1.57			
$C_6H_5CH_2CH_2Cl$			1.12			
$C_6H_5CH_2CH_2CH_2Cl$			1.72			
Ar =						
HC_6H_4				1.00	1.00	1.00
p-$CH_3OC_6H_4$				1.21	$0.81^{(c)}$	
p-$CH_3C_6H_4$					0.85	
p-FC_6H_4				1.79		
p-ClC_6H_4				1.89	2.17	1.73
p-BrC_6H_4				1.88	1.65	1.54
p-IC_6H_4				1.62	1.28	
p-$NO_2C_6H_4$				4.75	3.28	3.20
ρ (381)				0.590 ± 0.118	0.626 ± 0.097	0.642 ± 0.056

(a) Under the reaction conditions only Br is displaced.

(b) Rate constant was divided by two.

(c) At 75°C.

to be considerably smaller in the latter case. When the sulfur atom is converted to a sulfone group, as in aryl β-chloroethyl sulfones, the powerful inductive effect and dipolar nature of the sulfone group would be expected to be of overriding importance; yet the effect of substituents is about the same as in the former cases ($\rho = 0.642 \pm 0.056$) (381).

The fact that the products and course of almost all of these reactions have not been determined would alone suffice to render these data of uncertain significance. In addition, it is known that potassium iodide is incompletely dissociated in acetone solutions (page 605). The possibility that specific interactions between highly polar or polarizable organic solutes and potassium iodide ion-pairs can influence the kinetics of this reaction does not seem an unlikely one.

For these reasons, arguments based on the reaction of organic halides with potassium iodide in acetone must be made with circumspection. Nevertheless, to the extent that the relative rate changes in the potassium iodide reaction are valid and general, the argument based on Hine and Brader's results (which seem experimentally sounder) is weakened. The argument is also weakened to the extent that any dipole–dipole interactions between the heteroatom substituent and the reactive center are important.

iv. Substituted benzyl systems

The rate constant of bimolecular displacement by ethoxide ion in ethanol at 25°C. is 184×10^{-5} l./mole-sec. for benzyl bromide (87) and 6.2×10^{-5} l./mole-sec. for α-phenylethyl bromide (619). The thirtyfold rate difference is comparable to the difference between ethyl and isopropyl halides. It is interesting to contrast this rather large rate-retarding effect of a methyl group attached directly to the reacting center with a p-methyl substituent in the benzene ring. The relative rates given in table 7 show that such substitution generally *increases* the rate of displacement. The effect is exceedingly small and, moreover, there is one exception. The exceptional case, however, could conceivably involve reaction with the pyridine ring instead of an S_N2 displacement. Since the results of Bevan, Hughes, and Ingold (87) were presented in preliminary form with no experimental details, it is not possible to tell if they were indeed measuring an S_N2 reaction.

Although the rate enhancement shown for p-methyl substitution in all of the other cases is small, the effect is reproduced consistently and may be regarded as real. The effect is in the direction expected for extension of a π-bond system with an alkyl group as symbolized in structure XI. The dotted line to the R group in this structure represents the additional bonding of hyperconjugation consequent from the overlap of the π-bond system with the hybrid orbitals which compose the C—H and C—C bonds of the alkyl group (165, 184, 466; however, *cf.* 252). Such hyperconjugation can also be represented by the inclusion of structures such as XII in the resonance hybrid. The fact that a p-methyl group has only a slight rate-enhancing effect may be taken as an indication that the importance

TABLE 7

Relative direct displacement rates of some alkyl-substituted benzyl halides

Reactants	Solvent	Temperature	H	p-CH$_3$	m-CH$_3$	p-tert-C$_4$H$_9$	References
		°C.					
C$_6$H$_5$CH$_2$Cl + I$^-$	Acetone	20	1	1.17			(236)
C$_6$H$_5$CH$_2$Br + I$^-$	Acetone	0.0	1	1.46		1.36	(87)
C$_6$H$_5$CH$_2$Br + C$_2$H$_5$O$^-$	Ethanol	25	1	1.48		1.38	(87)
C$_6$H$_5$CH$_2$Br + t-C$_4$H$_9$O$^-$	t-C$_4$H$_9$OH	60	1	1.34		1.19	(87)
C$_6$H$_5$CH$_2$Cl + C$_2$H$_5$O$^-$	Ethanol	25	1	1.57		1.46	(87)
C$_6$H$_5$CH$_2$Cl + C$_2$H$_5$O$^-$	Ethanol	30	1	1.58	1.12		(263)
C$_6$H$_5$CH$_2$Br + pyridine	Acetone	20	1	1.66	1.17	1.35	(24, 26)
C$_6$H$_5$CH$_2$N$\overset{\oplus}{\diagup}\diagdown$ + C$_2$H$_5$O$^-$	Ethanol	20	1	0.50		0.69	(87)
C$_6$H$_5$CH$_2$Cl + OH$^-$	Aqueous acetone (50%)	30	1	1.35	0.91		(490)

TABLE 8
Reactivities of substituted benzyl halides

Substituent	Relative Rates (R = benzyl)									
	RCl, KI, acetone, 20°C. (75, 236)	$(CH_3)_3N$, RCl, benzene, 100°C. (605)	Aniline, RBr, 90% aqueous ethanol, 30.5°C. (22, 22a)	Pyridine, RBr, acetone, 20°C. (24)	Pyridine, RBr, 90% aqueous ethanol, 30.5°C. (22, 22a, 24a)	RCl, KOH, 50% aqueous acetone, 30°C. (490)	RF, C_2H_5ONa, 95% aqueous ethanol, 76°C. (457)	RBr, Br^-, $(CH_2OCOCH_3)_2$, 25°C. (595)	RCl, $S_2O_3^{--}$, 62% aqueous ethanol, 35°C. (580)	RCl, C_2H_5ONa, ethanol, 30°C. (263, 263a)
H	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
m-F	1.39			0.78			1.02			
m-Cl	1.64			0.88			1.22			1.38
m-Br	1.87	0.80		0.88		0.58	1.26			1.42
m-I	1.77			0.93			1.36			
p-F	1.44			1.21			1.37			
p-Cl	2.12		1.26	1.04	0.73		1.54			1.95
p-Br	2.36	1.16	1.17	1.06	0.67	1.08	1.51			
p-I	2.24		1.29	1.21	0.75		1.69			
m-CH₃				1.17		0.91	0.95			1.11
p-CH₃	1.17	1.42	2.48	1.65	2.16	1.35	1.07			1.58
p-CH₃O					~160			6.2		
m-NO₂	3.66		0.87	0.81	0.31		3.39		1.17	
p-NO₂	6.19	0.98	0.63	0.92	0.35			11.2	1.84	
m-CN						1.13				
p-CN						1.47		10.0		

of structures such as XII is small or that the amount of positive charge to be distributed is small (compare the rate acceleration provided by a p-methyl substituent in cases in which the amount of positive charge to be distributed is relatively large (table 34)).

$$\begin{array}{cc} \text{XI} & \text{XII} \end{array}$$
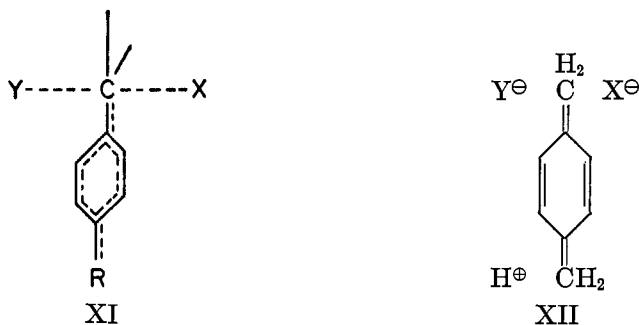
The situation is not as straightforward with electron-attracting substituents. Such groups increase the energy of a carbonium ion (*cf.* table 20); yet they frequently increase the rate of direct displacement (table 8). Swain and Langsdorf (605) have shown how this phenomenon is clearly demonstrated by Hammett's σ–ρ correlation (301, 381). Instead of the normal straight lines, benzyl systems in direct displacement reactions yield curves which are concave upward. An explanation of these results which is based on the discussion of Swain and Langsdorf (605) is the following: Electron-attracting groups will increase the positive character of the carbon atom of the C—X bond, made more polarizable by the benzene ring. Since the changes in charge on the reacting center in direct displacement reactions seem generally to be rather small, the resulting positive charge at the central carbon atom could be greater than at the transition state and would result in the observed changes in rate as a function of structure. This effect will account for only rather small rate accelerations by electron-attracting substituents in direct displacements, but the observed effect is small— most of the observed rate variations fall within a factor of 2 (table 8). The far larger effects of nitro and cyano groups are considered separately on page 600.

v. Allylic and acetylenic systems

The effect of alkyl substitution in allylic and acetylenic systems is more pronounced but in the same direction as in benzylic systems. 1-Chloro-2-butyne (XIII) reacts 50 per cent faster than propargyl chloride with potassium iodide in acetone (316).

$$CH_3C\equiv CCH_2Cl$$
XIII
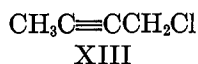
In allylic systems, methyl substitution at the reacting center causes a rate decrease of the same magnitude as in saturated systems; e.g., α-methylallyl chloride is less reactive than allyl chloride by a factor of 20 towards ethoxide ion in ethanol and by a factor of 36 towards lithium chloride in acetone (table 9).

TABLE 9

Direct displacement reactions of allylic chlorides[a]

Compound	Relative Rates		
	$C_2H_5O^-$ in ethanol 50°C.	KI in acetone 20°C.	LiCl in acetone 44.6°C.
$CH_2=CHCH_2Cl$	1.00	1.00	1.00
$CH_2=C(CH_3)CH_2Cl$	1.03	1.58	
$CH_3CH=CHCH_2Cl$ (*cis*)	5.14	8.35	2.52[b]
$CH_3CH=CHCH_2Cl$ (*trans*)	4.43	1.56	
$C_2H_5C(CH_3)=CHCH_2Cl$	20.0		
$CH_3CH=C(CH_3)CH_2Cl$ (*cis* CH_3, H)	4.37	41.8	
$CH_3CH=C(CH_3)CH_2Cl$ (*trans* CH_3, H)	3.92	5.27	
$(CH_3)_2C=CHCH_2Cl$	17[c]	28	21.3
$(CH_3)_2C=C(CH_3)CH_2Cl$		150	
$CH_2=CHCHClCH_3$	~0.05[c]		0.028

[a] References 313a, 318, 319, 319a, 618, 636, 649.

[b] A mixture of *cis* and *trans* isomers was used.

[c] At 44.6°C.

Alkyl substituents conjugated with the reacting center increase the rate, undoubtedly because of the same type of extension of the π-bond system which represented substituted benzylic systems. For the same reasons, alkyl substitution at the reacting center would be expected to increase the reaction rate were it not for a superimposed and dominant steric effect.

γ-Halogen substituents generally cause a rate increase in direct substitutions (table 14). The rate accelerations, which are substantial and are greater than in corresponding benzyl cases, are associated only with halogens conjugated directly with the reacting center, probably because a vinyl group conjugates more effectively than a phenyl group. β-Halogen substituents which are cross-conjugated show rate decreases which are associated predominantly with their inductive effects; e.g., the rate sequence seems to be β-F $<$ β-Cl $<$ β-Br (table 14).

vi. Energy and entropy of activation

Dostrovsky, Hughes, and Ingold (222) have treated steric hindrance as resulting from the energy required for compression of covalent radii at the transition state. Structure IV was used as a model of the transition state. Their calculations indicate that this compression energy is of only minor importance in the series methyl, ethyl, isopropyl, *tert*-butyl. Quite apart from the drastic approximations required both in the model assumed and in the method of calculation, another, perhaps more important, phenomenon which appears as a steric effect has been pointed out by Bauer, Ivanoff, and Magat (68, 380). The greater compactness of the transition state compared to the ground state causes a restriction in the number of configurations which may be assumed by the atoms involved and reduces the entropy of the system. As the number of atoms in the vicinity of the reacting center is increased, the degree of such restriction is likewise increased and the further reduction in entropy is rate-retarding.

This effect and others were included in the extensive calculations of energies

TABLE 10

Energies and entropies of activation of some displacement reactions

Reaction		CH₁	C₂H₆	i-C₃H₇	t-C₄H₉	C₃H₇	i-C₄H₉	Neo-pentyl	References
RI, I⁻, ethanol...............	$E^{\ddagger}$		20.4	20.9		18.1	18.8		(441)
	$\Delta S^{\ddagger}$		−9.0	−14.0		−17.6	−19.9		
RBr, Br⁻, 90% aqueous acetone.	$E^{\ddagger}$			22.9		18.1	20.2		(417)
	$\Delta S^{\ddagger}$			−11.6		−21.2	−19.9		
RBr, C₂H₅O⁻, ethanol........	$E^{\ddagger}$	20.0					22.8	26.2	(218)
	$\Delta S^{\ddagger}$	−8.6					−12.7	−19.9	
RBr, S₂O₃⁻⁻, 50% aqueous ethanol....................	$E^{\ddagger}$	15.6	18.5	20.1		18.0	19.6		(186, 226)
	$\Delta S^{\ddagger}$	−12.9	−12.3	−13.2		−15.3	−15.7		
RI, C₂H₅O⁻, ethanol..........	$E^{\ddagger}$	19.6	21.0			22.3			(325)
	$\Delta S^{\ddagger}$	−9.5	−9.5			−7.5			
RI, C₆H₅O⁻, ethanol..........	$E^{\ddagger}$	21.6	22.2			21.8			(556)
	$\Delta S^{\ddagger}$	−5.9	−6.9			−10.0			
RI, eugenoxide ion, ethanol....	$E^{\ddagger}$	18.9	19.0			21.0			(696)
	$\Delta S^{\ddagger}$	−8.9	−11.3			−11.6			
RI, (C₂H₅)₃N, nitrobenzene....	$E^{\ddagger}$	9.7	12.5	16.0					(115, 404)
	$\Delta S^{\ddagger}$	−34.7	−35.6	−33.7					
RI, pyridine, benzene..........	$E^{\ddagger}$	14.4	15.9	18.1		16.3			(654)
	$\Delta S^{\ddagger}$	−35.0	−35.5	−34.8		−36.5			
RI, pyridine, nitrobenzene.....	$E^{\ddagger}$	13.9	16.0	17.7					(114)
	$\Delta S^{\ddagger}$	−29.8	−28.8	−29.5					
RI, 2-methylpyridine, nitro-benzene.....................	$E^{\ddagger}$	14.0	16.5	19.2					(114)
	$\Delta S^{\ddagger}$	−31.0	−30.2	−29.8					
RBr, I⁻, acetone..............	$E^{\ddagger}$	16.3	18.8	20.5	22.0	18.7	19.9	24.0	(260)
	$\Delta S^{\ddagger}$	−8.4	−10.2	−13.9	−13.9	−11.1	−13.4	−13.9	
RI, Br⁻, acetone..............	$E^{\ddagger}$	16.3	17.7	18.5		17.5	18.8	23.1	(261)
	$\Delta S^{\ddagger}$	−8.4	−9.7	−13.9		−11.1	−13.4	−14.3	
RBr, Br⁻, acetone.............	$E^{\ddagger}$	15.8	17.5	19.7, 19.9	21.8	17.5	18.9	22.0	(196, 419)
	$\Delta S^{\ddagger}$	−11.5	−14.4	−16.1, −12.0	−10.2, −11.5	−15.6	−16.6	−21.1	
RBr, Cl⁻, acetone.............	$E^{\ddagger}$	15.7	17.6	18.8	21.0	17.5	18.1	21.7	(358)
	$\Delta S^{\ddagger}$	−17.0	−19.8	−23.8	−19.8	−21.1	−22.1	−26.2	
RI, Cl⁻, acetone..............	$E^{\ddagger}$	16.0	17.0	18.0		17.0	17.8	22.0	(358a)
	$\Delta S^{\ddagger}$	−17.5	−18.9	−22.5		−20.2	−22.5	−24.3	
RI, I⁻, acetone...............	$E^{\ddagger}$		17.4	19.4	21.5			22.0	(197)
	$\Delta S^{\ddagger}$		−7.9	−10.1	−5.6			−13.9	

and entropies of direct displacement reactions recently presented by de la Mare, Fowden, Hughes, Ingold, and Mackie (198). Structure IV was again used as the model of the transition state, but the calculations based on this model were more elaborate than the earlier results (222). The calculated energies and entropies of

activation for the reactions of ethyl, n-propyl, isopropyl, tert-butyl, isobutyl, and neopentyl halides with halide ion relative to the corresponding reactions of methyl halides agreed very well with the experimental results and represent one of the most successful attempts to compute the effect of structure on rate from first principles. Nevertheless, the calculated quantities are probably rather sensitive to the particular model used for the transition state. Furthermore, about half of the calculated changes in activation energy are the result of an assumed polarity parameter, taken such that the *inductive effect* of additional methyl groups would *increase* the activation energy. To the extent that the model chosen for the transition state is a valid one, the necessity for the assumed value and direction of this parameter may be taken as evidence for the assumed effect of inductive forces. On the other hand, if this assumed effect is wrong in direction (compare pages 586, 588), the calculations demonstrate a deficiency in the model.

A phenomenon which originates as a pure entropy or energy effect can alter both the energy and the entropy of activation. Consider the following argument: In the transition state for substitution on a methyl halide, the C—X and C—Y bond distances can be relatively short and can yield considerable bonding energy without significantly hampering the C—H bond vibrations. These vibrations would then contribute the same entropy to both the ground state and the transition state. If the transition state for substitution on an ethyl halide occurs at the same point along the reaction coordinate as for the corresponding substitution on the methyl halide—i.e., if the C—X and C—Y bond distances have the same values in both cases—the bonding energy at the transition state will be the same to a first approximation. These values for the bond distances may, however, involve serious restriction of the motions of the methyl group attached to the reacting center in the ethyl system with consequent reduction in the entropy of the system. If the transition state were to adopt such larger values of the C—X and C—Y bond distances that such restriction of methyl group motions became negligible, the total bond energy at the transition state would be low and would require a higher energy of activation. Actually, of course, the system will compromise with that structure which results in the smallest increase in free energy. The effects due to steric restrictions of motions will, of course, be all the more important if the structure of the transition state is not the planar model IV used by Dostrovsky, Hughes, and Ingold (222) but has instead the non-coplanar structure in figure 5.

In many displacement reactions α-alkyl substitution results mainly in a change in the energy of activation (table 10). The entropy of activation remains fairly constant throughout the series methyl, ethyl, isopropyl, tert-butyl, especially with the Menschutkin reactions (reactions with tertiary amines) and with the halide-exchange reactions in acetone.

vii. Steric requirements in the attacking nucleophile

Brown, Eldred, and Cahn (114, 115) have examined a corollary of the steric hindrance hypothesis by investigating the relative rates of reaction of methyl, ethyl, and isopropyl iodides with amines of comparable basicities but of widely

TABLE 11

Steric requirements of tertiary amines in displacement reactions

Solvent: nitrobenzene

RI	$\dfrac{k_{\text{quinuclidine}}}{k_{\text{triethylamine}}}$ 25°C. (115)	$\dfrac{k_{\text{3-methylpyridine}}}{k_{\text{2-methylpyridine}}}$ 60°C. (114)
Methyl......................................	57	4.1
Ethyl.......................................	252	8.0
Isopropyl...................................	706	25.6

different steric requirements. If interactions which restrict atomic motions at the transition state are important in displacement reactions, an alteration in the structure of the attacking nucleophilic species such that these interactions are reduced should cause an increase in rate. Quinuclidine (XIV), in which the substituents attached to the nitrogen are "pinned back," is more reactive than triethylamine (XV) with methyl iodide in nitrobenzene. Moreover, the magnitude of the rate factor increases with ethyl iodide and increases still more with isopropyl iodide (table 11).
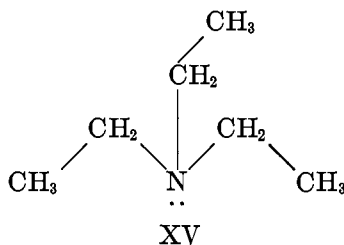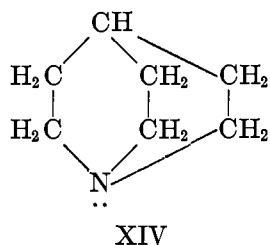
In a similar manner, the rate ratio $k_{\text{3-methylpyridine}}/k_{\text{2-methylpyridine}}$ increases for the series methyl, ethyl, and isopropyl. In both systems, increasing steric requirements of the nucleophilic species become a more important factor as the α-substitution about the reactive center of the substrate increases.

(c) Alkyl series: β-methyl substitution

The relative rates in table 5 also show the marked rate-retarding effect of β-methyl substitution; typical values of the relative rates for the series ethyl, propyl, isobutyl, neopentyl are $1.0:0.4:0.03:10^{-5}$. This effect is clearly to be interpreted as one of steric hindrance (51, 198, 222). The magnitude of the effect for the neopentyl group is particularly pronounced. For the same model of the transition state as used for the series methyl, ethyl, isopropyl, the calculations of Hughes and Ingold and coworkers (198, 222; *cf.* also 240) indicate that reasonable bond distances involve considerable compression of covalent radii. Bartlett and Rosen (51) have elegantly established that steric hindrance offers a satisfying explanation for the inertness of neopentyl halides. Their data in table 12 demonstrate that although the rate retardation becomes less as the *tert-*

TABLE 12

Reactions of some alkyl bromides with potassium iodide in acetone

Compound	Relative Rate at 25°C. (51)	Compound	Relative Rate at 25°C. (51)
(CH₃)₃CCH₂Br............	1*	CH₃CH₂CH₂CH₂Br............	470
(CH₃)₃CCH₂CH₂Br............	19	(CH₃)₃CC≡CCH₂Br............	23,000
(CH₃)₃CCH₂CH₂CH₂Br............	470	CH₃CH₂CH₂CH₂C≡CCH₂Br............	18,000

* This value is 100 times larger than that obtained by I. Dostrovsky and E. D. Hughes (219); however, the argument is not affected by the discrepancy.

butyl group is moved down the chain, the effect is not transmitted through a multiple bond. It is interesting to note that even the neohexyl system shows considerable steric hindrance.

Although the effects of α-alkyl substitution show up predominantly in the energies of activation, β-alkyl substitution affects both the energy and the entropy of activation (table 10). A possible explanation may be the following: For direct displacements on the systems methyl, ethyl, isopropyl, *tert*-butyl, the transition state structure is that in which the entering or the leaving group has a progressively larger bond distance with the central carbon. Such a situation is rather readily accommodated on the basis of the non-coplanar transition state in figure 5 (see Section IV,2,b). The larger bond distances imply lower bond energies and a higher energy of activation. In the cases of β-substitution, adoption by the transition state of the same bond distances and bond energies as in the unsubstituted cases might readily involve restrictions of motion of the β-substituents. A further readjustment of the distances is required to achieve the minimum free energy in many cases (however, *cf.* 198).

(d) α-Heteroatom substitution

Oxygen atoms in the α-position lead to greatly increased reaction rates (table 13). Chlorine, bromine, or iodine substituents lead to substantial reductions in displacement rates, although the effect of an α-fluorine atom seems to depend on the reaction conditions (table 13). Other, less extensive, investigations lead to the same conclusions (441, 502).

The observed relative rates due to α-heteroatom substituents are the resultants of several effects. The heteroatoms which are generally more electronegative than carbon are expected to destabilize a positive charge on carbon; hence they should increase the energy of structure II. This effect is apparently the predominant one for heteroatom substituents at the β-position. The effect should be more important at the α-position.

At the α-position the central p orbital of the reacting carbon, the "reaction orbital," can overlap with a p orbital of the adjacent heteroatom and provide the additional bonding characteristic of π-bonds. This effect can be represented by the inclusion of structures XVI (38a) and XVII for oxygen and chloride substituents, respectively, in the resonance representation of the transition state. Because carbon–oxygen double bonds are stronger than carbon–chlorine double

TABLE 13

Reactivities of α-heteroatom substituents

Compound	KI Acetone 50°C. (335)	CH₃ONa CH₃OH 50°C. (335)	KI Acetone 50°C. (158, 396)	LiCl Acetone 0°C. (38a)	C₂H₅ONa C₂H₅OH 0°C. (38a)
CH₃CH₂Br.....................	1.0	1.0			
FCH₂Br.......................	0.79	4.77			
ClCH₂Br......................	0.13	0.050			
BrCH₂Br[a]....................	0.041	0.0078			
ICH₂Br.......................	0.059	0.022[b]			
CH₃Cl........................				1.0	1.0
CH₃CH₂CH₂CH₂Cl............			1.0		
CH₃OCH₂Cl...................			900	~10⁵	~10⁵
CH₃COOCH₂Cl................			270		
C₆H₅COOCH₂Cl..............			59		

[a] Actual rate constants were divided in half.

[b] It is not known whether the actual rate constant measures displacement of bromine or iodine.

bonds, structure XVI may be expected to be relatively more important than structure XVII and provide for greater rate enhancement.

$$Y^{\ominus}$$
$$\begin{matrix} \diagup \\ C=\overset{\oplus}{O}-R \\ \diagup \end{matrix}$$
$$X^{\ominus}$$
XVI

$$Y^{\ominus}$$
$$\begin{matrix} \diagup \\ C=\overset{\oplus}{C}l: \\ \diagup \end{matrix}$$
$$X^{\ominus}$$
XVII

XVIII
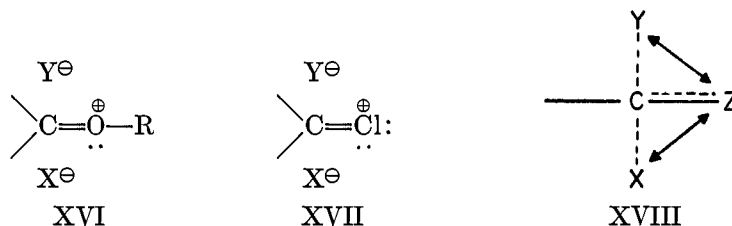
The size of the heteroatom substituent will be of importance in determining the amount of steric hindrance provided at the transition state. The use of rates relative to a β-methyl substituent as a standard is expected to reduce the contribution of this factor. Nevertheless, an iodine atom would be expected to lead to a lower rate than a fluorine atom on the basis of relative sizes. Closely related to that steric hindrance effect which involves restriction of atomic motions is an electronic effect which may be called "neighboring orbital overlap." This effect is seen most readily from an inspection of figure 8. Because atoms Y and Z, for example, are both overlapping with a p orbital of the central carbon atom, Y and Z must overlap with each other to some extent. Such overlap is shown as the shaded area in figure 8. Molecular orbital calculations indicate that this overlap is *antibonding* (592); i.e., the more extensive the overlapping, the higher the electronic energy of the system becomes and the lower the rate is expected to be. Neighboring orbital overlap amounts, in a sense, to an electronic repulsion which may be symbolized by structure XVIII.

The experimental results in table 13 would seem to indicate that neighboring orbital overlap is not important with the $2p$ orbitals of the first row elements but may be important with the much larger $3p$ and higher orbitals.

In halogen-substituted benzyl systems, the conjugation through the benzene ring is apparently so reduced that other effects become important, although there
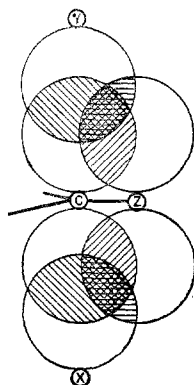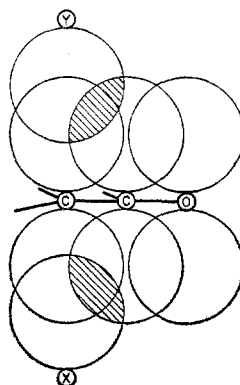
FIG. 8   FIG. 9

FIG. 8. Orbital representation of the transition state of a direct displacement reaction at a carbon bearing a heteroatom (Z), illustrating "neighboring orbital overlap."

FIG. 9. Orbital representation of the transition state of a direct displacement reaction on an α-halocarbonyl compound.

TABLE 14

Relative reactivities of haloallylic chlorides

Compound	Relative Rate (313a, 314, 315, 316a, 317, 319c)	
	C_2H_5ONa, C_2H_5OH, 50°C.	KI, acetone, 20°C.
$CH_2=CHCH_2Cl$	1.00	1.00
$CH_2=C(CH_3)CH_2Cl$	1.03	1.58
$CH_2=CClCH_2Cl$	0.47	0.72
$CH_2=CBrCH_2Cl$	0.82	0.87
$CHCl=CHCH_2Cl$ (*cis*)	2.78	8.58
$CHCl=CHCH_2Cl$ (*trans*)	3.47	2.90
$CHCl=C(CH_3)CH_2Cl$ (*cis* Cl, CH_2Cl)	2.64	32.8
$CHCl=C(CH_3)CH_2Cl$ (*trans*)	2.73	8.45
$CHCl=CClCH_2Cl$ (*cis*)	1.60	
$CHCl=CClCH_2Cl$ (*trans*)	2.27	
$CBr_2=CHCH_2Cl$	19.0	
$CCl_2=CHCH_2Cl$	12.1	
$CCl_2=C(CH_3)CH_2Cl$	7.42	
$CCl_2=CFCH_2Cl$	3.7	
$CCl_2=CClCH_2Cl$	9.0	
$CH_3CH=CHCH_2Cl$ (*cis*)	5.14	8.35
$CH_3CH=CHCH_2Cl$ (*trans*)	4.43	1.56
$CH_3CCl=CHCH_2Cl$ (*cis* Cl, CH_2Cl)	13.0	61.5
$CH_3CCl=CHCH_2Cl$ (*trans*)	4.05	20.6
$CH_3CCl=CClCH_2Cl$ (*cis*)	5.95	69
$CH_3CCl=CClCH_2Cl$ (*trans*)	6.66	23

seems to be a distinct difference between meta and para substituents (605) (*cf*. page 592). In a terminal allylic position the effect of conjugation is important, and both the inductive electron attraction of a halogen atom and the effect of neighboring orbital overlap are greatly reduced. Extension of the π-bonding of the allylic system to the heteroatom results in rate enhancement (table 14). A halogen in a cross-conjugating position, such as in β-chloroallyl chloride, is not effective in such conjugation (page 593).

(e) Hetero-unsaturated systems

It was shown in the last section that "neighboring orbital overlap" with an electron-rich atom is a destabilizing effect at the transition state. When, on the other hand, the adjoining atom is electron-deficient, such overlap constitutes additional bonding which stabilizes the transition state (592). In systems in which the central carbon atom is bound to a carbonyl or nitrile function, for example, orbital overlap such as that indicated by the shaded area in figure 9 is rate-enhancing. This energy-lowering effect may also be represented in valence-bond terms by the inclusion of structures such as XIX (42) as important contributors to the resonance hybrid of the transition state. These concepts provide a ready explanation for the high reactivity of α-halocarbonyl compounds and

TABLE 15

Relative displacement rates of α-halocarbonyl and α-halonitrile compounds

Reaction	Relative Rates					References
	C_3H_7X	$XCH_2COOC_2H_5$	$C_6H_5COCH_2X$	CH_3COCH_2X	XCH_2CN	
RBr + pyridine in methanol at 35°C.	1	85	450			(501)
RBr + thiourea in methanol at 35°C.	1	640	10700			(501)
RCl + KI in acetone at 50°C.	1	1600	97000	33000	2800	(158)
RBr + pyridine in ethanol at 55.6°C.	1	56	410	210		(148)
RCl + S₂O₃⁻⁻ in water at 25°C.	1	220	1600	1400		(578, 579, 580)

nitriles demonstrated in table 15. When the carbonyl group is sterically so situated that interactions of the type in figure 9 and formula XIX cannot occur, rate enhancement is not observed (56a).

$$-\overset{\displaystyle X}{\underset{\displaystyle Y}{\overset{\big\backslash}{\underset{\big/}{C}}}}-\overset{\displaystyle O^{\ominus}}{\overset{\big/}{C}}-R$$

XIX
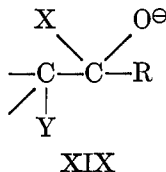
The same concept of neighboring orbital overlap may serve to explain the rather high reactivities of nitro- and cyano-substituted benzyl systems in some displacement reactions (table 8). These cases suggest that structures such as XX play a significant role.

The rate-enhancing effect in the case of heteroatom unsaturation seems to be more pronounced in cases in which the entering and the leaving groups are not

first row elements and hence have "large" orbitals for which "neighboring orbital overlap" might be expected to be more important. This generalization is not followed in a clear-cut way in the benzyl systems, in which the effects are so small that they may easily be masked by other small effects (page 592).

XX
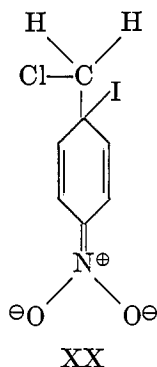
The pronounced reactivity of trimethylsilylmethyl chloride (XXI) towards potassium iodide in acetone (twenty times more reactive than propyl or butyl chloride) (160, 228) has been explained by the same sort of neighboring group interaction as symbolized by structure XXII (228). In this type of interaction silicon acts as an electron-deficient atom and the orbital overlap involved probably utilizes d orbitals. The fact that XXI is less reactive than n-hexyl chloride towards ethoxide ion (651) is consistent with the postulated importance of the relative "sizes" of electronic orbitals.

$(CH_3)_3SCH_2Cl$
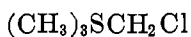
XXI
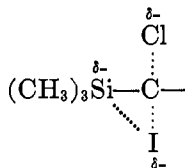
XXII

5. *Structural effects of the leaving group*

Empirically it is found that for displacements of similar charge type the relative rates for different leaving groups are remarkably constant. A number of common leaving groups and their relative rates are given in table 16. Among the halogens the order of ease of displacement, I > Br > Cl > F, parallels the decrease in C—X bond strength (499). In cases in which the leaving atom is the same, the ease of displacement parallels the ability of the leaving group to bear a negative charge. This generalization is demonstrated by the linear free energy

TABLE 16

Relative displacement rates for leaving groups

Leaving Group	Reaction	k_X/k_{Br}	Data of Reference	Average
Br..............		1.00		1.00
Cl..............	$C_3H_7X + C_2H_5O^-$, ethanol, 30°C.	0.016	159	0.02
	Allyl X + $C_2H_5O^-$, ethanol, 24°C.	0.019	159	
	$C_2H_5X + C_2H_5O^-$, ethanol, 40°C.	0.024	287	
	$CH_3X + S_2O_3^{--}$, water, 20°C.	0.023	460	
	$C_6H_5CH_2X$ + pyridine, 90% aqueous ethanol, 30.5°C.	0.020	22	
	C_2H_5X + LiCl, acetone, 25°C.	0.0056	195, 358	
I..............	C_2H_5X + pyridine, benzene, 80.5°C.	5.8	654	~3
	C_3H_7X + pyridine, benzene, 80.5°C.	5.2	654	
	$C_3H_7X + (CH_3)_3N$, benzene, 80.5°C.	5.6	654	
	$C_6H_5CH_2X$ + pyridine, 90% aqueous ethanol, 30.5°C.	1.2	22	
	C_2H_5X + sodium 3-phenyl-1-thiourazolate, 50% aqueous ethanol, 25°C.	3.1	2	
	$C_2H_5X + (C_2H_5)_3N$, acetone, 100°C.	6.3	453	
	$C_2H_5X + (C_2H_5)_3N$, benzene, 100°C.	6.8	453	
	$C_2H_5X + S_2O_3^{--}$, water, 25°C.	1.7	578	
	$C_2H_5X + C_2H_5O^-$, ethanol, 25°C.	1.9	444	
	Allyl X, $C_2H_5O^-$, ethanol, 24°C.	1.9	159	
	$C_3H_7X + C_2H_5O^-$, ethanol, 30°C.	1.3	159	
	C_2H_5X + LiCl, acetone, 25°C.	4.3	358, 358a	
	C_2H_5X + LiBr, acetone, 25°C.	8.7	196, 261	
	C_2H_5X + LiI, acetone, 25°C.	36	197, 260	
$OSO_2C_6H_5$.......	$C_2H_5X + C_2H_5O^-$, ethanol, 25°C.	5.8	444, 465	6
	$CH_3X + OH^-$, water, 25°C.	6.3	462, 567	
F...............	$C_4H_9X + C_2H_5O^-$, ethanol, 55°C.	1.4×10^{-4}	143, 206	10^{-4}
	$CH_3(CH_2)_3CHXCH_3 + I^-$, acetone, 120°C.	0.8×10^{-4}	81	
	$C_6H_5CH_2X + C_2H_5O^-$, ethanol, 76°C.	$\sim 2 \times 10^{-4}$	159, 457	
$\overset{+}{O}H_2$.............	$C_2H_5X + Br^-$, ethanol, 55°C.	1	296, 456	1*
ONO_2..........	$C_6H_5CH_2X + OH^-$, 60% aqueous dioxane, 50°C.	~0.02	86, 435	10^{-2}
	$C_2H_5X + OH^-$, 80% aqueous ethanol, 55°C.	0.01	25, 60	
$\overset{+}{S}(CH_3)_2$........	$CH_3X + OH^-$, water, 100°C.	10^{-4}	276, 556	0.5*
	$CH_3X + C_6H_5O^-$, ethanol, 100°C.	~0.1	276, 556	
	$CH_3X + C_2H_5O^-$, ethanol, 100°C.	~1	159, 276	

* Solvent-dependent; the values listed are for ethanol.

correlations between displacement rate and acidity found for the following systems:

$$X\text{—}\langle\text{—}\rangle\text{—}COOCH_3 + N(CH_3)_3 \rightarrow X\text{—}\langle\text{—}\rangle\text{—}COO^- + N(CH_3)_4^+ \quad (302)$$

$$X\overset{NO_2}{\underset{NO_2}{\text{—}\langle\text{—}\rangle\text{—}}}OCH_3 + (CH_3)_2N\text{—}\langle\text{—}\rangle\text{—}OCH_3 \rightarrow$$

$$X\overset{NO_2}{\underset{NO_2}{\text{—}\langle\text{—}\rangle\text{—}}}O^- + (CH_3)_3\overset{+}{N}\text{—}\langle\text{—}\rangle\text{—}OCH_3 \quad (330)$$

and

$$X\langle\underline{\quad}\rangle SO_3C_2H_5 + C_2H_5O^- \rightarrow X\langle\underline{\quad}\rangle SO_3^- + (C_2H_5)_2O \qquad (465)$$
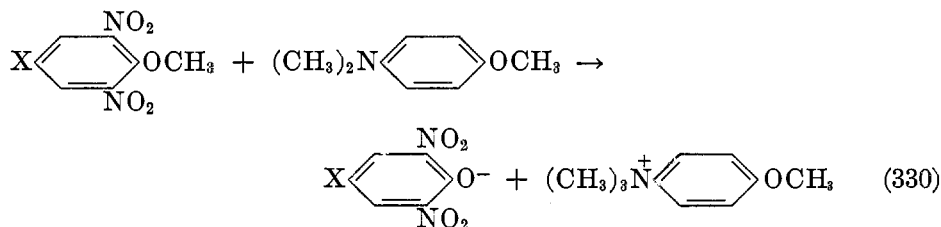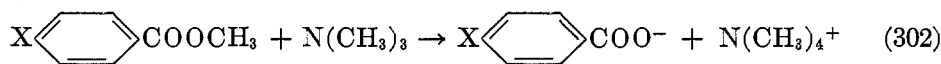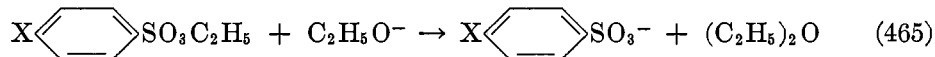
In each case, electron-attracting substituents facilitate reaction; i.e., these reactions follow the Hammett sigma–rho correlation with positive rho (301, 381).

Although water is quite readily displaced—as a leaving group it is about as reactive as bromide—there is no established case of displacement of hydroxide ion. This result agrees with thermodynamic considerations. Ogg (482) has calculated that the reaction of methyl bromide with hydroxide ion is exothermic by 16 kcal./mole. The equivalent increase in the activation energy of the reverse reaction corresponds to a factor of 10^{-12} in rate; i.e., the rate is far too slow to be observed. Since the reactions of alkyl halides with ethoxide, phenoxide, acetate, hydrosulfide, cyanide, thiosulfate, and sulfite ions are all exothermic by 10–20 kcal. (482), the reverse reactions will be slower by factors of 10^{-7} to 10^{-14} and will, therefore, not be observed except under most exceptional conditions.

6. *The effect of solvent*

In all direct displacement reactions ions are involved either as reactants or as products; consequently, solvation forces must be of major importance in determining the facility of reaction. Attempts to realize the Menschutkin reaction in the gas phase result in reaction occurring wholly or in part on the walls of the vessel (464). In saturated hydrocarbon solvents this reaction of alkyl halides with tertiary amines, in which charge separation is developed at the transition state, is catalyzed by the precipitated quaternary salt (506).

The simplest model of a solvent is that of a continuous dielectric medium. With reasonable assumptions, this model, although naive, can frequently predict the gross effects of solvent change for reactions of different charge type (161, 356). A high dielectric constant will facilitate reaction between two neutral molecules, since charge separation is generated at the transition state, but will greatly decrease the reaction between ions of opposite sign in which charge separation is being cancelled. For reactions between an ion and a neutral molecule, since the charge at the transition state is being dispersed, an increase in dielectric constant will decrease the rate. This changing effect of solvent depending on the charge type of the reaction puts a limitation on the usefulness of relative rates as a function of structure. This limitation is illustrated by the data for $-S(CH_3)_2^+$ as a leaving group in table 16. The rate of displacement relative to bromide as a leaving group varies from 10^{-4} in water to about 0.5 in the less polar solvent ethanol.

In the Menschutkin reaction initially neutral reactants form a transition state which has some separation of charge. From a crude application of Coulomb's law, the free energy of activation is expected to be inversely proportional to the dielectric constant of the solvent. In figure 10 the relative rates for the reaction of triethylamine with ethyl iodide at 100°C. are plotted on a logarithmic scale against the reciprocal of the dielectric constants for a number of solvents. There

is a decided trend towards higher rates in solvents of higher dielectric constant but the proportionality is far from exact. Of course, solvents are not continuous media and in the vicinity of the reacting species individual solvent molecules would undoubtedly play an important specific role. For example, in figure 10 a comparison of the rates in various solvents shows that for each functional group the use of a benzene derivative as solvent results in a higher displacement rate than does the use of the corresponding aliphatic derivative, although both may have about the same dielectric constant. For example, one finds the following rate ratios: chlorobenzene/propyl chloride = 4.3; diphenyl ether/diethyl ether = 22; ethyl benzoate/isobutyl acetate = 4.5; benzyl alcohol/isobutyl alcohol = 5.0, etc. The generality extends even to multiple rings: α-bromonaphthalene/bromobenzene = 4.2. This effect probably occurs because benzenoid solvent molecules close to the reacting system further stabilize charge separation by way of the high polarizability of the π-electrons of the aromatic ring.

The use of $(D - 1)/(2D + 1)$ (*cf.* footnote on page 620) has been proposed as a function proportional to the free energy of activation (395). The logarithms of the rates of some Menschutkin reactions give excellent linear plots against this function for benzene–alcohol mixtures but give definitely curved plots for benzene–nitrobenzene mixtures (275). Consequently, the dielectric constant
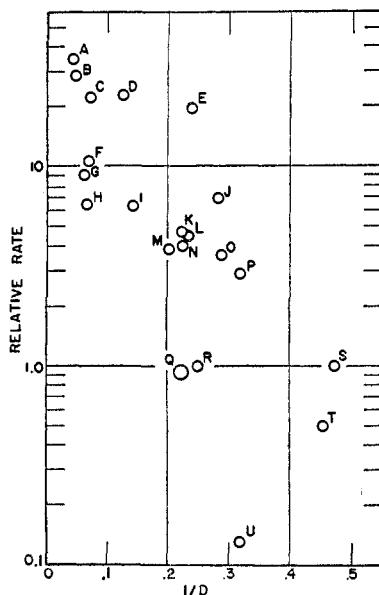
FIG. 10. Relative rates of the reaction of triethylamine with ethyl iodide in various solvents as a function of the dielectric constant (291, 447, 454). The letters refer to the solvents as follows: A, nitrobenzene; B, benzonitrile; C, acetophenone; D, benzyl alcohol; E, α-bromonaphthalene; F, acetone; G, methanol; H, ethanol; I, *o*-dichlorobenzene; J, anisole; K, bromobenzene; L, ethyl benzoate; M, ethyl acetate; N, chlorobenzene; O, phenetole; P, diphenyl ether; Q, *n*-propyl chloride; R, isobutyl acetate; S, benzene; T, xylene; U, ethyl ether.

alone gives an inadequate measure of solvating power, and, in fact, may actually play a rather minor role. Anions and cations require different solvating characteristics: hydrogen-bonding solvents make good anion solvators; solvents containing atoms having unshared electron pairs such as oxygen and nitrogen make relatively good cation solvators. Water and alcohols, which combine both requirements, can effectively solvate both anions and cations.

For the direct displacement of a neutral molecule by an ion, a number of cases are known in which a decrease in the solvating power of the solvent results in an increase in the rate (331, 418, 442), but, when the solvating characteristics are inadequate, complications set in. For such solvents the equilibrium between ion-pairs and the separated ions

$$M^+X^- \rightleftarrows M^+(\text{solvated}) + X^-(\text{solvated})$$
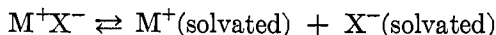
is not displaced completely to the right. The existence of this phenomenon is manifested by an increase in the second-order rate constant with a decrease in the total concentration of the ionic reactant. When the extent of ionic dissociation is independently measured and the observed rate constant is corrected for the actual amount of free ions present, the true rate constant thus obtained is found to be independent of the total salt concentration. This phenomenon has been recognized and correctly interpreted for ethanol solutions, at least, for many years (1, 2, 444, 475, 542, 543). Early results indicated that the dissociated ions and the ion-pairs have comparable reactivities, but more recent work shows that the ion-pairs are relatively unreactive (458, 696).

It is known that alkali halides are incompletely dissociated in acetone solutions (243, 244, 491, 494), although in methanol solutions complete dissociation apparently occurs (243, 244). Incomplete dissociation is undoubtedly the cause of the large negative salt effects noted in reactions of alkyl halides with alkali halides in acetone (196, 243, 244, 260, 261, 358, 358a).

The contrasting effects of solvent polarity on displacement rate and on ionic dissociation are clearly demonstrated in the reaction between p-nitrobenzyl bromide and lithium chloride in aqueous dioxane. The observed second-order rate constant first increases as the water content is increased from 10 per cent to 30 per cent and then decreases as the water content is increased further to 50 per cent (300).

The presence in the reaction mixture of agents which can complex with the leaving group results in a facilitation of the reaction. Since the complexing agent is already bonding at the transition state, a term involving the concentration of the agent will appear in the kinetic expression for the reaction. The first-order reaction of alkyl chlorides with pyridine in pyridine solution becomes a second-order reaction when silver nitrate is added (first order each in alkyl chloride and silver nitrate) and the reaction rate is greatly increased (637). The displacement of methyl iodide by nitrate ion in the presence of silver ion in acetonitrile solution has third-order kinetics, first order each in methyl iodide, silver ion, and nitrate ion (304).

Because hydrogen bonding is probably involved in the solvation of anions in

hydroxylic solvents, specific rate effects may be expected to arise from such hydrogen bonding at the transition state. Indeed, Swain and Eddy (603) have shown that the rate of displacement of methyl bromide by pyridine in benzene solution is enhanced by the addition of small amounts of not only such well-known halogen-complexing agents as mercurous bromide and aluminum bromide, but also of such hydrogen-bonding agents as methanol, phenol, and p-nitrophenol. In the latter cases, the rate enhancement increases with increasing acidity of the hydroxylic addend. The fact that third-order kinetics (first order each in methyl bromide, pyridine, and p-nitrophenol) was observed suggests that only one such hydrogen bond is necessary in the limiting case. In this sense, these hydroxylic compounds may be considered as electrophilic reagents in the same class as the Lewis acids mentioned above. It should be pointed out, however, that it is not valid to infer that halide ions in alcoholic or in aqueous solutions require such specific solvation with only one hydroxylic molecule; in fact, the reaction between methyl iodide and pyridine has the same rate in deuterium oxide as in water (599). If specific hydrogen bonding with one solvent molecule were involved, an isotope effect would have been expected.

IV. The Solvolysis Reaction

A. INTRODUCTION

1. Rate dependency on lyate ion

When displacement reactions are carried out in hydroxylic solvents a certain amount of reaction with the solvent (solvolysis) can occur. The extent of this reaction compared to other displacements depends strikingly on the structure of the substrate. Equation 9 gives the general kinetic expression for reaction with a hydroxylic solvent and with the lyate ion, in which the solvent is represented as SOH and the corresponding lyate ion as SO^-. k_2 is the second-order rate constant for displacement by SO^- and k_1 is a first-order constant which measures the rate of reaction with the solvent. Table 17 gives these rate constants for a wide range of systems.

$$- \frac{d[RX]}{dt} = k_1[RX] + k_2[RX][SO^-] \tag{9}$$

2. The Olson–Halford equation

The direct displacement mechanism for reactions with solvent,
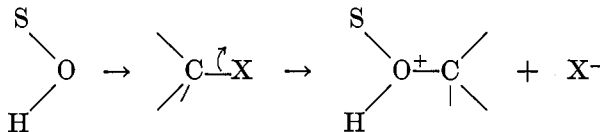
has been proposed by Olson and Halford (492), by Taylor (621, 622, 623), by Read and Taylor (518), and by Ogg (483). Olson and Halford (492) studied the solvolyses of *tert*-butyl chloride in aqueous ethanol and methanol mixtures. The concentration terms of the usual bimolecular rate equation were replaced by

TABLE 17

Rates of lyate-ion displacements and solvolyses

Substrate	Solvent	Temperature	$10^5 k_1$	$10^5 k_2$[a]	k_2/k_1[b]	References

Primary

		°C.	sec.⁻¹	l./mole-sec.		
Methyl bromide	80% Ethanol	55	0.349	2040	5840	(60)
Methyl benzenesulfonate	Ethanol	70	7.05	10300	1460	(544)
	Water	25	1.17	88	75	(507)
Sodium methyl sulfate	Water	138	0.77	46	60	(138a)
Ethyl bromide	80% Ethanol	55	0.139	171	1230	(60)
Ethyl benzenesulfonate	Ethanol	70	3.06	4010	1310	(544)
	Ethanol	25	0.024	37.2	1550	(628)
	Water	25	1.08	11.7	11	(385)
Ethyl tosylate	60.7% Aqueous dioxane	50	0.627	28.4	45	(439)
Sodium ethyl sulfate	Water	138	0.46	9.2	20	(138a)
n-Propyl chloride	50% Ethanol	101.6	0.97	58.1	60	(635)
	Ethanol	101.6	0.040	91	2300	(635)
n-Propyl benzenesulfonate	56% Aqueous acetone	40	0.163	12.5	77	(627)
Sodium isobutyl sulfate	Water	138	0.093	0.485	5.2	(138a)
1-Bromopentane	50% Aqueous acetone	50	0.0755	9.38	124	(489)
1-Bromohexane	50% Aqueous acetone	50	0.0688	8.54	124	(489)

Secondary

Isopropyl bromide	60% Ethanol	80	9.1	86	9.5	(376)
	80% Ethanol	80	2.9	128	44	(375)
Isopropyl benzenesulfonate	36.5% Acetone	25	2.37	~0	~0	(627)
	56% Acetone	40	2.84	~0	~0	(627)
	Isopropyl alcohol	50	0.388	46	119	(627)
	Ethanol	70	10.2	700	69	(544)
Sodium isopropyl sulfate	Water	99	0.34	0.27	0.8	(138a)
2-Bromohexane	50% Acetone	50	0.362	7.50	21	(489)
Sodium sec-butyl sulfate	Water	99	0.535	0.21	0.4	(138a)
2-Bromoöctane	60% Ethanol	80	5.2	79.5	15	(376)

Tertiary

tert-Butyl bromide	80% Ethanol	25	38.5	~0	~0	(72)
	60% Aqueous dioxane	10	28.9	~0	~0	(72)
tert-Amyl chloride	80% Ethanol	25	2.0	~0	~0	(374)

Allylic

Allyl chloride	50% Ethanol	25	0.0159	4.53	285	(8)
	Ethanol	44.6	0.0063	18	2900	(635)
	50% Dioxane	30	0.00158	4.3	2720	(398)
	50% Ethanol	44.6	0.168	28.0	167	(635)
Allyl bromide	50% Dioxane	30	0.032	115	3600	(398)
Allyl benzenesulfonate	Ethanol	25	0.79	484	612	(84)
Crotyl chloride	Ethanol	25	0.0511	6.16	121	(541)
	Ethanol	99.5	8.13	2720	335	(140)
	50% Ethanol	25	1.47	30.8	21	(699)
1-Chloro-3-methyl-2-pentene	Ethanol	25	0.332	24.2	73	(649)
1-Chloro-3-methyl-2-butene	Ethanol	44.6	6.5	270	41	(635)
α-Methylallyl chloride	50% Ethanol	25	1.22	~0	~0	(699)
	Ethanol	99.5	2.93	153	52	(140)

Arylmethyl

Benzyl chloride	Ethanol	50	0.0314	61	1950	(159, 263, 670)
	60.7% Dioxane	50	0.130	20	154	(86)
Benzyl tosylate	Acetic acid	40	1.72	<9	<5	(593)
α-Phenylethyl chloride	80% Ethanol	50	16.3	~0	~0	(646)
	Ethanol	70	3.75	16.7	4.5	(366)
	Methanol	70	43.5	24.6	0.6	(366)
	Acetic acid	50	0.55	~0	~0	(585)
Benzhydryl chloride	Ethanol	25	5.75	~0	~0	(647)
	Methanol	15	25.2	~0	~0	(72)

[a] ~0 means too small to be measured.
[b] ~0 means <1.

fugacities in order to account for the changes in activity coefficients with change in solvent. Their resulting rate expression was equation 10, in which k_w^0 and k_a^0 are the rate constants in pure water and in pure alcohol, respectively, and p_w, p_a, and p_{RCl} are the partial pressures of water, alcohol, and alkyl halide, respectively, for each particular solvent system. Although Olson and Halford assumed an outmoded activity rate equation, Bartlett (39) has shown that equa-

$$\text{Rate} = (k_w^0 p_w + k_a^0 p_a) p_{RCl} \qquad (10)$$

tion 10 can also be derived from the transition state theory with the same postulates of bimolecularity of reaction. The experimental rate constants were found to agree excellently with those derived from the equation (table 18).

Bateman, Hughes, and Ingold (63) pointed out, however, that the postulation of direct displacement by solvent requires that the relative amounts of product alcohol and ether, by reaction with water and with solvent alcohol, respectively, be directly proportional to the respective rate constants, $k_w^0 p_w$ and $k_a^0 p_a$. This relationship was found not to hold for the solvolyses of *tert*-butyl chloride in aqueous ethanol and methanol, for the amount of ether formed by reaction with solvent alcohol is greatly in excess of that predicted from the Olson–Halford equation (table 18). An attempt has been made to relate the product composition

TABLE 18

Solvolyses of tertiary butyl chloride in aqueous alcohols

Aqueous methanol; 25°C.

Solvent, Mole Per Cent Water	$10^5 k$ sec.$^{-1}$		Mole Per Cent t-C$_4$H$_9$OCH$_3$ Formed		
	Calculated by equation 10	Experimental	Calculated	Found (63)	(584)
49.7		9.64	12		43
49.0				36	
43.2	5.05	5.23	16		49
38.3	3.20	3.06	19		55
34.6	2.12	2.09	21		58
28.2	1.20	1.13	26		65
24.4				59	
23.0	0.755	0.706	31		71
17.5	0.454	0.428	37		78
16.4				68	
7.0	0.164	0.173	57		91
0.0		0.081			

Aqueous ethanol; 25°C.

Solvent, Mole Per Cent Water	$10^5 k$, sec.$^{-1}$		Mole Per Cent t-C$_4$H$_9$OC$_2$H$_5$ Formed	
	Calculated	Experimental	Calculated	Found (63)
82.9	137	130	4	
76.4	42.5	36.7	5	
68.4	13.5	12.6	6	16
58.1	3.50	4.03	7	
44.8	1.23	0.913	8	27
26.2	0.256	0.171	14	41
0.0		0.022		

TABLE 19

Solvolyses of n-butyl bromide in aqueous alcohols (63)

Aqueous methanol, 59.4°C.

Solvent, Mole Per Cent Water	10^5k, sec.$^{-1}$		Mole Per Cent n-C₄H₉OCH₃ Formed	
	Calculated by equation 10	Found	Calculated	Found
60.1		0.364	49	47
48.3	0.240	0.242	57	57
30.8	0.125	0.139	68	68
26.3	0.119	0.116	72	71
14.1	0.072	0.073	84	86
0.0		0.038		

Aqueous ethanol, 75.1°C.

Solvent, Mole Per Cent Water	10^5k, sec.$^{-1}$		Mole Per Cent n-C₄H₉OC₂H₅ Formed	
	Calculated by equation 10	Found		
73.7		1.11	32	29
56.2	0.586	0.567	37	41
25.8	0.243	0.248	55	55
0.0		0.078		

to the rate constants, but the additional assumptions and parameters required render the results of little significance (655).

Similar results were obtained in the ethanolysis of benzhydryl chloride, the rate of which is strongly accelerated by the addition of small amounts of water. The amount of benzhydrol formed is much less than that required for the explanation of the rate enhancement as a bimolecular displacement by water. In effect the addition of water catalyzes the alcoholysis (250).

One can also argue that if the solvolysis of *tert*-butyl or benzhydryl halides occurred by direct displacement by water, the far more nucleophilic hydroxide ion should cause a large acceleration in rate. In the solvolysis of these halides and of certain others, the lyate ion has no effect on the rate (table 17). On the other hand, for primary halides such as methyl and ethyl halides in solvents other than water, the rate ratio, k_2/k_1, is of the order of 10^3 or, if the solvolysis rate is reckoned as a second-order rate constant, 10^5. For these halides, the large acceleration in rate produced by the lyate ion suggests a direct displacement mechanism.

The solvolysis rates of n-butyl bromide in aqueous methanol and ethanol are accurately given by the Olson–Halford equation (equation 10) (table 19) (88, 298). Moreover, in these cases the proportions of product alcohol and ether formed fit excellently the predictions of the equation (table 19). The criterion of large rate acceleration by lyate ion as evidence for solvolysis by the direct displacement mechanism finds support in these results; however, a further mechanistic postulation seems required to interpret those cases in which lyate ion has no effect on the rate. Attention will be initially directed on these cases.

3. The ionization hypothesis

Ward (646) first observed that the rate of hydrolysis of α-phenylethyl chloride in 80 per cent aqueous ethanol is not affected by the addition of base. He pointed out that the similar observations for the ethanolysis of benzhydryl chloride (647) are consistent with a mechanistic sequence involving a preliminary ionization of the carbon–chlorine bond:

$$(C_6H_5)_2CHCl \rightarrow (C_6H_5)_2CH^+ + Cl^-$$

$$(C_6H_5)_2CH^+ + C_2H_5O^- \rightarrow (C_6H_5)_2CHOC_2H_5$$
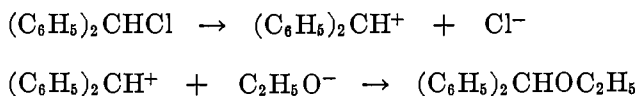
If the first step is postulated to be rate-determining, addition of ethoxide ion will not increase the overall rate.

In 1927, Ingold (377) advanced an ionization mechanism to explain observations concerning the hydrolysis of benzyl chloride which were later amplified by Ingold and Rothstein (379). Thereafter, Ingold and Hughes and their collaborators conducted an extensive investigation of the displacement reactions of alkyl halides. Originally they apparently considered that the reactions of all alkyl halides with hydroxylic solvents involved *preliminary ionization to carbonium ions, a general mechanism which they termed the S_N1 reaction* (substitution, nucleophilic, unimolecular) (276). Early examples which they considered included some reactions of trimethylsulfonium salts in ethanol solutions (276). The relatively rapid reactions of the hydroxide and phenoxide by second-order kinetics were interpreted as S_N2 displacements. The carbonate, bromide, and chloride, however, reacted by first-order kinetics and all gave the same rate constant. These results were interpreted as S_N1 reactions; the nucleophilic ability of these anions was considered to be too low to compete by displacement with the unimolecular ionization. In these examples, however, the experimental results could be explained equally well on the basis that displacement by carbonate, bromide, or chloride ions cannot compete with *displacement by solvent ethanol*, in which the mechanism could be S_N2 for all cases.[3] The reaction products were not identified.

B. THE S_N1 MECHANISM

The results of many experiments on solvolyses, particularly with tertiary alkyl and benzhydryl systems, cannot be interpreted as direct displacement reactions and are, on the contrary, consistent with the ionization hypothesis. At various times detailed descriptions of the S_N1 mechanism have been presented (59, 352, 354, 378, 535). Because of the importance of the concepts involved, the S_N1 hypothesis should be considered as being one of the most important developments in theoretical organic chemistry. Its general acceptance is marked by the aspects of it which have appeared in numerous books and texts (4, 42, 301, 355,

[3] Even as late as 1950, apparently, Ingold (378) considered these solvolyses to be S_N1 rather than S_N2 reactions.

522, 548). The S_N1 mechanism is considered in some detail in the sequel. Three steps are involved:

$$R\text{—}X \underset{(2)}{\overset{(1)}{\rightleftarrows}} R^+ \ X^- \xrightarrow[(3)]{B:} \text{products}$$
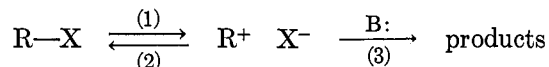
The first step consists in ionization of the carbon–halogen bond to liberate a carbonium ion and a halide ion. The second step is a reversal of the first—recombination of the carbonium ion and halide ion to re-form the alkyl halide. The third step is the reaction of the carbonium ion with any available nucleophilic agent to form the product or products. The S_N1 solvolysis reaction is the frequent case in which B: is a solvent molecule. Although formulated for halides, the mechanism applies in an obvious way to other leaving groups.

1. The ionization step

The ionization step is envisaged as simply a heterolysis of the carbon–halogen bond. Since a covalent bond is being broken, this step is normally endothermic and is the rate-determining step of the reaction.

(a) Triarylmethyl cations

A justification for even considering the possibility of ionization is the existence of such highly colored stable carbonium-ion complexes as those formed from triarylmethyl chlorides and $SbCl_5$, $SnCl_4$, $ZnCl_2$, $HgCl_2$, or $FeCl_3$ (21, 102, 285, 629). These complexes are analogous to stable carbonium salts such as the highly colored crystalline triarylmethyl perchlorates (101, 286, 337, 338), which were shown to be ionic by Hantzsch (307), who demonstrated that their nitromethane solutions conducted electricity about as well as did tetramethylammonium iodide. Walden (644) found that colorless, normally non-ionic triphenylmethyl bromide gave in liquid sulfur dioxide a yellow solution which was conducting. He attributed this phenomenon to the formation of the ions $(C_6H_5)_3C^+$ and Br^-. Quantitative measures of the extent of ionization of a number of such triarylmethyl halides have been determined in sulfur dioxide solution (428, 429, 703). These values correlate well with the energy differences calculated by simple molecular orbital theory (589). In general, the more stable the carbonium ion is relative to the initial halide, the greater is the degree of ionization. This theory incidentally predicts that the ionization of benzhydryl chloride is about 10^{-16} that of triphenylmethyl chloride (592) and, indeed, it has been reported that benzhydryl chloride and its m-chloro and p,p'-dimethyl derivatives are not measurably ionized in liquid sulfur dioxide (67; cf. 470).

Nitroalkanes have relatively high dielectric constants (D for nitromethane at 30°C. = 35.9; for sulfur dioxide at 0°C. D = 15) (447) and, like sulfur dioxide, cannot react with carbonium ions. Extensive measurements of the degree of ionization of triarylmethyl chlorides in nitroalkanes have recently been reported (78, 79, 238, 239, 241). The extent of ionization is reported to be greatly increased by the addition of Lewis acids such as mercuric chloride, which can coordinate with the separated halide ion (69, 77, 248).

It has been demonstrated that the ionized species exist in the solutions as ion-pairs. Electrical conductivity measures the amount of dissociated ions (428), whereas spectrophotometric methods measure the total amount of carbonium ion in ion-pairs and dissociated (41, 79). However, the measurements in nitro-alkanes are greatly dependent on the purity of the solvent; hence the results should be considered as questionable (42a). Triphenylmethyl chloride gives a *colorless* solution in *pure* acetonitrile [$D = 37.5$ at 20°C. (447)] (42a). Measurements of the ionization of triarylmethyl chlorides in acetic acid and in formic acid have recently been reported (242). In these solvents also, the ionic species are reported to be present almost entirely as ion-pairs.

During the reaction of trianisylmethyl chloride with pyrrole in benzene, the formation of a colored intermediate was observed, the spectrum of which was the same as that of trianisylcarbinol in sulfuric acid (603a). The results were accounted for by a carbonium-ion intermediate.

(b) Solvolysis of arylmethyl halides

Analogously to the ionizations in liquid sulfur dioxide, ionization of triaryl-methyl chlorides would be expected in the relatively highly solvating solvent ethanol, but in this case the solvent can and does react with the carbonium ions formed. Indeed, the rate of reaction is so great as to be comparable to the rate of solution (476). When ethanol is diluted with ether, however, the rate of reaction is sufficiently slow for convenient measurement. As shown in column 1 of table 20, the effect of substituents is essentially as expected for an ionization hypothesis. Groups such as *p*-methyl and *p*-methoxy, which can help distribute the positive charge, exert this effect at the transition state and cause an increased solvolysis rate. A strongly electron-attracting nitro substituent markedly decreases the rate.

Analogous studies (table 20) on the relative solvolysis rates of substituted benzhydryl halides and benzyl halides and tosylates show a closely similar pattern and are consistent with the application of the ionization hypothesis to these cases. The effect of a methoxyl group is particularly striking. In the para position a methoxyl group invariably produces a rather large rate enhancement, undoubtedly because the oxygen atom can accept a considerable fraction of the positive charge via resonance structures such as XXIII; i.e., an electron-rich oxygen $2p$ orbital readily becomes a part of the overall π-bonding. In the un-

XXIII
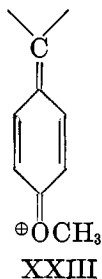
TABLE 20

Effects of ring substituents on solvolysis rates of arylmethyl systems

Substituent	Relative Rates									
	$(C_6H_5)_2CCl$, 60% ethyl ether–40% ethanol, 25°C. (476)	$(C_6H_5)_2CHCl$, ethanol, 25°C. (477, 478)	$C_6H_5CH_2OTs$, 76.6 mole per cent water in acetone, 25.3°C. (400)	$C_6H_5CH_2Cl$, 67% aqueous acetone, 60°C. (571)	$(C_6H_5)_2CHCl$, CH_3OH or $i\text{-}C_3H_7OH$, 25°C. (5)	$C_6H_5CH_2Cl$, 50% aqueous acetone, 69.8°C. (75)	$C_6H_5CH_2Cl$, 50% aqueous acetone, 60°C. (488, 490)	$C_6H_5CH_2Cl$, 48% aqueous ethanol, 83°C. (485, 486, 487, 488)	$C_6H_5C(CH_3)_2Cl$, 90% aqueous acetone, 25°C. (111)	$C_6H_5\text{-}CH_2OTs$, acetic acid, 40°C. (593)
H	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
o-CH₃O		93		108						
m-CH₃O			0.61	0.67						
p-CH₃O	>90		~25,000	~10,000	~5,000					
o-CH₃		2.9					4.2	4.7	3.63	
m-CH₃		2.1	1.8				1.2	1.4	2.00	2.6
p-CH₃	4.1	16.3	30			9.1	8.7	10.4	26.0	56.5
o-F						0.411			0.0502	
m-F						0.237			0.025	
p-F	0.76					1.70			2.14	
o-Cl		0.0096			0.013	0.289	0.30	0.35	0.0079	
m-Cl		0.022			0.026	0.232	0.20	0.23	0.0157	
p-Cl	0.32	0.40			0.47	0.587	0.58	0.62	0.305	
o-Br						0.254	0.28	0.28	0.0061	
m-Br			0.082			0.197	0.20	0.22	0.0144	
p-Br	0.28	0.33	0.41			0.462	0.51	0.50	0.208	
o-I						0.254	0.27	0.28	0.0111	
m-I						0.213	0.20	0.20	0.0233	
p-I	0.34					0.431	0.47	0.46	0.244	
o-NO₂							0.097	0.085		
m-NO₂						0.116	0.11	0.088		
p-NO₂	0.011		0.022		0.00068	0.105	0.10	0.073		

conjugated meta position such p-orbital overlap is not effective in assisting the distribution of charge; in fact, the electronegative oxygen atom, by virtue of its electron-attracting inductive effect, actually destabilizes the carbonium ion and causes a decrease in the rate of ionization. Resonance as in XXIII also occurs with an o-methoxy group, but the inductive effect, strongest in this position of close proximity to the reacting center, considerably reduces the rate enhancement.

These considerations apply as well to halogen substituents, although in these cases the effects are much smaller and less significant. An ortho substituent generally lowers the relative rate by steric inhibition of coplanarity of the carbonium ion with the aromatic ring.

(c) Alkyl cations

The rates of ionization of alkyl halides are also expected to depend on the stabilities of the corresponding carbonium ions. The energies required for a number of carbonium-ion reactions in the gas phase (table 21) clearly show the order of carbonium-ion stability to be tertiary > secondary > primary > methyl. The greater stability of the tertiary carbonium ion is also reflected in the solvolysis rates of alkyl halides (table 22). In the cases listed, $tert$-butyl bromide solvolyzes at least 10^3 times faster than does methyl, ethyl, or isopropyl bromide, in marked contrast to its relative unreactivity in S_N2 reactions (page 587).

In table 23 the effects of α-phenyl substitution on the reacting carbon are compared. Benzyl systems are comparable to secondary carbinyl. $tert$-Butyl chloride and α-phenylethyl chloride are alike in reactivities. A rough approximation is

TABLE 21

Energetics of gas-phase carbonium·ion reactions

$$RY \rightarrow R^+ + Y^-;\ \Delta H^{(a)},\ \text{kcal./mole}$$

R^+	$I^z(R)^{(b)}$	Y^-				
		H^-	Cl^-	Br^-	I^-	OH^-
H^+	312	400	328	317	308	382
CH_3^+	230	315	220 (223)	215 (214)	208 (204)	268
$CH_3CH_2^+$	201	282	192	183	176	239
$CH_3CH_2CH_2^+$	183	266	177	161	161	226
$(CH_3)_2CH^+$	171	250 (252)	(168)	150 (159)	149 (149)	214
$CH_3CH_2CH^+CH_3$	—	(242)	—	—	—	—
$(CH_3)_3C^+$	159	232	149 (150)	132	132	202
$CH_2{=}CHCH_2^+$	188	248	158 (161)	150 (154)	145 (147)	206
$C_6H_5CH_2^+$	178	239	(152)	(141)	(137)	—
$E_A(Y)^{(c)}$		16	87	82	76	49

$^{(a)}$ The endothermicity of each reaction was computed by combining heats of formation of the anion and appropriate alkane with the best values of the corresponding carbon-hydrogen dissociation energy, the ionization potential of the radical, and the electron affinity of the anion. Values in parentheses were determined by a direct computation from the measured appearance potential of R^+ in the mass spectrum of RY less the electron affinity of the halide. The table was compiled by D. P. Stevenson (586a).

$^{(b)}$ Ionization potential of radical.

$^{(c)}$ Electron affinity of Y.

TABLE 22

Relative solvolysis rates of some alkyl bromides

Solvent	Temperature	Methyl Bromide	Ethyl Bromide	Isopropyl Bromide	tert-Butyl Bromide	References
	°C.					
Ethanol.....................	55	2.60[a]	1.00	0.725	831	(299, 362, 670)
80% Ethanol...............	55	2.51	1.00	1.70	8600	(60, 368)
60% Ethanol...............	55	2.08	1.00	1.78	24100	(60, 620)
50% Ethanol...............	55	1.72	1.00	2.86	~48000[b]	(186, 220, 670)
Water......................	50	1.05	1.00[c]	11.6	1.2×10^{6}[b][d]	(670)
HCOOH....................	100	0.58	1.00	26.1	~10⁸[e]	(62)
90% Aqueous acetone.......	50	3.16	1.00	1.39	3530	(622)

[a] Extrapolated from 50°C., using $E^{\ddagger} = 19$ kcal./mole (670).
[b] Estimated using the Grunwald-Winstein correlation (equation 11).
[c] Extrapolated from 55°C., using $E^{\ddagger} = 25$ kcal./mole.
[d] Extrapolated from 25°C., using $E^{\ddagger} = 23.0$ kcal./mole.
[e] Estimated from the data of reference 61, using $E^{\ddagger} = 25$ kcal./mole.

that a phenyl group is as effective in stabilizing a carbonium ion as are two methyl groups (378).

(d) Effect of solvation

The ionization energies in table 21 are too high to permit any reasonable chemical reaction. In a condensed phase, however, these energies will be greatly lowered by solvation. Various attempts have been made to estimate the magnitude of this solvation energy to indicate whether the ionization mechanism is a reasonable one for these halides. In 1939 Ogg (483) likened carbonium ions to inorganic cations and obtained the result that the ionization of methyl bromide would require an energy greatly in excess of 50 kcal./mole. He considered all of the alkyl halides to be similar to methyl, and on this basis he discounted the possibility of an ionization process for the reaction of any alkyl halide. Data such as that in table 21 were not known at that time; it was not thought that the difference in the heats of formation of methyl and *tert*-butyl cations could be as high as the value now known to be 96 kcal./mole.

In 1946, Evans (234) undertook more extensive calculations using later, more abundant thermodynamic data. His results indicated that the ionization of methyl bromide in water would require some 87 kcal./mole, although *tert*-butyl bromide would require only 24 kcal./mole. The latter energy is readily accessible for chemical reactions in solution. Evans' calculations of the solvation energies of the various carbonium ions, however, were rather crude; his results could be in error by as much as 50 kcal./mole.

Recently Franklin (262) has attempted similar calculations using modern data. His method of calculating the energies and entropies of solvation of carbonium ions are as good as any available at present. Indeed, his final results are fortuitously close to the experimental values. The calculated energies of activation for the hydrolysis of *tert*-butyl halides in 80 per cent ethanol are the same as the experimental values within the limit of uncertainty of the latter. The

TABLE 23

Relative solvolysis rates of arylmethyl chlorides

Solvent	Temperature	Relative Rates						References
		t-C_4H_9Cl	$C_6H_5CH_2Cl$	$C_6H_5CHClCH_3$	$C_6H_5C(CH_3)_2Cl$	$(C_6H_5)_2CHCl$	$(C_6H_5)_3CCl$	
	°C.							
40% Ethanol, 60% ethyl ether	25	—	(1.0)[a]	—	—	(2000)[a]	(30,000,000)[a]	(476)
Ethanol	50	1.00	0.082	1.08	—	290	—	(19, 298, 366, 617, 670)
80% Aqueous ethanol	50	1.00	0.0121	0.90	—	~1300[b]	—	(350, 646, 647, 670)
50% Aqueous ethanol	50	1.00	0.00194	—	—	—	—	(350, 670)
Methanol	50	1.00	0.059	2.17[c]	—	1010[d]	—	(5, 185, 298, 366, 492, 670)
90% Aqueous acetone	25	1.00	—	—	620	23	—	(59, 111, 185)
85% Aqueous acetone	25	1.00	—	—	—	—	4,600,000	(185, 610)
80% Aqueous acetone	25	1.00	—	0.28[e]	—	40	—	(59, 185, 350, 366)
70% Aqueous acetone	25	1.00	0.0028[f]	—	—	25	—	(59, 185, 298, 571)
50% Aqueous acetone	25	1.00	0.0010	—	—	—	—	(75, 185, 333, 488)
Acetic acid	50	1.00	0.0054	1.99	—	—	—	(298, 524, 585)
Formic acid	15	1.00	~0.00017[g]	2.3	—	—	—	(61, 236, 367, 653a, 653b)

[a] Relative rates based on benzyl chloride.

[b] Extrapolated from 25°C., using $E^{\ddagger} = 19.7$ kcal./mole (1).

[c] At 70°C.

[d] At 25°C.

[e] At 70°C.

[f] Extrapolated from 60°C., using 20.4 kcal./mole, and estimated from 66.7 per cent aqueous acetone, using the Grunwald–Winstein correlation.

[g] Extrapolated from 25°C., using $E^{\ddagger} = 25$ kcal./mole.
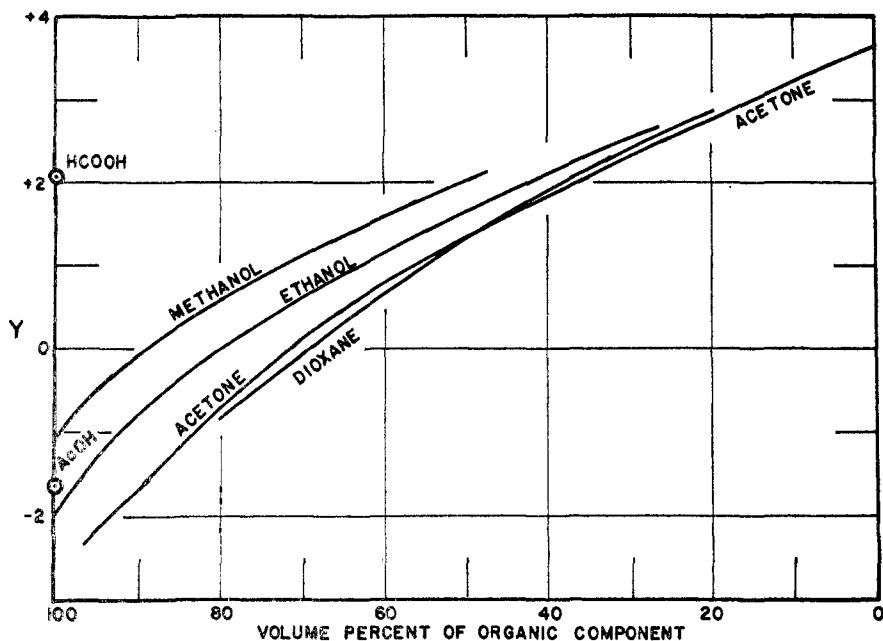
Fig. 11. Y values of various aqueous solvent mixtures

calculated rate constants for the hydrolyses are off by only a factor of ten. The calculations demonstrate that the ionic mechanism is not energetically unreasonable, at least for tertiary halides.

The various properties which contribute to the ability of a solvent to solvate ions may be termed collectively the "ionizing power" of the solvent. A measure of this ionizing power will be the rate of solvolysis of an alkyl halide which reacts by preliminary ionization. Grunwald and Winstein (298) have defined the ionizing power, Y, of a solvent as the logarithm of the rate of solvolysis of tert-butyl chloride therein relative to the rate of solvolysis in 80 per cent aqueous ethanol. Y values for a number of solvent systems are given in figure 11.[4]

Grunwald and Winstein found that the logarithms of the solvolysis rates of many compounds give linear correlations in Y which can be expressed by equation 11. k_0 is the rate of solvolysis in the standard solvent, chosen as 80 per cent aqueous ethanol.

$$\log k = mY + \log k_0 \tag{11}$$

The slope m measures the susceptibility of the substrate to the ionizing power of the solvent relative to tert-butyl chloride. A few representative values are given in table 24. The Grunwald–Winstein correlation has severe limitations (584, 653d). Different solvent systems yield different correlation lines. These dif-

[4] The Y values of acetic and formic acids and of aqueous ethanol and methanol mixtures were taken from Grunwald and Winstein (298). The values for aqueous dioxane and acetone mixtures were calculated from the more recent data of Cropper, Spieth, and Olson (185).

TABLE 24

Grunwald–Winstein constants for some alkyl halides

Alkyl Halide	Temper-ature	log k_0	m^*	References
	°C.			
tert-Butyl chloride..............................	25	−5.034	1.000	(298)
tert-Butyl bromide.............................	25	−3.472	0.940	(670)
tert-Amyl bromide..............................	25	−3.21	0.90	(123, 129, 161, 205)
α-Phenylethyl chloride.........................	50	−3.808	1.195	(298)
Neopentyldimethylcarbinyl chloride............	25	−3.661	0.858	(112)
α-Methylallyl chloride..........................	25	−6.314	0.894	(298)
Dineopentylmethylcarbinyl chloride............	25	−2.264	0.698	(112)
Benzhydryl chloride............................	25	−2.779	0.757	(298)

* Valid for ethanol-water mixtures.
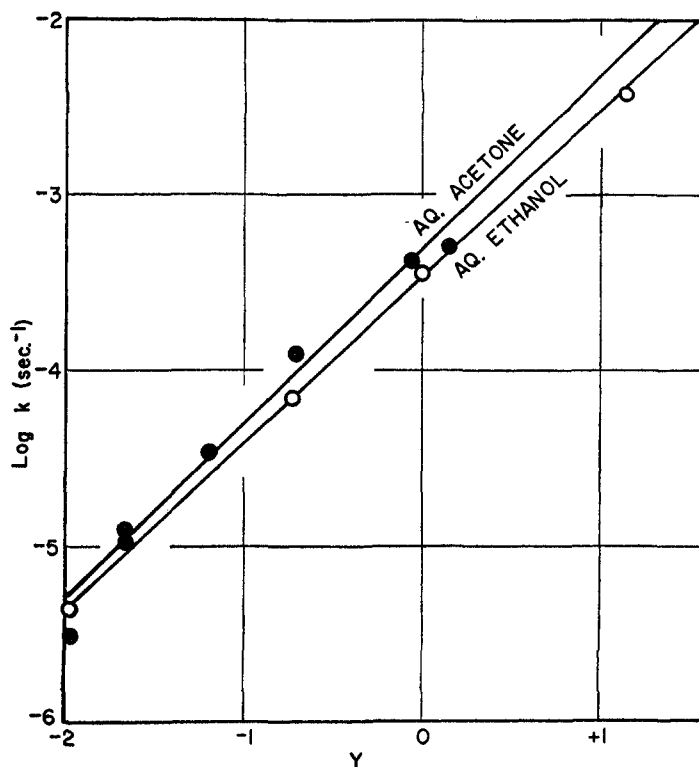
FIG. 12. Solvolysis rates of *tert*-butyl bromide as a function of **Y**

ferences are small when the system is structurally similar to *tert*-butyl chloride; for example, *tert*-butyl bromide gives slopes which differ only slightly for aqueous acetone and aqueous ethanol solutions (figure 12). Greater structural differences result in correlation lines for different solvent systems which may differ markedly from each other. Benzhydryl chloride in different solvent systems is a clear example (figure 13). These limitations imply that theoretical considerations
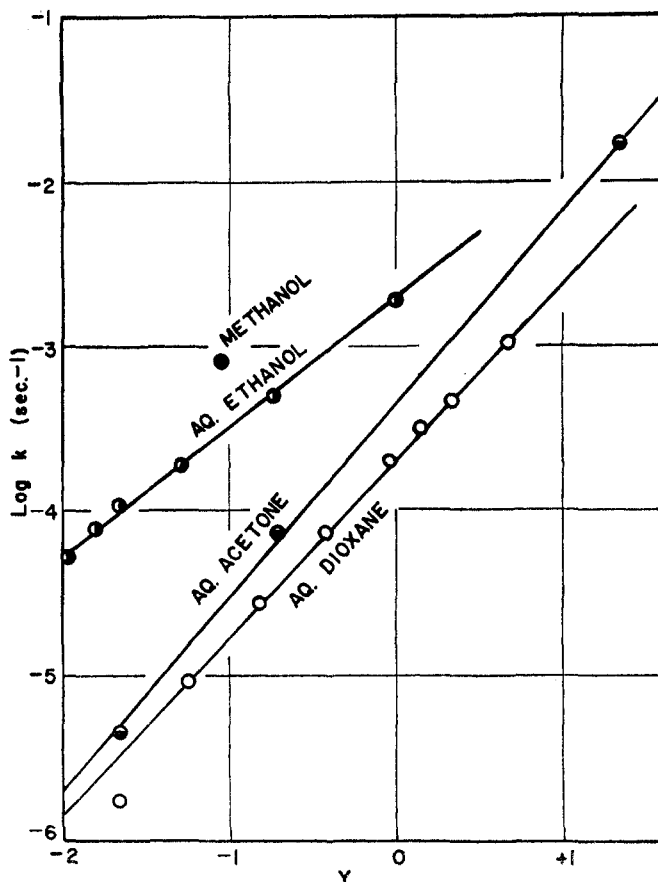
FIG. 13. Rates of solvolysis of benzhydryl chloride as a function of **Y**

based on the Grunwald–Winstein correlation must be made with circumspection. Nevertheless, the correlation is useful as a means of roughly estimating solvolysis rates and has been shown to account for the free energy of ionic solvation of potassium chloride in aqueous methanol mixtures (347a).

Swain, Dittmer, and Kaiser (600, 602) have extended a two-parameter equation to a variety of systems. Swain, Mosely, and Bown (607) have also proposed the use of a four-parameter equation. The computed values of the parameters are empirical constants which may be useful for estimating reaction rates but they have little theoretical value (see page 637).

The dielectric constant has long been considered to be one of the important attributes of overall solvent "ionizing power." Equation 12, which is due to Kirkwood (395), has been suggested (275) to correlate the effect of solvent change with the rates of reactions which involve dipolar ground states and transition states. In equation 12, D is the macroscopic dielectric constant of the solution, μ and $\mu_{\ddagger}$ are the dipole moments of the ground state and transition
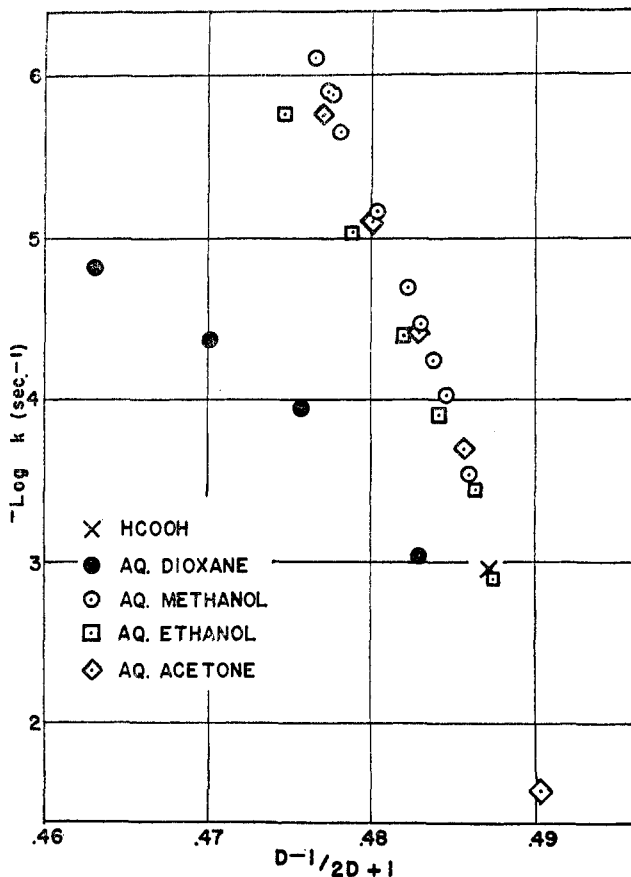
Fig. 14. Solvolysis rates of *tert*-butyl chloride in various solvent mixtures as a function of $(D - 1)/(2D + 1)$ at 25°C.

state, respectively, and r and $r_{\ddagger}$ are the respective molecular radii. Experimentally, linear relations between $\log k$ and the function $(D - 1)/(2D + 1)$ have been reported for several systems (166, 400).[5]

$$\ln k = \ln k_0 - \frac{1}{kT} \cdot \frac{D - 1}{2D + 1} \left(\frac{\mu^2}{r^3} - \frac{\mu_{\ddagger}^2}{r_{\ddagger}^3} \right) \tag{12}$$

The relationship, however, has its limitations. In figure 14 the rates of solvolysis of *tert*-butyl chloride in a variety of aqueous solvent mixtures are plotted logarithmically against the function $(D - 1)/(2D + 1)$. The various sets of points define the loci of curves which are distinctly non-linear. The curves for aqueous methanol, aqueous acetone, and aqueous ethanol mixtures are rather close together. The point for the homogeneous solvent formic acid fits in strik-

[5] Functions involving either $1/D$ or $(D - 1)/(2D + 1)$ have been used to correlate rates. If $(D - 1)/(2D + 1)$ is expanded in a power series of $1/D$, it is readily seen that above $D \cong 5$, $(D - 1)/(2D + 1)$ is essentially a linear function of $1/D$. The author is indebted to Dr. A. H. Fainberg for this observation.

ingly with these curves. The approximate slope for these groups of points is consistent with a C—Cl bond length ~ 0.5 A. greater than normal at the transition state. The locus of the points for aqueous dioxane is more strongly curved.

The dielectric constant, however, is frequently an inadequate measure of ionizing power. It has been emphasized recently that in mixtures of water and inert solvents, the actual water content is more important than any dielectric constant function (106a, 347a, 582a); e.g., in figure 11 the Y curves for aqueous dioxane and aqueous acetone solvents are closely similar, although the dielectric constants for particular mixtures differ widely (for example, at 20 volume per cent water: aqueous dioxane, $D = 11$; aqueous acetone, $D = 32$). Specific solvation of the leaving anion by four water molecules has been suggested (106a) (compare Section III,C,6).

(e) Effect of ionic strength

The ionizing power will be influenced by the ionic strength of the solution; an increase in the ionic strength generally causes an increase in solvolysis rate. Bateman, Church, Hughes, Ingold, and Taher (59) have treated the effect of ionic strength quantitatively by an extension of the Debye–Hückel theory to activity coefficients of dipoles. The resulting equations were tested by solvolyses of *tert*-butyl bromide in 90 per cent and 70 per cent aqueous acetone. The comparison of the theoretical curves with the experimental points showed good agreement. This agreement is all the more remarkable in that salt concentrations were used well above those for which the simple Debye–Hückel approximations are valid. Furthermore, in 90 per cent acetone salts are highly associated into ion-pairs (494). The effect of this point has recently been scrutinized by Nash and Monk (469), who found that the agreement was still fair, although not unique. Spieth and Olson (583) criticize this quantitative approach on the grounds that the theory does not work for known dipoles in aqueous solution and hence would not be expected to be successful with transition states.

(f) Effect of electrophilic catalysis

The effect of Lewis acids in enhancing the extent of ionization of triarylchloromethanes has been mentioned on page 611. In a sense, the ability of Lewis acids to coordinate with halide ions may be considered as a specific solvating effect which can reduce the energy of a dipolar transition state. Such Lewis acids as Ag^+ and Hg^{++} are well known in a qualitative way to enhance the reactivity of alkyl halides. Quantitative studies, however, frequently run into complications. Very strong Lewis acids will coordinate with the hydroxylic solvent and will not be available to the alkyl halide. Silver and mercuric cations have received considerable study as mild Lewis acids which do not complex with the solvent. The precipitated silver halide formed, however, is itself a catalyst for the reactions of alkyl halides (361, 519, 558), the more so apparently when photosensitized (467). These heterogeneous reactions may result in complex kinetics. The kinetic orders which have been reported for the reaction of alkyl halides with silver nitrate vary from second to higher non-integral kinetic orders ranging up to 3.5 (136, 221, 445, 509, 510, 512). The system has been used,

however, for determining the relative reactivities of alkyl halides (23, 135, 221, 445, 467, 480, 511).

Mercuric halide produced when mercuric ion is used as an electrophilic catalyst remains in solution, although the salt is largely unionized. Early work (473, 519) showed that mercuric salts are indeed catalysts for the solvolysis reactions of alkyl halides and indicated that the catalyst is deactivated by the formation of halide complexes of the type HgX_4^-. The active agent has been shown to be Hg^{++} (70, 525). The equilibria involving the various species Hg^{++}, HgX^+, and HgX_2 have been explicitly considered in the derivation of a kinetic equation which yields meaningful rate constants (70). The rate constants for a number of alkyl halides have been determined in this manner (70, 480).

Optically active α-phenylethyl chloride is known to racemize in liquid sulfur dioxide by a process which cannot be a direct displacement reaction since the rate is unaffected by chloride ion (80). The postulate that the racemization involves the symmetrical α-phenylethyl carbonium ion and that styrene is not involved is supported by the absence of loss of any deuterium during the racemization of α-trideuteromethylbenzyl chloride in phenol (308a). Similarly, α-mesitylethyl chloride racemizes in acetone by first-order kinetics (145).

The racemization of α-phenylethyl chloride in a variety of solvents in the presence of Lewis acids has been used as a system for estimating relative electrophilic powers (90). In at least some of these cases, styrene has been demonstrated not to be an intermediate; e.g., in the presence of stannic chloride in benzene solution at room temperature, racemization occurs rapidly without the production of styrene, even though styrene was shown to be stable under the reaction conditions (93). Although ionization to a racemic carbonium ion which subsequently combines with chloride ion has been the commonly accepted interpretation of these racemization experiments (324), Farinacci (249) has assumed complete inversion at each step of the reaction sequence and has developed kinetic expressions which fit the data of Bodendorf and Böhme (90). So many adjustable parameters were required, however, that the significance of this interpretation is uncertain.

Kornblum, Smiley, Blackwood, and Iffland (400a) have recently discussed the effect of electrophilic catalysis in changing the course of reaction.

(g) Proton catalysis

The solvolyses of *tert*-alkyl fluorides are catalyzed by acids (144), presumably because of the marked hydrogen-bonding characteristics of fluoride ion. In aqueous alcohol and aqueous acetone solutions, triphenylmethyl fluoride (606) gives about the same types of Grunwald–Winstein correlations referred to *tert*-butyl chloride as does benzhydryl chloride (figure 13). In acetic acid, however, the rate of solvolysis of triphenylmethyl fluoride is $\sim 10^3$ faster than the correlation would predict (606). The rate enhancement is undoubtedly due to specific interactions between the leaving fluoride ion and the acidic solvent.[6]

_____

[6] Swain and Mosely (606) apparently did not consider this interpretation of their results.

Other halides are not subject to acid catalysis, at least in hydroxylic solvents. Acceleration by proton donors in various reactions in non-hydroxylic solvents is nevertheless known. The rearrangement of camphene hydrochloride to iso-bornyl chloride (page 698) in inert solvents is catalyzed not only by the usual Lewis acids but also by phenols and by hydrogen chloride (50, 451). Specific solvation of the leaving halide ion by hydrogen-bonding is plausibly involved. Consistent with this postulation is the fact that the acceleration of the rate is proportional to the acidity of the phenolic catalyst (43). Similar hydrogen-bonding catalysis has been demonstrated for reactions of *p*-methoxybenzhydryl chloride in nitrobenzene solutions (48), of *tert*-butyl bromide in nitromethane solutions (274), and of triphenylmethyl chloride in benzene solutions (321, 604).

tert-Butyl chloride solvolyzes only 0.73 as rapidly in 90 per cent D_2O–10 per cent dioxane as in 90 per cent H_2O–10 per cent dioxane. This result has been explained on the basis that solvent deuterium bonds to the leaving halide are not as effective as hydrogen bonds (599). In 50 per cent D_2O–50 per cent acetone *n*-hexyl bromide solvolyzes 0.84 as fast as in 50 per cent H_2O–50 per cent acetone (489), although solvolysis of methyl chloride or iodide occurs at the same rate in water and in deuterium oxide (599).

Acid catalysis is involved in many reactions in which a carbonium ion is formed by the breaking of a carbon–oxygen bond. Examples important as solvolytic displacement reactions are the acid-catalyzed hydrolyses of certain carboxylic esters (corresponding to the hydrolysis mechanism A″1 of Day and Ingold (194) and A_{AL} of Ingold (378)). Alkyl–oxygen fission was elegantly established for solvolyses of esters of tertiary alcohols by Cohen and Schneider (155) and has since been amply confirmed (133, 154, 214, 217, 588, 702). Many examples of alkyl–oxygen fission are known for benzhydryl and some allyl esters, although in a number of these cases desirable control experiments are lacking (6, 27, 28, 29, 30, 31, 33, 36, 37, 38, 188, 227, 386, 387). The mechanism of such acid-catalyzed reactions can be represented as:

$$RCOOR' + H^+ \rightleftharpoons R\overset{\overset{\displaystyle O^+H}{\|}}{C}\text{—}OR' \rightarrow RCOOH + R'^+ \rightarrow \text{products}$$
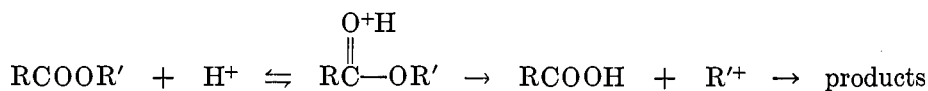
Alcoholysis of triphenylmethyl benzoate with alkyl–oxygen fission is accomplished without acid catalysis (305). This result suggests that when the stability of the carbonium ion is sufficiently high, a carboxylate ion itself can split off:

$$(C_6H_5)_3COCOC_6H_5 \rightarrow (C_6H_5)_3C^+ + {}^-OOCC_6H_5$$
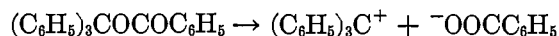
Analogous results have been obtained in solvolyses of triphenylmethyl acetate (131).

2. The recombination step

According to the ionization hypothesis, the carbonium ion formed in the first step can react with any available nucleophilic species in solution. If this reaction

occurs with the halide ion formed, the original alkyl halide is regenerated. The kinetic expression for this case is given by equation 13.

$$-\frac{d[RX]}{dt} = \frac{k_1[RX]}{\frac{k_2}{k_3}[X^-] + 1} \tag{13}$$

The subscripts on the rate constants in equation 13 refer to the various steps in the overall mechanism (page 611). If the halide ion cannot compete with solvent for the reactive intermediate, $k_2[X^-] \ll k_3$, and the left-hand side of the denominator will be small compared to 1. For such cases, equation 13 reduces to the equation for simple first-order kinetics. If the term $\frac{k_2}{k_3}[X^-]$ is appreciable, it will become progressively more important as halide ion builds up during the course of the reaction. The instantaneous rate represented by the differential will become progressively smaller than that expected for simple first-order kinetics; i.e., the reaction is slowed down by a "mass action" effect or "external return" (663a).

Such progressive slowing down of the first-order reaction will be counteracted to a greater or lesser extent by the increase in ionic strength during the course of the reaction as halide ion is liberated. This change in the ionic strength could very probably be "swamped out" by the use of a high concentration of an inert salt such as lithium perchlorate. Unfortunately, no investigations of the "mass law" effect have been reported using this technique (however, cf. page 720).

The rate of hydrolysis of triphenylmethyl chloride in 85 per cent aqueous acetone is *decreased* fourfold by 0.01 M sodium chloride (611). This result is a striking demonstration of the mass law effect, since other, "non-common ion," salts effected no change in the rate. The solvolysis of p,p'-dimethylbenzhydryl chloride in aqueous acetone shows marked deviations from simple first-order kinetics even in rather dilute solutions (65). Similar deviations, smaller in magnitude, are reported for the reactions of p-alkylbenzhydryl chlorides in 80 per cent aqueous acetone, although in 90 per cent aqueous acetone the instantaneous rates rise during the course of the reaction (147). The difference was interpreted (147) as the resultant of opposing mass law and ionic strength effects. The latter is more important in less aqueous solvents and for these compounds it is the predominating effect in 90 per cent aqueous acetone. A similar line of argument has been suggested to explain the behavior of benzhydryl chloride itself, which accurately follows first-order kinetics in 80 per cent aqueous acetone (146). The supposition in this case that the two opposing effects exactly cancel is supported to some extent by the fact that in 90 per cent aqueous acetone the instantaneous rates again show the progressive rise of a predominating ionic strength effect.

The contrast between the two effects has been satisfactorily demonstrated by the comparison of the initial rates of solvolyses of benzhydryl bromide and chloride, alone and in the presence of added chloride and bromide ion (71, 582a). The use of initial rates avoids the complications arising from the constantly changing system. The procedure for evaluating the rate constants used by Benfey, Hughes,

TABLE 25

Solvolysis rates of benzhydryl halides with halide ion

Added Salt	Initial Solvolysis[a] Rates in 80 Per Cent Aqueous Acetone at 25°C., $10^5 k$ (sec.$^{-1}$)		
	$(C_6H_5)_2CHBr$ (71)	$(C_6H_5)_2CHCl$ (71)	(582a)[b]
None	153	7.00	6.06
0.1 M LiBr	133	8.16	8.03
0.1 M LiCl	194	6.09	5.22
0.1 M LiClO₄			8.51

[a] Rates listed are equivalent to the rates of liberation of halide ion.

[b] In aqueous acetone containing 50.4 mole per cent water (~80.2 per cent by volume) at 24.8°C.

and Ingold (71) has been criticized by Spieth (582a). Her procedure yields rate differences which are similar qualitatively but differ quantitatively. Some of the results of both sets of investigators are given in table 25. These results show that the initial rates are decreased by the common ion and increased by the non-common ion. Explanation of these results in terms of a simultaneous hydrolysis and direct displacement by halide ion requires that the salt effect on the hydrolysis reaction be negative for lithium bromide and chloride but positive for lithium perchlorate (582a).

The rate of solvolysis of benzyl chloride in 60.7 per cent (by weight) aqueous dioxane is slightly decreased by the presence of small amounts of sodium chloride or hydrochloric acid (86). The use of this result as evidence for a mass law effect in this system is, however, invalidated by the extreme sensitivity of the reaction rate to slight changes in the medium (86).

In aqueous acetone *tert*-butyl halides show a slight increase in the instantaneous rate which has been attributed to an ionic strength effect (64). A mass law effect for *tert*-butyl chloride has been reported (484), but the magnitude is very small. Its significance is all the more questionable in view of the quantitatively different rate-enhancing effects found for different salts towards the solvolysis of *tert*-butyl halide in aqueous acetone solutions (583). No mass law effect could be detected in the solvolysis of *sec*-butyl bromide in 75 per cent aqueous alcohol (149).

For reactions of the carbonium-ion intermediate with nucleophilic species other than the solvent, the use of an inert solvent makes possible the detection of otherwise unobservable mass law effects. In dilute benzene solution the rate of exchange of triphenylmethyl chloride with a quaternary ammonium radiochloride is independent of the chloride-ion concentration (604). A rate-determining ionization to triphenylmethyl cation is consistent with the results. In benzene solution, of course, the ionic species must be present as ion-pairs or as higher aggregates.

tert-Butyl chloride in formic acid solution exchanges with radioactive chloride ion by a process which is not bimolecular (401). For the assumption of an ionization mechanism,

$$RCl \underset{k_2}{\overset{k_1}{\rightleftarrows}} R^+ + Cl^-$$
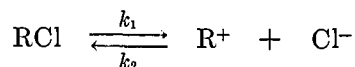
k_1 was determined to be 3×10^{-4} sec.$^{-1}$ at 15°C. (401). In formic acid containing small amounts of water, *tert*-butyl chloride hydrolyzes at a rate independent of the water concentration (61). The first-order rate constant, 3.7×10^{-4} sec.$^{-1}$ (61), is that of the postulated rate-determining ionization step and is in good agreement with the value derived from the exchange experiments.

The reactions of benzhydryl halides and of *tert*-butyl halides with amines in liquid sulfur dioxide are also postulated to involve a preliminary ionization. Both systems show rate retardations typical of a mass law effect (89, 130).

It should be emphasized that the mass law effect discussed in this section results from the reaction of a carbonium ion with a leaving group which has become equilibrated in the mixture. It should not be confused with the reaction of the carbonium ion with the *same* group to which it was originally attached, for in this case no mass law effect is possible (compare with internal return, pages 658 and 720).

3. The product step

(a) Reaction of the carbonium-ion intermediate with anions

The nature of the reaction of the carbonium-ion intermediate with nucleophilic species to form stable covalent compounds can be investigated directly for those few carbonium compounds which can be isolated as such. A well-known example of this type is the alkaline fading of crystal violet (XXIV), in which the reaction of the dye cation with hydroxide ion forms the colorless carbinol base (XXV). The most careful investigation of this reaction is probably that of Turgeon and LaMer (631; *cf.* also 409).
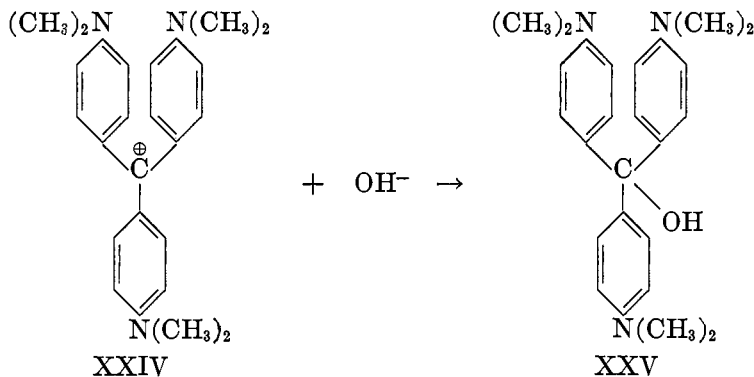
The reaction is second order, with an activation energy of 15 kcal./mole, and shows a primary salt effect behavior which is excellently interpretable on the basis of the Debye–Hückel theory (631).

Since triphenylmethyl chloride is appreciably ionized in several inert solvents, it is possible in principle to study directly the reaction of its carbonium ion with hydroxylic compounds. The only work of this kind which has been reported (274) is discussed in detail on page 654 (*cf.* also page 649).

More common are solvolyses run in the presence of an added nucleophilic

species. In such cases the intermediate can react either with solvent or with the addend. The mass law effect (page 624) results from that example in which the nucleophilic addend is the same species as the leaving group.

Kinetic expressions have been published for the reactions of triphenylmethyl cation (611):

$$(C_6H_5)_3CX \xrightarrow{k_1} (C_6H_5)_3C^+ + X^-$$

$$(C_6H_5)_3C^+ + Y^- \xrightarrow{k_Y} (C_6H_5)_3CY$$

$$(C_6H_5)_3C^+ + H_2O \xrightarrow{k_0} (C_6H_5)_3COH_2^+ \rightarrow (C_6H_5)_3COH + H^+$$
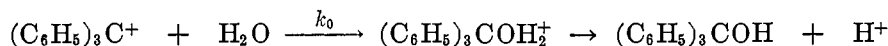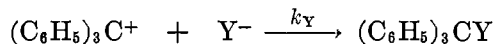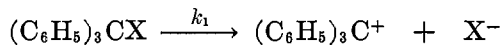
The ratio k_Y/k_0 measures the ability of a nucleophilic reactant to compete with water for the carbonium ion. The derivation is essentially that of Ogston (484), with the exception that Ogston's definition of the competition factor does not take explicit account of the concentration of water in the solvent. It is a necessary condition for the carbonium-ion mechanism to hold that the competition factor of any Y must be independent of the nature of X. Competition factors for several ions towards triphenylmethyl fluoride, chloride, and thiocyanate show rather fair agreement for a variety of solvent mixtures (table 26).

Competition factors towards benzhydryl cation are considerably lower than towards the triphenylmethyl cation; e.g., k_Y/k_0 for azide ion is 1.7×10^2 and 2.8×10^5, respectively; the corresponding values for chloride ion are 1.2×10^2 and 3.1×10^3, respectively (611). This change is intelligible on the sound basis that triphenylmethyl cation requires a greater free energy of activation for its destruction than does the less stable benzhydryl cation. If the free energy of activation is greater, a greater range is possible of values which depend on the nucleophilicities of the competing bases. As an example, if $\Delta F^{\ddagger}$ for the reactions of two carbonium ions with water is, respectively, 10 and 5 kcal./mole, the reaction with a substance twice as nucleophilic as water will, to a first approximation, halve these values to 5 and 2.5 kcal./mole, respectively. The differences correspond to competition factors of 4000 and 60, respectively. *The less stable a carbonium ion is relative to its reaction with one nucleophilic substance, the less sensitive its reactivity will be to the nucleophilicities of other reactants.*

The difference in solvolysis reactivities of the respective halides implies that

TABLE 26

Competition factors towards triphenylmethyl cation

Source of Carbonium Ion	Solvent	Temperature	$10^{-4}k_Y/k_0$ (611)		
			N₃⁻	OH⁻	S₂O₃⁻⁻
		°C.			
(C₆H₅)₃CF..................	80% Aqueous acetone	25	24	—	—
	50% Aqueous acetone	25	28	5.3	1.9
(C₆H₅)₃CNCS..............	50% Aqueous acetone	25	31	4.9	—
(C₆H₅)₃CCl..................	85% Aqueous acetone	−34	11	—	—
	92% Acetone, 2% dioxane, 6% water	25	9	1.0	0.3

tert-butyl cation is less stable than the benzhydryl cation (table 23); correspondingly, the competition factor of azide ion towards *tert*-butyl cation is only 3.9 (611), about one-fiftieth the value towards benzhydryl cation.

The ability of azide ion to compete with solvent for carbonium ions was first demonstrated for benzhydryl systems (65, 146, 147). The experimental results exclude the possibility that bimolecular displacement of the alkyl halide by azide ion is important for these systems. When the solvolysis of p,p'-dimethyl-benzhydryl chloride in 85 per cent aqueous acetone is carried out in the presence of 0.05 M sodium azide, the initial first-order rate constant is increased by a factor of 1.5 (65). This increase is understandable as a salt effect, especially since other salts produce a corresponding rate increase. The product, however, consists of 60 per cent p,p'-dimethylbenzhydryl azide and 40 per cent of the corresponding carbinol. For this amount of alkyl azide to arise as a result of a direct displacement reaction, the initial rate would have to increase by a factor of 2.5, if salt effects are neglected. Other attempts to account for product compositions as resultants of S_N2 reactions have also failed (59).

The temperature coefficient of the competition factor in this system corresponds to an energy of activation for the reaction of the carbonium ion with azide ion that is 4.0 kcal./mole higher than the corresponding reaction with solvent (320). This result clearly demonstrates that the reaction of the carbonium ion with an anion is a process requiring definite activation, and has been explained on the grounds that the electrostatic bonding of the solvation shells of the ions is destroyed in the process (320).

The nature of reactions with azide ion has been placed in some question recently by Swain and Kreevoy (604), who found that the second-order reaction of triphenylmethyl chloride with tetraalkylammonium azide in benzene solution is faster than the first-order reaction with chloride ion. Since ionization is the rate-determining step of the latter reaction, these results necessitate some direct reaction with azide ion, perhaps of the direct displacement type. In benzene solution, however, the reactions are undoubtedly occurring within ionic aggregates (604) and the interpretation is far from clear-cut.

Benzhydryl chloride has been reported to give a good yield of benzhydryl isothiuronium chloride (XXVI) with thiourea in ethanol at a rate only slightly higher than the rate of solvolysis with ethanol alone (394). The many examples of the reactions of substituted benzhydryl esters with various nucleophilic compounds are undoubtedly reactions involving intermediate carbonium ions, although in many cases desirable kinetic data are lacking (27, 28, 30, 31, 35, 36, 37, 38, 386). The hydrogen phthalates in dilute alkali undergo dismutation rather

$$(C_6H_5)_2CHSC \overset{\displaystyle NH_2}{\underset{\displaystyle NH_2^{\oplus}}{}} \quad Cl^{\ominus}$$

XXVI
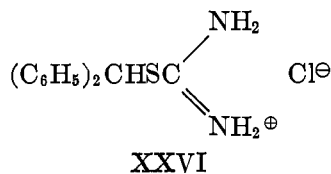
readily to give the dialkyl phthalate, a result which indicates that the ester anion itself can compete effectively with solvent for the intermediate carbonium ions.

Reaction with sodium p-toluenesulfinate produces the corresponding sulfone; reaction of the carbonium ion with the salt produces a new sulfur–carbon bond rather than an oxygen–carbon bond. Bonding does not necessarily occur at the same atom in a nucleophilic species for reaction with a carbonium ion as for a direct displacement reaction. Thus, the formation of p-tert-butylphenol in the reaction of tert-butyl chloride with alcoholic sodium phenoxide is undoubtedly the result of a carbonium-ion reaction (page 588). In a recent discussion (400a), an attempt has been made to generalize this phenomenon.

As in the case of the mass law effect, the kinetic differences due to the competition between various nucleophilic agents are accentuated in an inert solvent. In liquid sulfur dioxide benzhydryl chloride reacts at approximately the same rate with fluoride ion, water, pyridine, and triethylamine (66). Similar observations are obtained with m-chlorobenzhydryl chloride (66, 89). The reactions of tert-butyl bromide in nitromethane with bromide ion, chloride ion, nitrite ion, pyridine, water, ethanol, and phenol occur at approximately the same initial rate (130, 199). Initial rates are compared in this system, since elimination occurs and adds a complication to the kinetics. These results, however, are certainly consistent with a rate-determining ionization of the alkyl halide.

(b) Elimination to olefin

When the carbonium-ion intermediate possesses a β-hydrogen, elimination of a proton is possible with the consequent production of a double bond. *A necessary consequence for the ionization hypothesis to be valid is that the proportion of solvolysis products and elimination products must be independent of the nature of the leaving group* (369). The several tests of this corollary which have been provided show indeed that for those reactions for which the S_N1 mechanism is postulated the proportion of reaction which results in elimination is, within experimental error, independent of whether a chloride, bromide, iodide, or dimethylsulfonium salt is used (table 27).

A further corollary is that the proportions of isomeric olefins formed by elimination should also be invariant with respect to the leaving group. The ethanolyses of tert-amyl bromide and of tert-amyldimethylsulfonium ion give, respectively, 82 per cent and 87 per cent of 2-methyl-2-butene and 18 per cent and 13 per cent of 2-methyl-1-butene (163). The differences are no greater than

TABLE 27

Proportion of elimination in solvolysis of RX

R	Solvent	Temperature	X = Cl	X = Br	X = I	S(CH₃)₂⁺	Reference
			Per cent elimination				
		°C.					
2-Octyl	60% Ethanol	100	13	14			(369)
tert-Butyl	80% Ethanol	25	17	13	13		(162)
	80% Ethanol	65.3	36			36	(163)
tert-Amyl	80% Ethanol	25.2	33	26	26		(374)
	80% Ethanol	50	40			48	(163)
Dimethylneopentylcarbinyl	85% Aqueous n-butyl cellosolve	25	65	65	65		(124)

TABLE 28

Solvolysis products from crotyl chloride (primary) and
methylvinylcarbinyl chloride (secondary)

Reaction Conditions	Chloride Used	X	Product Composition		Reference
			$CH_3CH=CHCH_2X$	$CH_3CHXCH=CH_2$	
			per cent	*per cent*	
Ethanol, 78°C.	Primary	OC_2H_5	92	8	(140)
	Secondary	OC_2H_5	82	18	
AgOH, H_2O, 25°C.	Primary	OH	45.2	54.8	(699)
	Secondary	OH	33.8	66.2	
CH_3COOAg, CH_3COOH, 25°C.	Primary	$OCOCH_3$	60	40	(541)
	Secondary	$OCOCH_3$	56	44	

the probable experimental error. The olefin mixtures from the solvolyses of di-methylneopentylcarbinyl chloride, bromide, and iodide in 85 per cent aqueous *n*-butyl cellosolve solution consist in each case of 81–82 per cent 2,4,4-trimethyl-1-pentene and 18–19 per cent 2,4,4-trimethyl-2-pentene (124). The olefin mixtures from the acetolyses of 2-pentyl tosylate and 2-pentyl brosylate at 70°C. consist in both cases of 16 per cent 1-pentene, 35 per cent *cis*-2-pentene, and 49 per cent *trans*-2-pentene (127).

4. Allylic rearrangement

The ionization of an allylic halide would produce a mesomeric cation which could react at either positive center. In an unsymmetrical allylic system the same carbonium ion will be produced from either of two isomeric allylic halides. The postulate that these halides solvolyze by preliminary ionization to a carbonium ion requires that each halide must produce the same product mixture. This criterion has been applied to reactions of crotyl chloride (XXVII: R = CH_3, R' = H) and methylvinylcarbinyl chloride (XXVIII: R = CH_3, R' = H). This system is somewhat unsatisfactory as a test of the criterion, since the rates of solvolyses are somewhat dependent on lyate-ion concentration (table 17). Nevertheless, solvolyses of these halides generally produce a mixture of isomeric products (table 28). The two isomers do not give exactly the same proportions of product isomers but the differences are in the direction consistent with the postulation that part of the solvolysis in each case occurs by bimolecular displacement. Many additional examples are available in a recent comprehensive review (700).

RCH=CHCHClR'
    XXVII $\searrow -Cl^-$

$$[RCH\text{---}CH\text{---}CHR']^+ \xrightarrow[-H^+]{ROH}$$

     $\nearrow -Cl^-$

RCHClCH=CHR'
    XXVIII   RCHORCH=CHR' + RCH=CHCHORR'
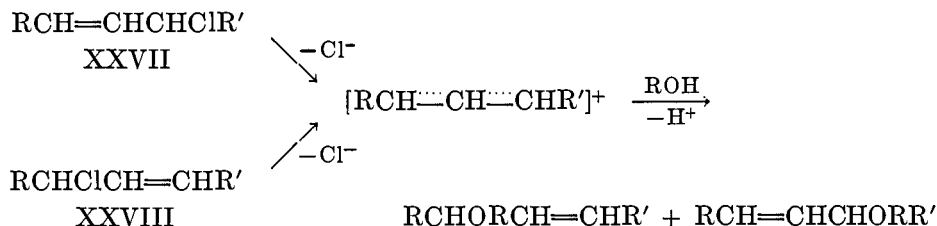
5. Stereochemistry

The simple concept of a carbonium ion as a planar system surrounded by a solvent shell requires that any asymmetry which may have existed at the reacting center must vanish during reaction; i.e., an optically active compound in which the single asymmetric carbon atom becomes a carbonium ion must produce totally racemic products. This requirement is met in several systems involving carbonium ions of the benzhydryl type.

The hydrogen phthalate of p-methoxybenzhydrol readily racemizes in a number of solvents (29). The hydrogen phthalates of p-phenoxybenzhydrol (38) and of p-anisyl-1-naphthylcarbinol (31) manifest reactions suggesting carbonium-ion formation and give racemic products. For example, the sodium salts in the presence of sodium p-toluenesulfinate yield the corresponding racemic p-tolyl sulfones. On standing in aqueous solution, the sodium salts of the hydrogen phthalates deposit the *half-racemized* neutral dialkyl phthalates. In these cases a consistent interpretation is that the carbonium ion which results from cleavage of one ester molecule reacts with the anion of another, which, having a negative charge, can compete effectively with solvent water as a reactive nucleophile. The original alkyl group of the ester has unchanged configuration; that which came from the carbonium ion is completely racemized.

Complete racemization in solvolyses of esters of arylmethylcarbinols is frequently observed (13, 30, 31, 227) but is not general. The stereochemistry of reactions of the parent α-phenylethyl system has been studied in some detail. Solvolysis of the chloride in ethanol or in methanol yields the corresponding ether with a small but definite net inversion of configuration (366, 389). In 60 per cent and 80 per cent aqueous acetone, α-phenylethyl chloride yields the alcohol with 5 per cent and 2 per cent inversion, respectively (366). One may question the significance of the incomplete racemization obtained, for in these systems the addition of base causes a small increase in rate (table 17). The inverted product could be said to have arisen from a competing direct displacement by solvent. This argument cannot be applied to the results of the acetolysis of α-phenylethyl chloride, since acetate ion causes no increase in rate (table 17) (585). Nevertheless, Steigman and Hammett found that the α-phenylethyl acetate formed is 15 per cent inverted and 85 per cent racemized (575). The result must be taken to indicate that in this system any intermediate involved cannot always have lost its asymmetry. Similar results have been obtained using α-phenylethyl tosylate. In acetic acid, the acetate is formed with 12 per cent net inversion; in ethanol, the ethyl ether is produced with 20 per cent inversion; in butanol, the butyl ether is formed with 27 per cent inversion (391).

The fact that racemization is accompanied by varying degrees of inversion of configuration renders very important the study of systems for which any bimolecular displacement reaction is exceedingly slow. α-Phenylneopentyl tosylate in acetic acid yields the corresponding acetate with 10 per cent net inversion of configuration (683).

Even with *tert*-alkyl systems, complete racemization is not observed. Solvolyses of 3,7-dimethyl-3-octyl acetate and chloride are reported to give partial

inversion (359; *cf.* 217). The methanolysis of hydrogen 2,4-dimethylhexyl-4 phthalate yields 4-methoxy-2,4-dimethylhexane with predominant inversion and only 40 per cent racemization (212, 213, 217). Under the same conditions hydrogen 2-phenylbutyl-2 phthalate yields a methyl ether with about 10 per cent inversion and 90 per cent racemization (702).

In each of the systems considered above a reactive intermediate is demonstrable by other criteria. The stereochemical approach can be readily applied to other systems in which the existence of an intermediate cannot be directly determined by other criteria. Secondary alkyl systems give results ranging from almost complete inversion to extensive racemization. 2-Butyl tosylate in ethanol produces 2-ethoxybutane with at least 90 per cent inversion of configuration (390). The products from the reaction of 2-bromoöctane with 60 per cent aqueous ethanol are about 70 per cent inverted (360). Ethanolysis of 1-phenyl-2-propyl tosylate is accompanied by 86 per cent net inversion, although acetolysis gives a 30 per cent yield of inverted product (660).

The stereochemistry of a primary aliphatic system has recently been studied by the use of hydrogen–deuterium asymmetry at the reacting center. The formolysis and acetolysis of butyl-1-*d* brosylate were found to yield almost completely inverted esters (591).

6. *"Lifetime" of the carbonium ion*

The stereochemical results of solvolysis demand that the simple picture of a symmetrical carbonium-ion intermediate be modified. In the Hughes–Ingold S_N1 mechanism (59) the stereochemical results are accommodated by the postulation of a "lifetime" for the carbonium ion. This lifetime is defined by the "time-lag" between reactions 1 and 3 in the following sequence, in which SOH represents a solvent molecule:

$$\text{R—X} \xrightarrow{\text{(1)}} \text{R}^+ + \text{X}^- \xrightarrow[\text{SOH}]{\text{(3)}} \text{ROS} + \text{X}^- + \text{H}^+$$
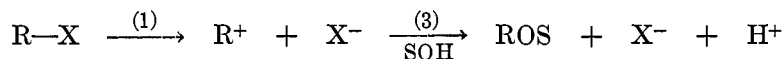
When this time-lag is large, the carbonium ion is able to become completely free. The free ion is symmetrical and is postulated to be electrostatically solvated by a surrounding solvent shell. Reaction 3 is postulated to occur by a simple collapse of the solvent shell. Totally racemic products will, of course, result. The assumption is implied that the more stable a carbonium ion is inherently, the longer will be its lifetime. Hence, the solvolyses of benzhydryl systems may be described in terms of long lifetimes for the carbonium ion which account for the complete racemization observed.

When the time-lag is relatively short, reaction 3 is postulated to occur before the leaving group has had a chance to recede very far. This group will then partially "shield" the frontside of the carbonium ion, and products with partial net inversion will result. The solvolyses of *tert*-carbinyl and α-phenylethyl systems are to be described in these terms.

This mechanism has been called both unimolecular (59), because only one

covalent bond is involved in the process, and polymolecular (250, 585), because many solvent molecules are required for solvation at the transition state.

For the cases in which the time-lag has vanished, reactions 1 and 3 are synchronous and the mechanism is that of S_N2 displacement. Some solvolyses of primary systems are to be so described. Hence, the S_N1 and S_N2 mechanisms are intended to be extremes of a continuous sequence with no dividing line defining the extremes. It is convenient to refer to an intermediate set of "borderline cases." Most solvolyses of secondary alkyl halides are to be described as belonging in this category.

The more ionizing the solvent and the more stable the carbonium ion, the longer will be the lifetime of the intermediate. The time-lag between reactions 1 and 3 will be longer and more racemization will result. At long lifetimes of the carbonium ion, addition of lyate ion should not affect the rate of reaction. At the opposite extreme, for S_N2 solvolyses, lyate ion enormously increases the reaction rate. For a continuous sequence from S_N2 to S_N1 mechanisms, varying degrees of facilitation of rate by added lyate ion will be observed. This postulate has recently been formalized (89); however, the authors of this scheme have never attempted a structural description of the mechanism of solvolysis of a borderline case. Unfortunately, although Hughes and Ingold and their collaborators have emphasized that borderline cases are to be represented by some sort of intermediate mechanism (59, 89, 276, 368), in several papers (204, 222, 365) such cases have been regarded as mixtures of S_N1 and S_N2 solvolyses. Thus, for example, we find the following statement (222): "In all these cases a fairly large part of the reaction in aqueous alcohol is bimolecular . . ."

7. Inadequacies of the S_N1 mechanism

Of fundamental importance in the S_N1 mechanism is the postulation of a carbonium-ion intermediate. A wide variety of evidence does point to the presence of an electron-deficient intermediate of some sort in many systems. Most of the criticism of the theory has related to the manner in which stereochemical results are accommodated. The concept of an independent carbonium ion shielded by the leaving group has caused no little confusion; for example, "if ionization were complete enough to permit the reaction to be called unimolecular, then the ion R^+ would be free enough from shielding effects so that a completely racemic product would result" (655). This objection was answered by defining unimolecular ionization as being essentially complete as soon as the system has passed over its energy barrier (59). Nevertheless, the shielding hypothesis has not met with general acceptance.

Shielding by the leaving group was placed on a sounder conceptual basis by Hammett (301), who suggested that the product of the ionization step is an ionpair. He implied that reaction with solvent, before dissociation of the ion-pair, would occur with inversion of configuration. Hammett's interpretation requires but little modification to account for the several recent phenomena, such as internal return, which are difficult to reconcile with the S_N1 mechanism. These results will be discussed in the sequel.

1. Hypotheses resulting from kinetics

(a) The "push-pull" termolecular mechanism

Bartlett and Nebel (48) studied the kinetics of the reaction of *p*-methoxybenz-hydryl chloride with small amounts of methanol in nitrobenzene solution. Both a first-order and a second-order kinetic dependence on methanol were found and were interpreted by solvation of the leaving chloride ion by one or by two methanol molecules. The alternative that one methanol molecule was attacking the central carbon atom directly was not ruled out but was thought less probable.

From the results of closely similar experiments, Swain was led to stress the importance of *specific* ionic solvation, not only of the leaving group but of the reacting carbon atom (597, 598, 603). The reaction of triphenylmethyl chloride with methanol in benzene solution in the presence of pyridine was found to have third-order kinetics, first order in triphenylmethyl chloride and second order in methanol (597). Pyridine was found not to affect the rate; the use of other tertiary amines such as quinoline and dimethylaniline led to approximately the same rate constants. The amines were used to react with the hydrogen halide liberated in the reaction. The addition of phenol, which alone reacts relatively slowly with triphenylmethyl chloride, caused one phenol molecule to replace one methanol in the third-order rate equation together with a sevenfold increase in the rate constant. *p*-Nitrophenol caused a greater than twentyfold increase in the rate. One reagent molecule was assigned a role specifically solvating the leaving halogen by hydrogen-bonding. The remaining methanol was considered to solvate the central carbon atom by a predominantly ionic bond. These conclusions were then extrapolated to encompass all solvolyses (597): "Simultaneous attack on both atoms is required to effect any reaction. In the rate-determining step one and only one molecule forms a solvation bond (chiefly ionic) to carbon; similarly one and only one hydroxylic molecule becomes bound by a hydrogen bond (ionic bond) to halogen. The result is always a push-pull termolecular mechanism with exactly third-order kinetics." This extrapolation can be criticized because of the vastly different solvation characteristics of benzene and such typically hydroxylic solvents as water and alcohol. Furthermore, Swain's interpretation is not a unique one; in fact, the evidence favors an alternative hypothesis (page 649). Bartlett (42) has also postulated that the rearward participation by a solvent molecule is to be regarded as a purely electrostatic solvation.

For reaction with a lyate ion, the solvent molecule at the rear is considered to be replaced by the ion; the resulting kinetics can then be described by the two-term equation 9 (603) and develops Swain's contention that there is only one mechanism for displacement. These proposals still do not account for the variation with structure of the relative rate ratios of the reactions represented by each term of equation 9. This variation is one of the distinctive features of the "borderline region." In particular, if the solvent is to be considered to assist at the rear by ionic bonding, it is difficult to see why *negative ions* are not more effective than they are in many cases.

The conception of a concerted termolecular displacement reaction later led to a modification in terms of the total bonding at the transition state (605). The postulates made were that the greater the nucleophilicity of the group attacking the reacting carbon at the rear, the greater the extent of "bond-making" at the transition state; the greater the electrophilic ability of the group attacking the leaving halogen, the greater the degree of "bond-breaking" at the transition state. The relative amounts of "bond-making" and "bond-breaking" are considered to vary widely from case to case. Support for these proposals was obtained by a study of the effect of substituents on the reactions of benzyl halides (page 648). Inherent in these proposals is the suggestion that *covalent* bonding to solvent at the rear may be important in solvolytic displacements.

(b) Variation of solvent nucleophilicity and ionizing power

Rates of solvolysis as a function of structure were summarized by Winstein, Grunwald, and Jones (670) in terms of solvent ionizing power, $\mathbf{Y}$, and nucleophilic character, $\mathbf{N}$, by equation 14. Because water, methanol, and ethanol are

$$ d \log k = \left(\frac{\partial \log k}{\partial \mathbf{Y}} \right)_\mathbf{N} d\mathbf{Y} + \left(\frac{\partial \log k}{\partial \mathbf{N}} \right)_\mathbf{Y} d\mathbf{N} \tag{14} $$

of comparable nucleophilicity, the second term approximately vanishes ($d\mathbf{N} \lesseqgtr 0$) for solvolyses in mixtures of these solvents. For such cases,

$$ \left(\frac{\partial \log k}{\partial \mathbf{Y}} \right)_\mathbf{N} = m $$

where m is the slope of the Grunwald–Winstein correlation (equation 11, page 617) for these solvent mixtures. Acetic acid and formic acid may similarly be regarded as having approximately equal but low nucleophilicity. Formic acid, however, has much greater ionizing power than acetic acid ($\Delta \mathbf{Y} = 3.71$). From rates of solvolyses in the two acids, an apparent m value may be calculated which is also a measure of $\left(\dfrac{\partial \log k}{\partial \mathbf{Y}} \right)_\mathbf{N}$, although for a much smaller value of $\mathbf{N}$ than the m value obtained from aqueous alcohol mixtures. Both m values and apparent m values have been included for a number of compounds in table 29. In all the cases which involve reaction at a primary or a secondary carbon atom (borderline cases), the apparent m value is greater than the m for aqueous alcohol solvents. If the assumption of equal nucleophilicity for formic acid and acetic acid is correct, the inference is that at low solvent nucleophilicities, the reaction rate of borderline cases is more dependent on ionizing power; if incorrect, the error is in the direction which requires formic acid to be more nucleophilic than acetic acid.

A rough measure of $\left(\dfrac{\partial \log k}{\partial \mathbf{N}} \right)_\mathbf{Y}$ may be obtained by comparing solvolysis rates in solvents of different $\mathbf{N}$ but identical $\mathbf{Y}$. Convenient for this purpose are the rate ratios $k_{\text{aq.alc.}}/k_{\text{HCOOH}}$ or $k_{\text{aq.alc.}}/k_{\text{CH}_3\text{COOH}}$, in which $k_{\text{aq.alc.}}$ is the rate in the aqueous ethanol solution having the same $\mathbf{Y}$ value as that of the carboxylic acid (670). Such estimated rate ratios are listed in table 29 for a number of sub-

TABLE 29

Effect of solvent nucleophilicity on solvolysis rates

Compound	Temperature	m (Aqueous Alcohol)	Apparent m (RCOOH)	$\left(\dfrac{k_{\text{aq.alc.}}}{k_{\text{RCOOH}}}\right)_Y$		References
				CH$_3$COOH	HCOOH	
	°C.					
Methyl bromide................	50	0.26			200	(682)
Methyl tosylate................	75	0.23[a]	0.30	97	55	(682)
Ethyl bromide..................	55	0.34			80	(682)
Ethyl iodide...................	50	0.27				(228a)
n-Propyl chloride..............	101.6	0.39			~30	(635, 636)
n-Propyl bromide..............	95	(0.34)[b]			63	(221)
Ethyl benzenesulfonate.........	50	0.28				(682)
Ethyl tosylate.................	50	0.26	0.44,[c] 0.37[d]	80	18	(682)
n-Butyl brosylate..............	60	0.32[e]	0.38	30	23	(410, 591)
Isopropyl bromide..............	50	0.54			20	(682)
Isopropyl brosylate............	70	0.41	0.66[c]	6	2	(682)
2-Pentyl tosylate..............	58.2	(0.41)[b]	0.68	4	0.4	(424)
3,3-Dimethyl-2-butyl brosylate..	70	0.71	0.83[c]	0.4		(298, 682)
tert-Butyl chloride............	25	(1.00)	(1.00)	(1)	(1)	(298)
tert-Butyl bromide.............	25	0.94				(298)
1-Bromobicyclo[2.2.2]octane....	100	0.88	0.92	0.7	0.5	(209)
Benzyl chloride................	50	0.43	0.66	58	4	(236, 324a, 523, 524)
Benzyl tosylate................	25	0.39		30		(682)
p-Methylbenzyl chloride........	50	0.57				(236, 488)
α-Phenylethyl chloride.........	50	0.81		2.5		(19, 366, 585, 646)
Allyl chloride.................	44.6	0.40			40	(236, 635, 636)

[a] Value for methyl benzenesulfonate at 50°C. used.
[b] Assumed value.
[c] At 25°C.
[d] At 75°C.
[e] Value for n-butyl benzenesulfonate used.

stances. Secondary sulfonates are only slightly dependent on nucleophilicity ($[k_{\text{aq.alc.}}/k_{\text{RCOOH}}]_Y < 10$). Isopropyl bromide and methyl and ethyl systems are definitely dependent on solvent nucleophilicity ($[k_{\text{aq.alc.}}/k_{\text{RCOOH}}]_Y = 20\text{--}200$). The relative sensitivity of a compound to solvent nucleophilicity is comparable to the relative sensitivity of the compound to the addition of lyate ion (table 17).

The relative values of the partial differentials have been qualitatively treated by Winstein, Grunwald, and Jones (670) in terms of the contributing resonance structures (XXIX, XXX, and XXXI) of the transition state. The greater the

$$\text{Z: R—X} \leftrightarrow \text{Z—R :X} \leftrightarrow \text{Z: R :X}$$
$$\text{XXIX} \qquad\qquad \text{XXX} \qquad\qquad \text{XXXI}$$
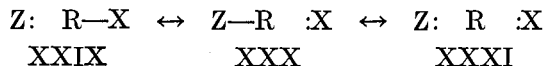
ability of the system to sustain a positive charge, the greater the contribution of structure XXXI, the greater will be m, the measure of $\left(\dfrac{\partial \log k}{\partial Y}\right)_N$, and the smaller will be the measure of $\left(\dfrac{\partial \log k}{\partial N}\right)_Y$. Systems for which $\left(\dfrac{\partial \log k}{\partial N}\right)_Y = 0$ are defined as "limiting" and will generally include those systems which are said to react by a "pure" S$_N$1 mechanism in the Hughes–Ingold scheme. Systems for which $\left(\dfrac{\partial \log k}{\partial N}\right)_Y$ is large could also be said to be S$_N$2 solvolyses. The postulate that the

differentials may assume a continuous range of values may be considered to define either a "range of mechanisms" or a "single mechanism." The difference is only one of words and not one of meaning.

Swain, Mosely, and Bown (607) have extended the Grunwald–Winstein correlation (page 617) to the four-parameter equation 15, in which k^0 is the solvolysis rate in the standard solvent, c_1 and c_2 measure the sensitivity of the substrate to nucleophilic and electrophilic (ionizing power) character, respectively, of the solvent, and d_1 and d_2 are measures of the nucleophilic and electrophilic character, respectively, of the solvent system; d_1 and d_2 are defined as 0 for the solvent taken as the standard.

$$\log (k/k^0) = c_1 d_1 + c_2 d_2 \qquad (15)$$

Differentiation of equation 15 yields equation 16, which is identical to equation 14 except for symbols. Equation 15 may be derived by integrating equation 14 (or 16) with the assumptions that $\log k$ is independently a linear function of $\mathbf{N}$ and $\mathbf{Y}$ (or d_1 and d_2).

$$d \log k = c_1 dd_1 + c_2 dd_2 \qquad (16)$$

A large number of rate data were processed to derive the least-squares best fit values of c_1, c_2, d_1, and d_2 for a variety of systems after arbitrary standard values were set up to define the range of values. Some of the results are given in table 30. The use of four adjustable parameters is expected to result in overall better agreement with experiment than the use of only two such parameters, as in the Grunwald–Winstein correlation. The values of the parameters in table 30 therefore may be useful for predictive purposes.

The values of c_2 which are supposed to measure sensitivity to solvent electrophilicity are rather close in many cases to the m values (tables 24 and 29). Unfortunately, because of the conventions adopted in setting up the c_1 values, these have no theoretical significance. The definition that $c_1 = 1.00$ for tert-butyl chloride leads to the completely inconsistent result that methyl bromide is *less* sensitive to solvent nucleophilicity than the tertiary halide. The many such in-

TABLE 30

Constants in Swain's four-parameter equation (68)

Compound	c_1	c_2	Solvent	d_1	d_2
Triphenylmethyl fluoride	0.37[a]	1.12[a]	Formic acid	−4.40	+6.53
Benzhydryl chloride	1.24	1.25	Acetic acid	−4.82	+3.12
Benzyl tosylate	0.69	0.39	Ethanol	+0.53	−1.03
tert-Butyl chloride	1.00[b]	1.00[b]	80% Ethanol	0.00[b]	0.00[b]
1-Bromobicyclo[2.2.2]octane	0.96[c]	0.99[c]	Water	−0.44	+4.01
Isopropyl bromide	0.90	0.58	50% Acetone	−0.25	+0.97
n-Butyl bromide	0.77	0.34	90% Acetone	−0.53	−1.52
Ethyl bromide	0.80	0.36	Methanol	−0.05	−0.73
Methyl bromide	0.80[d]	0.27[d]			

[a] $c_1/c_2 = 0.33$ by definition.
[b] By definition.
[c] Calculated from the data of reference 209 at 100°C.
[d] $c_1/c_2 = 3.00$ by definition.

compatible values in table 30 demonstrate that the c_1 values are completely empirical parameters which bear no resemblance to the actual sensitivities of the substrates to nucleophilic character. The most startling discrepancy occurs in the case of 1-bromobicyclo[2.2.2]octane (XXXIX), which is structurally protected from attack at the rear. This compound fits equation 15 better than does *tert*-butyl chloride. Swain's viewpoint then leads to the conclusion that XXXIX is more sensitive to backside attack than methyl bromide! A more propitious starting point would have been the definition, $c_2 = 0.00$, for *tert*-butyl chloride (*cf.* page 642). The adoption of this definition would, of course, change all of the values in table 30; in particular, the d_2 values would become identical with the values of **Y**.

2. A structural hypothesis

The term "reaction mechanism" has meaning on several levels. On its lowest level, which is also the classical use of the term, a reaction mechanism is a sequential account of the isolable intermediates of a set of reactions. A somewhat higher level, which is obtained directly from investigations of kinetic order, is a description of the atoms involved at the transition state of the rate-determining step. Specification frequently may be made of the composition of other transition states and also of intermediates. At a rather high level a reaction mechanism is a structural description of each transition state and each intermediate involved in the reaction or reaction sequence. Specification in terms of chemical structures implies, at least in principle, the spectra, dipole moments, optical activity, and other *macroscopic* phenomena. Thermodynamic properties such as energy, entropy, and free energy are also implicated. The structural description has the important advantage that the semantic difficulties inherent in many so-called reaction mechanisms vanish.

An attractive structural hypothesis for many displacement reactions lies in the molecular orbital representation of the carbonium-ion intermediate which was introduced by Doering and Zeiss (page 640). The hypothesis implies a number of corollaries which relate to the structure of the rate-determining transition state. Although the arguments to be presented are formulated with orbital pictures, they could have been developed equally well in valence-bond terms. The orbital pictures, however, are perhaps more easily visualized.

(a) Structural hypothesis of the transition state

For those cases in which the presence of an intermediate is demonstrable, the structural hypothesis of a planar carbonium ion implies that the transition state of the rate-determining step leading to this intermediate occurs before the system has become coplanar. Such a transition state can be represented by structure XXXII, in which the C—X bond, formed originally from a carbon sp^3 tetrahedral hybrid, is formed from a hybrid intermediate between sp^3 and pure p; the other three bonds to the central carbon are formed from hybrid orbitals intermediate between sp^3 and sp^2. Concomitantly, the bond angle between these bonds is intermediate between 109° and 120°. The hybridization of the atoms attached to the central carbon is not important.

XXXII   XXXIII
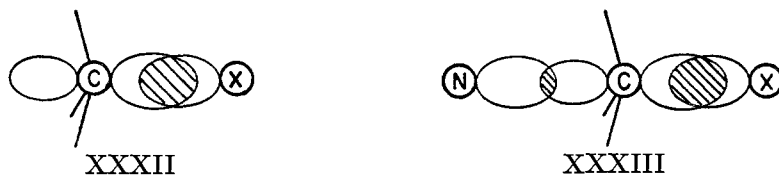
The solvation forces on the leaving group, whether electrostatic, hydrogen-bond, or Lewis acid complex in type, render this group effectively more electronegative, which, in turn, causes electron deficiency on the central carbon atom. A correlative postulate asserts that the greater these solvation forces, the more they will stabilize charge separation; hence, *the closer the transition state structure will be to tetrahedral.* The effects of solvent nucleophilicity and substrate structure relate to the dispersal of the positive charge retained by the central carbon. This positive charge may be distributed among several atoms in the substrate by π-bonding (conjugation), overlap with neighboring σ-orbitals (hyperconjugation), neighboring group participation (Section V), or by interaction with an external nucleophilic grouping (e.g., solvent). *The greater the ability of the system to internally disperse the positive charge* (i.e., the more stable the carbonium ion), *the closer to tetrahedral the transition state structure will be.* These postulates are extensions of Hammond's postulate (303), and are shown diagrammatically in figure 15. As a reaction system is altered to stabilize the intermediate, the free energy of activation decreases (first hump is lowered) and the structure of the transition state resembles the reactants more ($t'' \rightarrow t'$).

In molecular orbital terms, a nucleophilic reagent, N, can share the positive charge by overlapping with the "tail" end of the reaction orbital as represented in structure XXXIII. Some implications of this orbital representation may be more immediately obvious than the corresponding resonance structures XXIX, XXX, and XXXI. Because systems which can better internally stabilize the charge are closer to tetrahedral at the transition state, the amount of orbital available at the rear is smaller and overlap is energetically less important. Further-
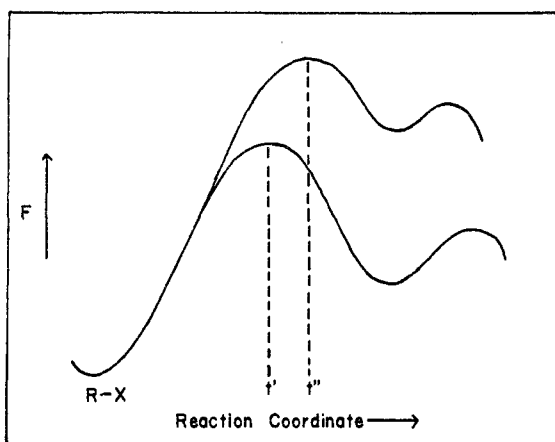

Fig. 15. Free energy curves for solvolysis reactions illustrating the effect of the stability of the intermediate on the position of the first transition state along the reaction coordinate.

more, a system which is closer to tetrahedral is less "open" at the rear and there is greater steric opposition to close approach of a nucleophilic molecule. In the extreme, the structural specificity of the system is such that the bond energy gained by overlap with a nucleophilic molecule at the rear does not compensate for the loss in entropy associated with the restriction of the motions of the nucleophilic molecule. Such systems are not sensitive to nucleophilic properties; they correspond to the "limiting" cases of Winstein, Grunwald, and Jones (page 636).

Because the structure of the transition state is postulated to be closer to tetrahedral the greater the solvation forces on the leaving group, an increase in these forces implies a lesser sensitivity of the system to nucleophilic character; hence the structural hypothesis explains why "the two kinds of driving force are roughly complementary." (670)

(b) Structural hypothesis of the intermediate

The concept of the transition state, which invokes to some extent an overlapping of a nucleophilic grouping at the rear of the bond undergoing reaction, leads logically to the structural hypothesis of the intermediate as the pentacovalent[7] carbonium ion (XXXIV), introduced by Doering and Zeiss (203, 212, 216, 217, 591). In this structure both lobes of the central p orbital of the carbonium ion overlap with orbitals of two Lewis bases, B_1 and B_2. Each of these bonds is generally rather weak and should be considered at best as a half-bond. The three remaining bonds are formed from sp^2 hybrid orbitals. This hypothesis is further supported by the consideration that an empty p orbital in an environment rich
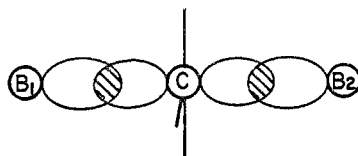
XXXIV

in unshared electron pairs may represent an unstable arrangement (526). It should be recalled (page 577) that a linear combination of atomic orbitals as represented in formulas XXXIII and XXXIV will form three molecular orbitals, two of which, a bonding and a non-bonding orbital, contain the total of four electrons implicated. Depending on the bonding forces involved and on the effective electronegativities of B_1 and B_2 (in XXXIV) a varying degree of positive charge is sustained by the central carbon atom. Essentially the same type of result would undoubtedly be obtained by application of the valence-bond method (page 636). The Lewis bases, B_1 and B_2, may be solvent molecules, other nucleophilic addends, or the leaving group. Since the atomic orbitals on these atoms may be any of a variety of hybrid orbitals, it is convenient to refer to the C—B bond simply as a p_σ bond. At reasonable values for the C—B p_σ bond distance (about 0.5 A.
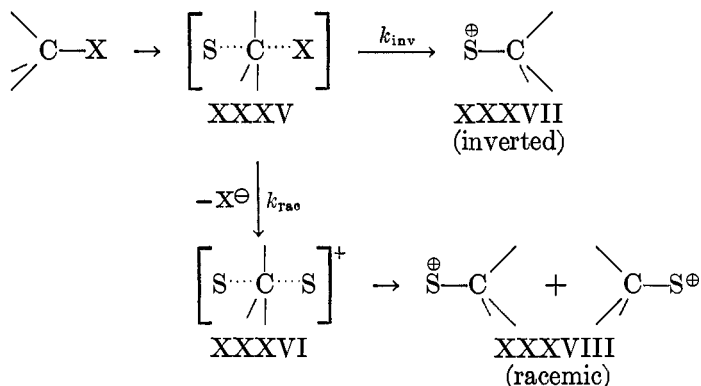
[7] The term "pentacovalent" is used since the central carbon atom is bonded to five other atoms, although two of these bonds may be exceedingly weak.

longer than the normal C—B bond distance), the amount of such orbital overlap is appreciable (591).

The similarity of structure XXXIV with the structure usually written for the transition state of a direct displacement reaction has been pointed out (217). The difference is simply one of energetics. The electronegativity of B_1 and B_2 imposes a positive charge on the central carbon. In some systems the arrangement is one of extreme instability; in others, the arrangement is a more or less stable representation and can be described as an intermediate.

(c) Stereochemistry

As discussed by Doering and Zeiss (217), an exchange of the leaving group for a solvent molecule may occur which depends on the strength of the p_σ bond to the leaving group. Such exchange arises from the relative weakness of the p_σ bonds which, consequently, may be broken more or less readily. Exchange with solvent (k_{rac}) will yield a new intermediate, XXXVI, which is symmetrical and which must produce racemic products such as XXXVIII. Instead of further reaction with the solvent, the first intermediate (XXXV) may simply rehybridize (k_{inv}), yielding a completely inverted product (XXXVII). The free energy pic-

ture of a typical example is represented in figure 16. The overall rate of reaction is determined by $\Delta F^\ddagger$. In the particular case illustrated $\Delta F^\ddagger_{rac}$ is equal to $\Delta F^\ddagger_{inv}$, and the product, XXXVII and XXXVIII, would be 50 per cent inverted and 50 per cent racemized. The stereochemical outcome of the reaction is thus a function of a precisely defined concept: the relative rates of competing reactions of a structurally specific intermediate. The rather vague concepts of "time-lag," "lifetime," and "shielding" are avoided.

3. Application to specific systems

(a) Tertiary carbinyl systems

The insensitivity of the rates of solvolysis of tertiary systems to the nucleophilic properties of the solvent or to the addition of lyate ion or other bases strongly suggests that the transition state of the rate-determining step in these systems is best represented by structure XXXII; i.e., there is no participation by
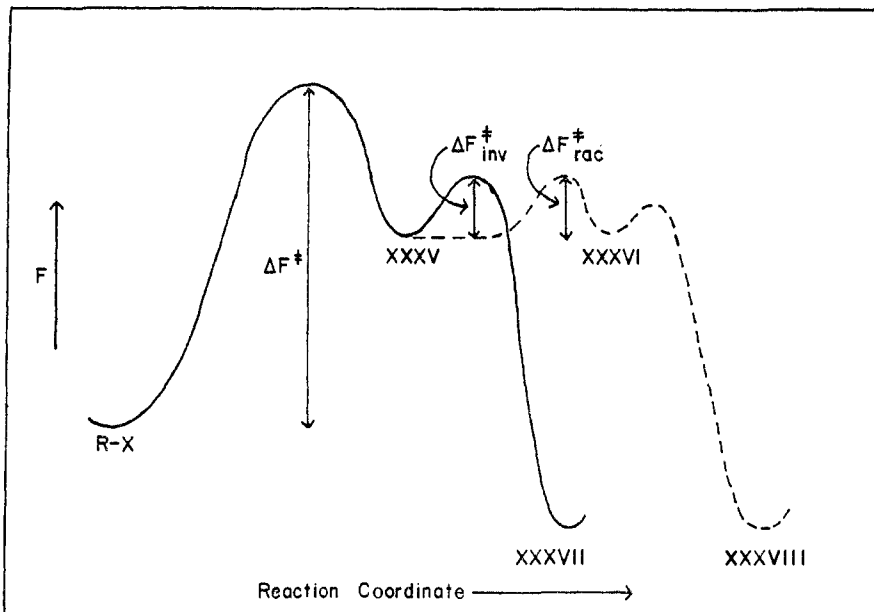
Fig. 16. Free energy curves illustrating the stereochemical outcome of a solvolysis reaction.

a solvent molecule at the rear. An interesting variant of this approach is instructive.

Solvolysis of 1-bromobicyclo[2.2.2]octane (XXXIX) cannot conceivably in-

$$
\begin{array}{c}
\text{CH} \\
\diagup \quad | \quad \diagdown \\
\text{H}_2\text{C} \quad \text{CH}_2 \quad \text{CH}_2 \\
| \qquad | \qquad | \\
\text{H}_2\text{C} \quad \text{CH}_2 \quad \text{CH}_2 \\
\diagdown \quad | \quad \diagup \\
\text{C} \\
| \\
\text{Br}
\end{array}
$$
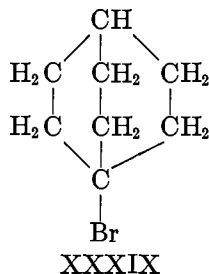
XXXIX

volve a carbonium ion specifically solvated at the rear of the reacting bond. The rates of solvolysis of XXXIX are relatively slow, presumably because of the strain involved in generating a flat carbonium ion at the bridgehead; however, the rates in various solvents bear essentially the same relative relationship as do the rates of solvolysis of *tert*-butyl chloride in the same solvents (209). Application of the Grunwald–Winstein correlation (page 617) yields a value for m of 0.91 (at 100°C.) comparable to the value, 0.94 (at 25°C.), given by *tert*-butyl bromide. The value of m derived from two aqueous ethanol mixtures, 0.88, does not differ significantly from the value, 0.92, derived from acetic and formic acids. Finally, the values of $(k_{\text{aq.alc.}}/k_{\text{HCOOH}})_Y$ and $(k_{\text{aq.alc.}}/k_{\text{CH}_3\text{COOH}})_Y$ do not differ significantly from unity (table 29). If a solvent molecule were required in a

nucleophilic capacity at the rear of the reacting *tert*-butyl system, the relative rate pattern in solvents of varying nucleophilic character of XXXIX, in which such solvation is impossible, would be expected to be significantly different.

The results are consistent with the representation of *tert*-carbinyl systems as "limiting" and justify the use of the rates of solvolysis of *tert*-butyl chloride as measures of solvent "ionizing power." The transition state structure, intermediate between tetrahedral and trigonal, possesses a relatively small "tail" lobe of the reaction orbital which is, moreover, flanked by three bulky alkyl groups. Such a structure is consistent with ineffective covalent solvation at the rear. The transition state leading to any intermediate or product must contain all of the atoms which are involved in the intermediate or product. Consequently, the first intermediate in the solvolyses of *tert*-carbinyl systems must be represented by XL. In this structure the solvation forces on the leaving group, although very important, have been omitted for convenience. When X is leaving as a negative ion, the C—X bond in XL has a large amount of ionic character. Consequently, such intermediates have been referred to as ion-pairs (663a). The ion-pair terminology is not satisfactory, however, when X is leaving as a neutral molecule.

In XL a larger orbital is available for bonding with the solvent and the steric opposition by the three surrounding alkyl groups is greatly reduced. Further

XL
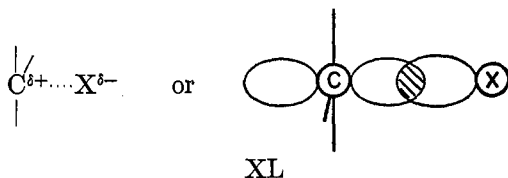
reaction to form the more stable intermediate XXXV will doubtless be exceedingly rapid. The detailed interpretation of the available facts thus requires the free energy picture of the initial phase of the reaction of these systems to be similar to that in figure 17.
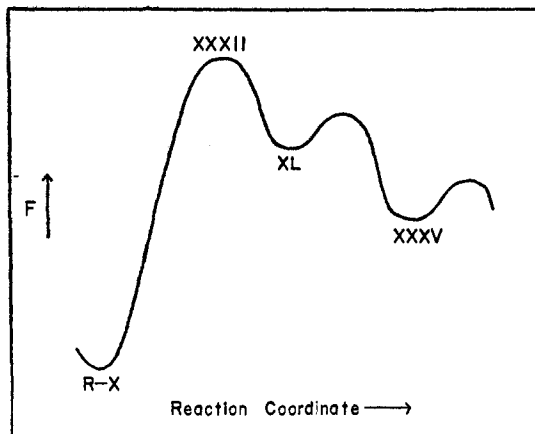

FIG. 17. Free energy curve for the solvolysis of a tertiary halide

The three alkyl groups in XXXV are sufficiently spread out that steric hindrance is probably not serious. The calculations of Dostrovsky, Hughes, and Ingold (222) for such a model showed only a small amount of steric compression energy. An increase in solvent nucleophilicity should increase the stability of XXXV *relative to the first transition state*, XXXII. This conclusion should hold also for the reactions of tertiary halides with highly nucleophilic substances in an inert solvent, in which the major driving force is derived from nucleophilic overlap at the rear; i.e., in direct displacement reactions on *tert*-carbinyl systems, the transition state probably does not have the planar trigonal structure. The free energy curve must therefore be a two-humped curve (figure 4).

In the subsequent competing reactions of the intermediate, XXXV, an increase in solvent nucleophilicity should increase k_{inv} relative to k_{rac} and should produce a less racemized product. In this manner, the relatively high nucleophilicity of an alcohol accommodates the rather large figure of 60 per cent inversion found for the methanolysis of hydrogen 2,4-dimethylhexyl 4-phthalate (212, 216, 217).

(b) Secondary carbinyl systems

Because a secondary carbonium ion is less stable than a tertiary, the transition state in solvolysis has a structure closer to the sp^2 hybrid. In such a structure the "tail" of the reaction orbital is larger, and, together with the smaller degree of steric hindrance to close approach provided by two rather than three surrounding alkyl groups, orbital overlap with a nucleophilic group at the rear is more important than in the corresponding tertiary case (tables 17 and 29). The degree of importance is less than in the case of primary systems.

Because of the relative stabilities of the carbonium ions (table 21), secondary carbinyl systems are less sensitive to the ionizing power of the medium (lower m) than tertiary carbinyl systems, but more so than primary compounds. In cases in which the nucleophilicity is high, as in direct displacement reactions (table 5) or in reaction with ethanol (table 32), isopropyl bromide is less reactive than ethyl bromide. As the ionizing power of the solvent is increased, the relative reactivity of the secondary halide increases (table 32). For example, $k_{i\text{-}C_3H_7Br}/k_{C_2H_5Br}$ for solvolysis rises from 0.73 in ethanol to 2.9 in 50 per cent aqueous ethanol; in formic acid the ratio is 26.

Because tertiary systems are not dependent on nucleophilicity and secondary systems are, there is a predictable change in relative rates with change in solvent; $k_{t\text{-}C_4H_9Br}/k_{i\text{-}C_3H_7Br}$ is $\sim 10^6$ in formic acid, ~ 17000 in 50 per cent ethanol, and only 1140 in absolute ethanol (table 22). The figure 10^6, which corresponds to 8.5 kcal./mole, represents the minimum stabilization of a tertiary carbonium ion relative to a secondary in a limiting solvolysis (682).

Consistent with this general picture, the addition of mercuric bromide to solvolytic systems in aqueous acetone produces rate enhancements in the order *tert*-butyl bromide > isopropyl bromide > ethyl bromide > methyl bromide (519).

The relative stabilities of the carbonium ions imply also that the p_σ bonds of

the intermediate are stronger for secondary compounds than for tertiary. Consequently, k_{inv}/k_{rac} is higher for the secondary derivatives (page 641). Under the same conditions a decrease in ionizing power increases the net amount of inversion. The 2-ethoxyoctane produced by the solvolysis of optically active 2-octyl tosylate is 80.9 per cent inverted in 80 per cent ethanol and 91.5 per cent inverted in absolute ethanol (at 78°C.) (594). The 2-octanol simultaneously produced in 80 per cent ethanol is 83.4 per cent inverted (16.6 per cent racemized) (594).

(c) Primary carbinyl systems

The low stabilities of primary carbonium ions imply that the transition state of the rate-determining step is rather close to sp^2 in structure, but probably not as close as in direct displacement reactions in which the driving force for the reaction is provided almost wholly by the nucleophilicity of the displacing base. In the latter case, the order of the relative rates as a function of structure seems to be rather constant and independent of the nature of the displacing base (page 583). In various solvolysis reactions, however, the relative rates vary significantly in different solvents (table 31). For example, $k_{CH_3OTs}/k_{C_2H_5OTs}$ ranges from 2.3 in ethanol to 0.56 in formic acid. In direct displacement reactions, methyl compounds *always* react faster than the corresponding ethyl compounds, usually by factors of about 30 (table 5).

As solvent ionizing power increases and the reaction becomes more limiting, the energetics of the transition state are less dependent on nucleophilic overlap and the type of steric hindrance encountered in direct displacement reactions becomes less important. These generalizations are strikingly demonstrated by the relative solvolysis rates of isobutyl and neopentyl derivatives in which such steric hindrance is exceedingly important in direct displacement reactions (page 596). In ethanol, the solvolysis rates form a pattern much like that for direct displacement (table 31). In this reaction, the position of the transition state along the reaction coordinate must correspond closely to that for direct displacement. The intermediate in the ethanolysis, if one exists, must be very unstable. In

TABLE 31

Relative solvolysis rates of some primary compounds [a]

Reaction	R = Methyl	R = Ethyl	R = Isobutyl	R = Neopentyl	Reference
Average S_N2 reaction	30	1.0	0.03	0.00001	Table 5
ROTs,[b] C_2H_5OH, 75°C	2.3	1.0	0.046	0.00057	(682)
RBr, 50% C_2H_5OH, 95°C	1.94	1.0	0.075	0.00625	(222)
RBr, 70% C_2H_5OH, Ag+, 64°C	0.81	1.0	0.085	0.013	(222)
RBr, 70% aqueous dioxane, Hg++, 55°C	—	1.0	0.14	—	(70)
$ROSO_3^-$, H_2O, 138°C	1.79	1.0	0.15	0.090	(138a)
$ROSO_2C_6H_5$, H_2O, 60°C	1.05	1.0	0.235	0.109	(410)
ROTs, CH_3COOH, 75°C	1.11	1.0	0.31	0.11	(682)
RBr, HCOOH, 95°C	0.64	1.0	—	0.57	(222)
ROTs, HCOOH, 75°C	0.56	1.0	1.22	1.0	(682)

[a] This table was adapted from reference 682.

[b] Ts = tosylate.

formic acid, however, the solvolysis rates of methyl, ethyl, isobutyl, and neopentyl tosylates vary by only a factor of two. One possible conclusion is that these formolyses are limiting and independent of steric effects. This conclusion is almost certainly wrong for the following two reasons: In those cases in which steric hindrance is not important, weaker solvent bonds at the transition state imply weaker p_σ bonds in the intermediate and more facile interconversion of Lewis bases, hence more racemized products. The formolysis of optically active butyl-1-d brosylate gave almost completely inverted butyl-1-d formate (591); hence a reasonably strong nucleophilic solvent bond is indicated at the transition state of the rate-determining step.

It was shown (page 644) by the comparison of the relative rates of formolysis of secondary and tertiary halides that the positive charge delocalizing ability of a methyl group is worth at least a factor of 10^6 in the rate of a limiting solvolysis. Winstein and Marshall (682) have pointed out that comparable rate increases should be expected throughout the series methyl, ethyl, isopropyl, *tert*-butyl for limiting solvolyses. It is shown in table 32 that all known solvolyses of primary systems yield relative rate factors far from that expected for a limiting reaction and, consequently, must be far from limiting.

Since a reasonably strong solvent bond at the rear is demonstrated, the fact that the formolyses of isobutyl and neopentyl tosylates are as fast as that of ethyl tosylate has been interpreted on the basis of a rate-enhancing rearrangement (page 707) (682).

(d) Benzyl systems

Benzyl systems combine the low steric hindrance to nucleophilic attack of primary compounds with a carbonium-ion stability somewhat greater than that of secondary alkyl systems (table 21). These compounds are more reactive than the corresponding primary or secondary aliphatic compounds, but the relative rates vary somewhat with solvent in a predictable way.

TABLE 32

Relative rate effects of methyl substitution[a]

Reaction	$k_{C_2H_5}/k_{CH_3}$	$k_{i-C_3H_7}/k_{C_2H_5}$	Reference
RBr, C_2H_5OH, 50°C	0.37	0.76	(670)
RBr, 80% C_2H_5OH, 50°C	0.39	1.4	(670)
ROTs,[b] 50% aqueous dioxane, 50°C	0.47	1.42	(544)
$ROSO_2C_6H_5$, CH_3OH, 50°C	0.49	4.9	(544)
ROTs, C_2H_5OH, 75°C	0.44	5.0	(682)
$ROSO_2C_6H_5$, 80% C_2H_5OH, 50°C	0.45	6.0	(544)
RBr, H_2O, 50°C	1.08	10	(670)
$ROSO_2C_6H_5$, 50% C_2H_5OH, 50°C	0.53	13.2	(544)
$ROSO_3^-$, H_2O, 138°C	0.56	16	(138a)
ROTs, CH_3COOH, 75°C	0.9	51	(682)
RBr, HCOOH, 100.2°C	1.7	27	(62)
$ROSO_2C_6H_5$, H_2O, 50°C	0.95	68	(410)
RBr, 70% aqueous dioxane, Hg^{++}, 25°C	—	145	(70)
ROTs, HCOOH, 75°C	1.8	202	(682)
Expected for limiting solvolysis	$\sim 10^6$	$\sim 10^5$	(682)

[a] This table was adapted from reference 682.

[b] Ts = tosylate.

TABLE 33

Relative rates of solvolysis of benzyl, isopropyl, ethyl, and allyl systems

Reaction	Relative Rates				References
	Benzyl	Isopropyl	Ethyl	Allyl	
RCl, 80% C_2H_5OH, 50°C.	100	0.70	—	52	(375, 636, 670)
RCl, 50% C_2H_5OH, 50°C.	100	3.0	—	24	(527, 636, 670)
RCl, CH_3COOH. 100°C.	100	3.0[a]	—	—	(149, 523, 524)
ROTs, CH_3OH, 25°C.	100	0.74[b]	0.15	—	(544, 670)
ROTs, C_2H_5OH, 25°C.	100	0.69	0.26	8.6[c]	(84, 544, 670)
ROTs, 80% C_2H_5OH, 25°C.	100	0.88[d]	0.17[e]	—	(544, 670)
ROTs, 50% C_2H_5OH, 25°C.	100[f]	1.89	0.16[e]	—	(544, 670)
ROTs, CH_3COOH, 25°C.	100	3.0[g]	0.045	—	(670, 682)

[a] Estimated from the rate of solvolysis of isopropyl bromide, using $k_{RCl}/k_{RBr} = 0.04$.

[b] Calculated from the rate of solvolysis of isopropyl benzenesulfonate at 50°C., using $E^{\ddagger} = 22.9$ kcal./mole and $k_{ROTs}/k_{ROSO_2C_6H_5} = 0.63$ (544).

[c] Calculated from the rate of solvolysis of the benzenesulfonate, using $k_{ROTs}/k_{ROSO_2C_6H_5} = 0.63$.

[d] Extrapolated from 50°C., using $E^{\ddagger} = 22.5$ kcal./mole.

[e] Extrapolated from 50°C., using $E^{\ddagger} = 21.5$ kcal./mole.

[f] Estimated from other aqueous alcohol mixtures, using the Grunwald–Winstein correlation.

[g] Estimated from isopropyl brosylate, using $k_{ROTs}/k_{ROBs} = 0.32$.

As the solvent nucleophilicity is increased, the relative rates of benzyl systems increase with respect to the corresponding secondary systems but decrease with respect to the primary systems (table 33). This effect is demonstrated by the rate ratios $k_{C_2H_5OH}/k_{CH_3COOH}$, which for the tosylates are: benzyl, 22; isopropyl, 5; ethyl, 126 (544, 670, 682). Conversely, because of the greater role played by nucleophilic character in benzyl systems, the sensitivity of rate to solvent ionizing power is less than for secondary carbinyl compounds. The large difference in carbonium-ion stabilities means that benzyl systems will be more sensitive to ionizing power than primary carbinyl systems. Examples are found in table 33 and in the tosylate solvolysis rate ratios, $k_{50\%\ C_2H_5OH}/k_{C_2H_5OH}$, for the tosylates: benzyl, 23; isopropyl, 62; ethyl, 14 (670).

An increase in the substitution about the reactive carbon atom in a benzyl system (e.g., α-phenylethyl chloride) leads to a decreased sensitivity of the solvolysis rates to solvent nucleophilicity and an increased sensitivity to solvent ionizing power. This trend is suggested in the relative rates in table 23; for example, $k_{C_2H_5OH}/k_{CH_3COOH}$ at 50°C. is 21 for benzyl chloride (523, 524, 670) and 1.3 for α-phenylethyl chloride (19, 366, 585); $k_{80\%\ C_2H_5OH}/k_{C_2H_5OH}$ at 50°C. is 7.1 for benzyl chloride (670) and 40 for α-phenylethyl chloride (19, 366, 646).

Substituents in the meta and para positions of the benzene ring do not affect steric hindrance at the reactive center, but they do affect the ability of the system to bear a positive charge. Swain and Langsdorf (605) have proposed the use of Hammett's sigma–rho equation (301, 381) in this connection by the use of the postulate that the reaction constant, ρ, is a measure of the change in electronic charge on the benzenoid system between the ground state and the transition state. Displacement reactions and solvolyses on benzylic systems do not give good linear Hammett relations (the plots show definite curvature); hence ρ is difficult to define for these systems. The postulate is applied just as well by

TABLE 34

p-Methyl rate enhancements in benzylic solvolyses

Compound	Solvent	Temperature	$k_{p\text{-CH}_3}/k_H$	References
		°C.		
XC₆H₄CH₂Br	90% Ethanol	30	4.3	(28)
	90% Ethanol, AgNO₃ added	30	45	(476)
	HCOOH	25	57.9	(87)
XC₆H₄CH₂Cl	80% Ethanol	50	5.05	(236, 670)
	48% Ethanol	30	9.4	(488)
	50% Acetone	30	8.0	(490)
XC₆H₄CH₂OTs	Aqueous acetone, 29 mole per cent H₂O	25.3	19.2	(400)
	Aqueous acetone, 55 mole per cent H₂O	25.3	24.6	(400)
	Aqueous acetone, 67 mole per cent H₂O	25.3	32.2	(400)
	Aqueous acetone, 76 mole per cent H₂O	25.3	29.8	(400)
	CH₃COOH	40	56	(593)
XC₆H₄CHClCH₃	CH₃COOH	50	35	(425, 585)
XC₆H₄C(CH₃)₂Cl	90% Acetone	25	26	(111)
XC₆H₄CHCl₂	50% Acetone	50	71.8	(17a)
XC₆H₄CHClC₆H₅	Ethanol	25	16.3	(477)
	Ethanol	25	23.2	(616)
	90% Acetone	25	20.6	(59)
	80% Acetone	25	22.1	(59)
	80% Acetone	25	21.4	(371)
XC₆H₄CHClC₆H₄Cl-p	2-Propanol	25	15.7	(5)
(XC₆H₄)₂CHCl	Ethanol	25	413	(478)
	90% Acetone	0	396	(59)
	80% Acetone	0	296	(59)
XC₆H₄C(C₆H₅)₂Cl	60% Ether–40% ethanol	25	4.1	(476)
	SO₂	0	17.6*	(428)
	CH₃NO₂	20	4.6*	(237)
(XC₆H₄)₃CCl	CH₃NO₂	20	123*	(237)

* Relative equilibrium constants for ionization.

comparing the effect of a single substituent on the rates of various reactions (605). The substituent illustrated in table 34 is the *p*-methyl group. The greater the positive charge on the system at the transition state of the rate-determining step, the greater the rate enhancement provided by *p*-methyl substitution. For benzyl halides in aqueous acetone and aqueous alcohol solutions, the ratio $k_{p\text{-CH}_3}/k_H$ varies from 4.3 to 9.4. The value is much higher in the presence of a Lewis acid (45 with Ag⁺) and in the poorly nucleophilic, highly ionizing solvent formic acid (57.9). The fact that sulfonic acid esters tend to be more limiting than the halides is shown by the comparison of the rate ratios in aqueous acetone: benzyl chloride, 8.0; benzyl tosylate, 29.

(e) Benzhydryl systems

A second benzene ring on a benzyl system has a rate-enhancing effect on solvolysis which amounts to several powers of ten (table 23). The increased ability to support a positive charge is also shown by the relatively high $k_{p\text{-CH}_3}/k_H$ values provided by diphenylmethyl compounds (table 34); concomitantly, the p_σ bonds of the carbonium-ion intermediate are weaker. Thus the reaction step involving rehybridization to a tetrahedral product will have a lower rate relative to the reaction which exchanges the p_σ-bonded Lewis bases. The stereochemical

outcome of such solvolyses is essentially complete racemization. Furthermore, other agents such as azide ion and halide ion can compete with solvent in reactions with the intermediate which give rise to mass law and common-ion effects (page 624).

(f) Triarylmethyl halides

In 85 per cent aqueous acetone, triphenylmethyl chloride undergoes solvolysis 130,000 times as fast as benzhydryl chloride (table 23). This high reactivity is probably due entirely to the stability of the triphenylmethyl cation. The stability of the first transition state in triarylmethyl halide solvolysis is expected to be as little dependent on nucleophilicity as that for benzhydryl systems, although this view is clearly inconsistent with the interpretation of the third-order kinetics found for the methanolysis of triphenylmethyl chloride in benzene as a termolecular process which requires nucleophilic solvation at the rear (page 634). However, Swain and Kreevoy (604) have recently demonstrated with new experimental observations a complete consistency with the view that the rate-determining step in this case is the reaction of methanol with the triphenylmethyl cation which arises from a rapid reaction of triphenylmethyl chloride with methanol acting as an electrophilic catalyst:

$$(C_6H_5)_3CCl + CH_3OH \underset{\longleftarrow}{\overset{rapid}{\longrightarrow}} \quad \underset{C_6H_5}{\overset{C_6H_5}{\underset{|}{C^+}}} \cdots Cl^- \cdots H-O-CH_3 \xrightarrow[\text{determining}]{\text{rate-}}$$

$$CH_3-O \cdots \underset{H \quad C_6H_5}{\overset{C_6H_5}{\underset{|}{C^+}}} \cdots Cl^- \cdots HOCH_3 \rightarrow (C_6H_5)_3COCH_3$$
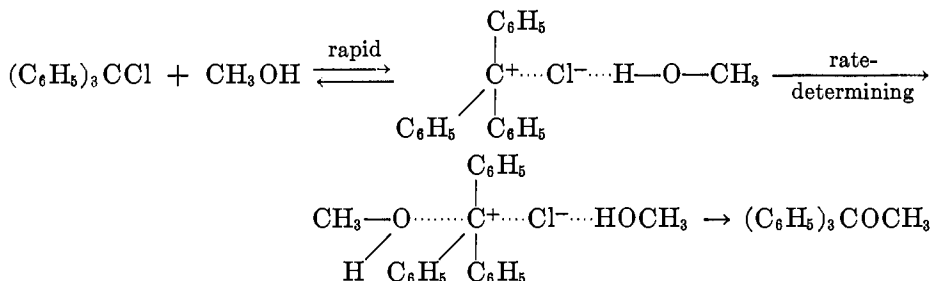
The dotted lines which Swain had considered as predominantly ionic bonds may just as readily be regarded as p_σ bonds.

Also consistent with this mechanism are the recent results of Hawthorne and Cram's (321) study of the reactions of substituted benzyl alcohols with triphenylmethyl chloride in benzene solution. These reactions, like that with methanol, follow third-order kinetics; the rate is greater with electron-attracting groups. For example, the relative rates of p-CH$_3$, H, and p-NO$_2$ substituents are, respectively, 0.82, 1.0, and 3.1. The third-order rate constants with phenol as the electrophilic catalyst were essentially the same for all of the benzyl alcohols studied. This observation clearly demonstrates the unimportance of a nucleophilic contribution at the rear of the transition state structure of the ionization step. The observed differences in the rates of the reactions with the substituted benzyl alcohols in the absence of phenol are ascribable to differences in hydrogen-bonding ability. Electron-attracting groups should facilitate removal of chloride and lead to a higher equilibrium concentration of the carbonium-ion intermediate. The subsequent reaction of this intermediate is expected to be less susceptible to slight differences in nucleophilicity.

TABLE 35

Reactivities of allylic systems

| Compound | Second-order reaction with ethoxide ion in ethanol, 44.6°C. | Relative Rates (635, 636) Solvolysis | | | $\dfrac{k_{50\%\ C_2H_5OH}}{k_{C_2H_5OH}}$ | m (Aqueous Alcohol) | $\left(\dfrac{k_{\text{aq. alcohol}}}{k_{\text{HCOOH}}}\right) Y$ |
		C_2H_5OH 44.6°C.	50% C_2H_5OH 44.6°C.	HCOOH 100°C.			
$CH_2{=}CHCH_2Cl$	1.00	1.00	1.00	1.00	27	0.40	40[a]
$CH_2{=}C(CH_3)CH_2Cl$	0.89	1.26	1.53	0.47	32	0.42	130[b]
$CH_3CH{=}CHCH_2Cl$	2.62	16	91	2060	150	0.61	2.3
$CH_2{=}CHCHClCH_3$	0.05	3.3	81	2940	654	0.79	2.0
$(CH_3)_2C{=}CHCH_2Cl$	15	1030	130,000	—	3300	0.98	—
$CH_2{=}CHC(CH_3)_2Cl$	—	2950	550,000	—	4900	1.03	—
$CH_3CH{=}CHCHClCH_3$	—	6600[c]	—	—	—	—	—
$C_6H_5CH{=}CHCH_2Cl$	6.83	139	7700	—	1470	0.89	—
$CH{\equiv}CCH_2Cl$	1.03	—	0.049	—	—	—	—
$CH_3CH_2CH_2Cl$	0.027	—	0.07[d]	0.038	24[c]	0.39[c]	30[f]
$(CH_3)_2CHCl$	—	—	0.12[g]	~0.1[h]	—	—	—
$(CH_3)_3CCl$	—	24[i]	2100[j]	—	3770[k]	1.00	1.00

[a] From table 29.

[b] The rate in formic acid was extrapolated from 100°C.; $E^{\ddagger}$ was assumed to be the same as for allyl chloride.

[c] Extrapolated from 30°C., using $E^{\ddagger} = 22.2$ kcal./mole (278).

[d] Extrapolated from 101.6°C.

[e] At 101.6°C.

[f] This value is lower than that given by other primary halides (table 29).

[g] Extrapolated from higher temperatures (527).

[h] Calculated from isopropyl bromide (62), assuming $k_{RCl}/k_{RBr} = 0.02$.

[i] Extrapolated from other temperatures (298).

[j] Extrapolated from other temperatures (350).

[k] At 25°C.

(g) Allylic systems

The effects of the relative stabilities of primary, secondary, and tertiary carbonium ions are reproduced in the changes in reactivity of allylic systems. The relative rate data in table 35 are due predominantly to the recent kinetic studies of Vernon (635, 636).

A positive charge developed as allyl cation can be shared by two carbon atoms, both of which are primary. Allyl chloride is comparable to benzyl chloride in many respects which concern reactivity (table 33), although the allyl system is somewhat less reactive and more dependent on reagent nucleophilicity. An interesting comparison is afforded by the displacement rates with ethoxide ion relative to the solvolysis rates with ethanol (k_2/k_1 in table 17): allyl chloride, 2900; n-propyl chloride, 2300; benzyl chloride, 1995. The importance of nucleophilic character in the solvolyses of allyl chloride is also demonstrated by the m value in aqueous alcohol, 0.40 ($m = 0.39$ for n-propyl chloride) and by the value of 40 for $(k_{\text{aq.alc.}}/k_{\text{HCOOH}})_Y$ (table 35). The effect of solvent nucleophilicity and ionizing power is also demonstrated by comparison of the relative rates of allyl chloride, crotyl chloride, and methylvinylcarbinyl chloride in ethanol, 1.0, 16, and 3.3, respectively, and in formic acid, 1.0, 2060, and 2940, respectively (table 35). Nucleophilic forces are far more important for the unsubstituted allyl chloride.

The γ-substituted allyl chlorides—crotyl chloride and γ,γ-dimethylallyl chloride—take on more the character of secondary and tertiary carbinyl chlorides, respectively, even though the carbon–chlorine bond is still primary. With increase in the carbonium-ion stability nucleophilicity is again of decreased importance; e.g., the ratio $k_2(C_2H_5O^-)/k_1(C_2H_5OH)$ for these structural changes becomes: allyl chloride, 2900; crotyl chloride, 121; γ,γ-dimethylallyl chloride, 42 (table 17). Correspondingly, dependency on solvent ionizing power becomes more marked; e.g., the ratio $k_{50\% \ C_2H_5OH}/k_{C_2H_5OH}$ becomes: allyl chloride, 27; crotyl chloride, 150; γ,γ-dimethylallyl chloride, 3300 (table 35). Similar comparisons hold for other allylic systems.

In short, an allylic system compares roughly to the aliphatic system which corresponds to the sum of the substitution about both conjugated carbons; e.g., allyl corresponds roughly to isopropyl, and crotyl or α-methylallyl (methylvinylcarbinyl) corresponds roughly to tert-butyl. α,γ-Dimethylallyl chloride with two secondary carbon atoms undergoes solvolysis 630 times faster than tert-butyl chloride in 75 per cent aqueous acetone (14, 185).

The structure of the transition state for direct displacement at an allylic system has been represented as shown in formula VII and figure 7. The structural postulates may be applied to accommodate allylic rearrangements (page 630) in much the following manner: The first transition state in the solvolysis of allyl chloride will have a structure akin to that shown in formula VII and figure 7, but the system will not be coplanar. The first intermediate may well be represented by formula VII and figure 7. This intermediate could rehybridize to a product with inversion of configuration and without rearrangement or it could rearrange

to a structure such as XLI in which both carbons have become equivalent. In an obvious way, two (rather than one) solvent molecules may be involved in
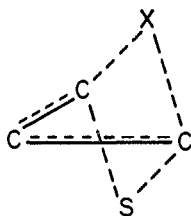
XLI

the rearward bonding. This structure implies rearranged products. The rate dependency of allyl chloride itself on nucleophilic properties suggests that the formation of intermediate XLI cannot readily compete with the direct formation of products; i.e., allyl chloride will probably produce solvolysis products rather generally with little rearrangement or racemization.

In a crotyl system, however, rearrangement to a structure such as XLI has the result of placing more of the positive charge burden on a secondary carbon and is, therefore, likely. The methylvinylcarbinyl system is so little dependent on nucleophilic properties that the same intermediate might well form as the first step. Looked at in this manner, the reaction sequence in solvolysis would be as follows (S represents a solvent molecule):

$$CH_3 CH = CHCH_2 Cl \xrightarrow{S}$$

$$CH_3 CH = CHCH_2 S^+ \quad + \quad Cl^-$$

$$k'' \Big\downarrow$$

$$CH_3 CH = CHCH_2 S^+ \quad + \quad Cl^-$$
$$+$$
$$CH_2 = CHCH(CH_3)S^+ \quad + \quad Cl^-$$
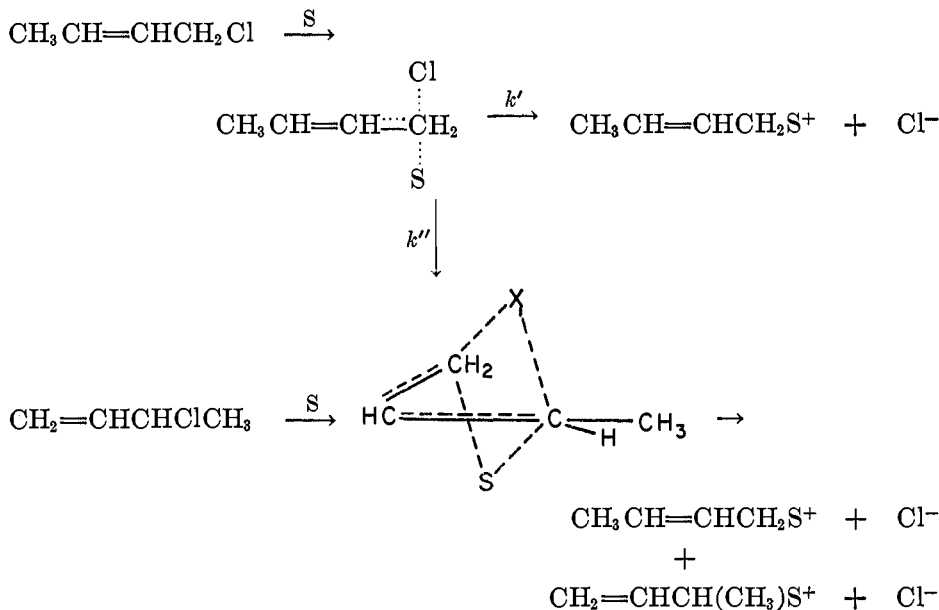
If k'' is large compared to k', both isomers will yield the same mixture of solvolysis products. Such a result is observed in solvents of low nucleophilicity such as acetic acid. In the more nucleophilic ethanol, k' is apparently appreciable and

greater quantities of the primary isomer are obtained (table 28). One mechanistic sequence is sufficient to account for the diversity of products. The alternate explanation in terms of simultaneous S_N1 and S_N2 reactions is wholly unnecessary.

(h) Acetylenic halides

A triple bond has lower conjugating power and higher inductive electron attraction than a double bond. The solvolysis rate ratio of α,α-dimethylallyl chloride to α,α-dimethylpropargyl chloride (XLII) is $\sim 10^5$ in aqueous ethanol.[8] XLII is only one-fortieth as reactive as *tert*-butyl chloride in 80 per cent aqueous ethanol (134, 329, 350). That conjugation of the reactive center with the triple bond does occur, however, is shown by the rate in 80 per cent ethanol of XLIII

$$HC\equiv CC(CH_3)_2\,Cl \qquad\qquad CH_3\,C\equiv CC(CH_3)_2\,Cl$$
$$\text{XLII} \qquad\qquad\qquad\qquad \text{XLIII}$$

relative to XLII, i.e., 2200 (134). This rate enhancement is roughly the same as the effects of comparable structural change in allylic systems; for example, α,γ-dimethylallyl chloride undergoes solvolysis 2000 times faster than α-methylallyl chloride in ethanol (table 35).

(i) Relative rates of leaving groups

The rate of solvolysis is dependent upon the nature of the leaving group. Relative rates for a variety of common leaving groups in different systems have been compiled in table 36. The order of reactivity seems generally to be $F < Cl < Br < I <$ benzenesulfonate.

4. *Additional evidence for the structural hypothesis*

The pentacovalent carbonium ion, which includes *covalent bonds* to solvent and to the leaving group, was originally postulated to account for the simple stereochemistry of the solvolysis reaction (216) and has been shown in the preceding sections to account for the effects of structure on rate. Various lines of evidence, however, substantiate more directly the assumptions required.

(a) Ionization of triarylmethyl chlorides

The solvolysis of triphenylmethyl chloride involves a transition state necessarily with only partial charge separation. In an ether–alcohol solvent a *p*-methyl substituent increases the rate of solvolysis by 4.1-fold (table 34). As the amount of charge separation is increased, the facilitation by a *p*-methyl group is also expected to increase. Yet, the *equilibrium constant* for the ionization of triphenylmethyl chloride in nitromethane is increased only 4.6-fold by a *p*-methyl substituent (table 34). The equilibrium involves a carbonium ion–halide ion ion-pair which does not dissociate into separated ions (79). The ion-pair has the same ultraviolet spectrum as the carbonium ion formed when triphenylcarbinol is dissolved in sulfuric acid. Both triphenylmethyl moieties, consequently, must have

[8] Estimated from the data of references 329 and 635.

TABLE 36

Relative rates of solvolysis of leaving groups

Leaving Group, X	CH₃X C₂H₅OH 70°C.	C₂H₅X C₂H₅OH 50°C.	i-C₃H₇X 80% C₂H₅OH 50°C.	Cyclohexyl X		t-C₄H₉X 80% C₂H₅OH 25°C.	t-C₅H₁₁X 80% C₂H₅OH 25°C.
				CH₃COOH 75°C.	HCOOH 25°C.		
F.................						10⁻⁵	
Cl................			1.72 × 10⁻⁴			1.00	1.00
Br................	0.0393[a]	0.033[d]	0.0131			39.4	42.1
I.................		0.052				99	113
ONO₂.............	0.0015[b]					38[b]	
S(CH₃)₂⁺.........	0.031[c]					0.020	0.076
OSO₂C₆H₄H.......	1.00	1.00	1.00				
OSO₂C₆H₄OCH₃-p..	0.45						
OSO₂C₆H₄CH₃-p...	0.64	0.62	0.60	1.00	1.00		
OSO₂C₆H₄Cl-p.....		2.21					
OSO₂C₆H₄Br-p.....	2.20		2.57[e]	2.90	2.73		
OSO₂C₆H₄NO₂-p....	9.28						
OSO₂C₆H₄NO₂-m...	11.0						
References.........	(25, 276, 544, 670)	(228a, 296, 628, 670)	(149, 298, 375, 544)	(668, 684)	(676, 684)	(25, 60, 116, 129, 161a, 163a, 350)	(116, 129, 161, 163a, 370, 374, 565)

[a] At 50°C.

[b] The Grunwald–Winstein correlation (298) was used to extrapolate to this solvent.

[c] At 100°C. The rate constant was divided by the statistical factor of 3.

[d] At 55°C.

[e] Extrapolated from other temperatures, using $E^{\ddagger} = 22.0$ kcal./mole.

the same π-bond structure; yet the effect of methyl substitution on the ion-pair equilibrium suggests that the carbonium ion in the ion-pair has less than a full unit of positive charge. This type of result is understandable if partial covalent bonding to solvent or to the chloride ion is involved. If such bonding were of the p_σ type, the π-electronic system would not be greatly affected; however, the argument is weakened by the extent to which the experimental data are questionable (page 612).

Gelles, Hughes, and Ingold (274) have studied the reactions of the triphenyl-methyl cation in nitromethane with added water, ethanol, and phenol. Because of the development of hydrogen chloride in these reactions, equilibrium is reached when only a small amount of reaction has taken place. Excess pyridine, therefore, was added to react with the hydrogen chloride as formed. Addition of pyridine to the solution, however, was found to discharge the color due to the carbonium ion, undoubtedly because of the formation of triphenylmethylpyridinium chloride. Nevertheless, reaction with excesses of the hydroxylic addends under these conditions proceeded to completion by pseudo·first-order kinetics. The kinetics was of zeroth order in the substituting agent except when these were in small concen-

tration.[9] The rates of the reactions were independent of pyridine concentration. The first-order rate constants at 0°C. could be expressed by equation 17.

$$10^5 k_1 \text{ (sec.}^{-1}) = 4.0 + 125[\text{H}_2\text{O}] + 500[\text{C}_2\text{H}_5\text{OH}] + 25[\text{C}_6\text{H}_5\text{OH}] \quad (17)$$

The reactivities are in the order of the relative nucleophilicities: $\text{C}_2\text{H}_5\text{OH} > \text{H}_2\text{O} > \text{C}_6\text{H}_5\text{OH}$.

These observations cannot be explained by the mechanistic sequence:

$$[(\text{C}_6\text{H}_5)_3\text{C-Pyr}]^+ \underset{\longleftarrow}{\overset{\text{fast}}{\longrightarrow}} (\text{C}_6\text{H}_5)_3\text{C}^+ + \text{pyridine}$$

$$(\text{C}_6\text{H}_5)_3\text{C}^+ + \text{ROH} \xrightarrow{\text{rate-determining}} \text{products}$$
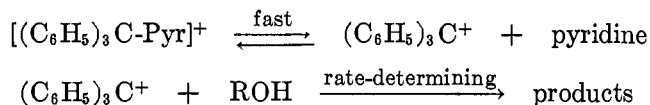
In this sequence the equilibrium concentration of triphenylmethyl cations, and hence also the rate, would be dependent on the pyridine concentration. Neither can the following sequence be correct:

$$[(\text{C}_6\text{H}_5)_3\text{C-Pyr}]^+ \xrightarrow{\text{slow}} (\text{C}_6\text{H}_5)_3\text{C}^+ + \text{pyridine}$$

$$(\text{C}_6\text{H}_5)_3\text{C}^+ + \text{ROH} \xrightarrow{\text{fast}} \text{products}$$

In this sequence the kinetics would be independent of the presence of hydroxylic addend.[10] A direct displacement mechanism, although consistent with this body of facts, is implausible on other grounds.

The facts are, on the other hand, completely in accord with the hypothesis of a p_σ-bonded carbonium ion. This hypothesis is developed in the following manner, in which only the kinetically significant entities are depicted:

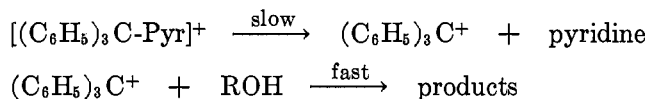$$[(\text{C}_6\text{H}_5)_3\text{C-Pyr}]^+ \underset{\longleftarrow}{\overset{\text{fast}}{\longrightarrow}} \left[\begin{array}{c} \text{C}_6\text{H}_5 \\ | \\ \text{C}\cdots\text{Pyr} \\ \diagup\ | \\ \text{C}_6\text{H}_5 \quad \text{C}_6\text{H}_5 \end{array} \right]^+ \xrightarrow[\text{rate-determining}]{\text{ROH}} \text{products}$$
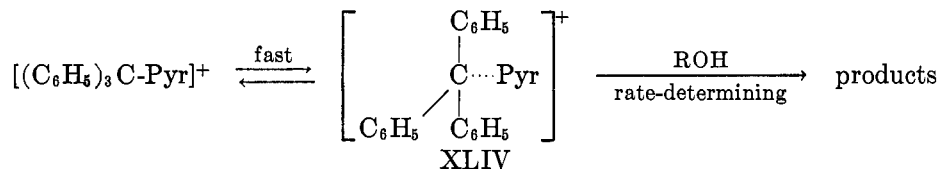
<div align="center">XLIV</div>

The tetrahedral pyridine complex, like the chloride, is to be considered in rapid equilibrium with the p_σ-bonded isomer (XLIV). The disappearance of color when pyridine is involved demonstrates that XLIV is present in very small concentration. In XLIV the triphenylmethyl system is now flat and open to attack by the hydroxylic addend in the rate-determining step. Note that the reactive intermediate (XLIV) cannot be described as an ion-pair in this case, because only a single charge is involved!

<div align="center">(b) Stereochemistry of the solvolysis in mixed solvents</div>

The solvolysis of optically active hydrogen 2,4-dimethylhexyl-4 phthalate (XLV) in methanol is acid-catalyzed and yields 4-methoxy-2,4-dimethylhexane

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[9] The authors' statement that the reactions were pseudo-first order even at low concentrations of the hydroxylic addend is contradicted by the experimental data which they present.

[10] This is the mechanism actually adopted by the authors.
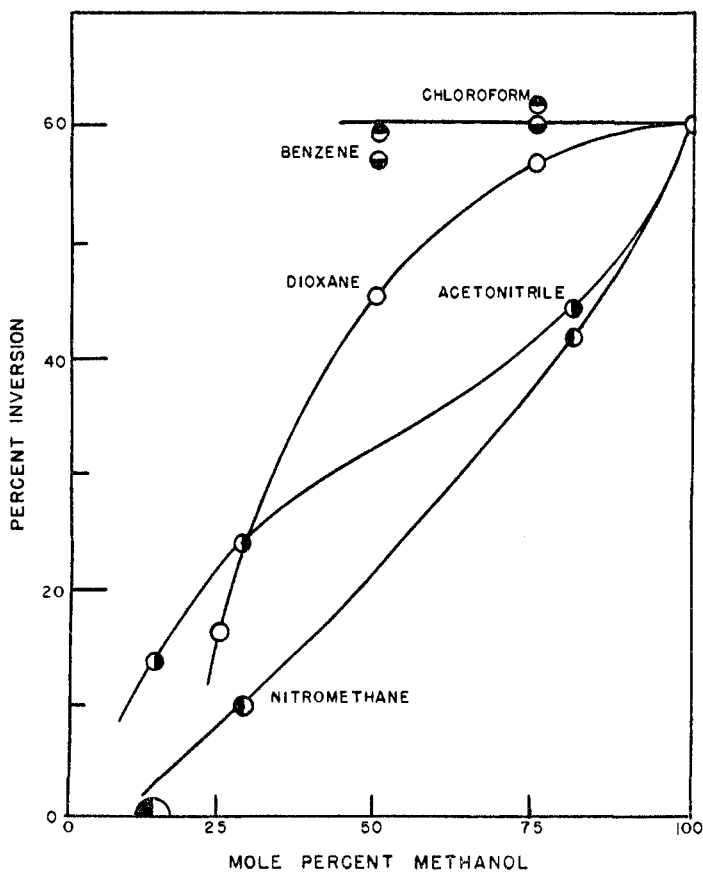
FIG. 18. Stereochemistry of the methanolysis of hydrogen 2,4-dimethylhexyl-4 phthalate in various solvent mixtures.

(XLVI) with 60 per cent inversion of configuration and 40 per cent racemization.

XLV   XLVI
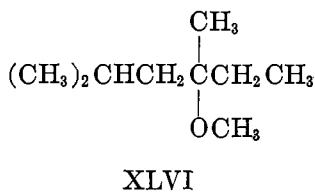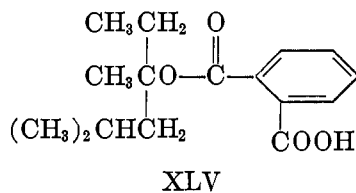
When the methanol is diluted with benzene or chloroform, the stereochemical outcome of the methanolysis is virtually unchanged. The addition of dioxane, acetonitrile, or nitromethane to the solution causes an increased degree of racemization (figure 18) (213, 214). In the several cases in which unreacted hydrogen phthalate was recovered, its rotation was unchanged. The self-racemization of XLVI under the conditions used was demonstrated to be too slow to account for the results.

The observations cannot be accommodated by any reasonable picture which invokes the "lifetime" of the carbonium ion, for there is no consistent correlation between the dielectric constant or ionizing power of the solvent and the extent of racemization. One must postulate the involvement of *intermediates* in which the leaving group and specific solvent molecules are bound in some way to the central carbonium ion. Since the reaction is acid-catalyzed, phthalic acid itself is undoubtedly the leaving group:

$$
XLV \ + \ H^+ \ \rightleftharpoons \qquad
\begin{array}{c}
C_2H_5 \\
\backslash \\
CH_3\!-\!\overset{\displaystyle |}{C}\!-\!O\!-\!\overset{\displaystyle \overset{\oplus O\nearrow H}{\|}}{C}\!\!-\!\!\langle\text{ring}\rangle \\
\diagup \qquad \qquad \diagup \\
(CH_3)_2CHCH_2 \quad HOOC
\end{array}
\ \rightarrow
$$

$$
\begin{array}{c}
C_2H_5 \qquad\qquad OH \\
| \qquad\qquad\qquad | \\
\oplus C\cdots\cdots\cdots O\!=\!C\!-\!\langle\text{ring}\rangle \\
\diagup| \qquad\qquad\qquad \diagup \\
CH_3\ | \qquad\qquad\qquad \\
(CH_3)_2CHCH_2 \quad HOOC
\end{array}
$$
XLVII

The results can be readily accounted for by a logical extension of the reaction sequence used to interpret the simple stereochemistry of solvolysis (page 641):

XLVII

$$
\begin{array}{ccc}
Q\cdots\overset{|}{C}\cdots X & \qquad & P\cdots\overset{|}{C}\cdots X \ \rightarrow \ P\!-\!C\!\big\langle \\
\diagup| & & \diagup| \qquad\qquad \text{Inverted} \\
& & \swarrow XLVIII \\
Q\cdots\overset{|}{C}\cdots Q \ \rightleftarrows \ P\cdots\overset{|}{C}\cdots Q \\
\diagup| \qqu\qquad \diagup| \\
L \qquad\qquad \\
\Updownarrow \qquad\qquad \Updownarrow \\
Q\cdots\overset{|}{C}\cdots P \ \rightleftarrows \ P\cdots\overset{|}{C}\cdots P \ \rightarrow \\
\diagup| \qquad\qquad \diagup| \\
& XLIX
\end{array}
$$

Inverted

P—C⟨ + ⟩C—P
Racemic

In this diagrammatic scheme P and Q represent components of the solvent mixture of which only P is capable of forming a stable compound with the carbonium ion. If the addend to the methanol has unshared pairs of electrons able to participate in p_σ-bonding to a carbonium ion yet does not form a stable com-

pound with the reacting system, such an addend cannot but increase the extent of racemization through such intermediates as L and the like. Dioxane, nitromethane, and acetonitrile are to be placed in this class. If the addend is unable to participate in such bonding, it cannot compete with the methanol for the carbonium ion. In this case only intermediates XLVIII and XLIX can be involved, and the stereochemical outcome is the same as in the absence of the addend.

Analogous results have been obtained with a primary system (594). Solvolysis of optically active butyl-1-d p-nitrobenzenesulfonate in acetic acid at 114°C. gave butyl-1-d acetate with 85 ± 2 per cent inversion and 15 ± 2 per cent racemization. In a mixture of 90 per cent nitrobenzene and 10 per cent acetic acid, the acetate formed showed 51 ± 2 per cent inversion and 49 ± 2 per cent racemization. Similarly, in a mixture of 75 per cent dioxane and 25 per cent acetic acid at 97°C. the acetate was only 46 ± 2 per cent inverted, although replacement of the dioxane by o-dichlorobenzene caused formation of the acetate with 93 ± 6 per cent inversion. The p-nitrobenzenesulfonate and acetate esters were shown to be optically stable to the reaction conditions; hence the stereochemical results pertain to the solvolysis reactions.

Nitrobenzene and dioxane, which have electron pairs available for bonding, cause increased racemization, although dichlorobenzene, which is far less nucleophilic, effects essentially no change. The pattern of the results resembles closely that obtained in figure 18, although, of the systems compared, one is primary and the other is tertiary; in one case the leaving group is a negative ion and the intermediates involved can be called ion-pairs, while in the other the leaving group is a neutral molecule and the intermediates involved cannot be considered as ion-pairs. The differences between the various systems seem to be of degree rather than of kind.

(c) Internal return in allylic systems

A number of investigations of allylic systems have provided important evidence for the existence in solvolysis of *intermediates in which the leaving group is still bonded to the reacting system.*

The acetolysis of α,α-dimethylallyl chloride (LI) is accompanied by a rearrangement to γ,γ-dimethylallyl chloride (LII) (701). The rate of rearrangement follows first-order kinetics and is independent of added chloride ion; hence the rearrangement must be intramolecular. A similar rearrangement accompanies solvolysis in 75 per cent aqueous ethanol but not in absolute ethanol (200). When the solvolysis of either LI or LII in aqueous ethanol is carried out in the presence of excess $^{36}Cl^-$, the unreacted rearranged allylic halide recovered contains some of the isotopic chlorine *but not the amount which corresponds to the*

$$CH_2{=}CH\overset{\displaystyle CH_3}{\underset{\displaystyle CH_3}{C}}Cl \qquad\qquad (CH_3)_2C{=}CHCH_2Cl$$
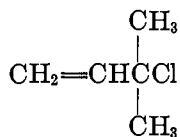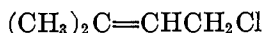
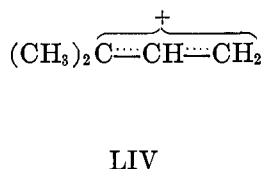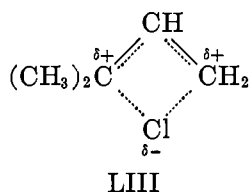LI   LII

equilibrium value. Part of the rearranged halide must result from an intramolecular rearrangement and the rest must come from some reaction involving chloride ion in solution.

There are two general ways of interpreting the results: either the intramolecular rearrangement is a reaction completely independent of the concurring solvolysis or the intramolecular rearrangement and the solvolysis involve a common intermediate. de la Mare and Vernon (200), who prefer the former alternative, propose two simultaneous reactions, an intramolecular cyclization involving structure LIII as a *transition state*, the $S_N i'$ reaction, and an $S_N 1$ ionization reaction to the free carbonium ion (LIV). The ion can react with solvent to give a mixture of products or with chloride ion to give a mixture of LI and LII.

$$(CH_3)_2 \overset{\delta+}{C} \underset{\overset{\displaystyle Cl}{\delta-}}{\overset{\displaystyle CH}{\diagdown}} \overset{\delta+}{CH_2} \qquad\qquad (CH_3)_2 \overset{+}{\overbrace{C \text{---} CH \text{---} CH_2}}$$

LIII   LIV

Young, Winstein, and Goering (701) suggest instead that structure LIII is an *intermediate* which is common to all of the reactions. This intermediate can revert back to either LI or LII or it can react with solvent to form either the primary or the tertiary acetate. LIII could also react with chloride ion in solution. With labeled chloride ion such an exchange reaction would result in a similar intermediate with isotopic chlorine. The subsequent reactions of this intermediate would result in both LI and LII containing isotopic chlorine.

The distinction between the two alternatives, although subtle, can be made on the following basis: de la Mare and Vernon consider that since LIII is a structure with considerable charge separation, the $S_N i'$ reaction is facilitated by more polar solvents. This assumption is required by the observed increase (45-fold) in the isomerization rate in going from acetic acid to 75 per cent aqueous ethanol (table 37). The experimental results then require that ethanol be considered to be too weakly polar to permit the isomerization! Yet the isomerization is readily observable in acetic acid, which has a far lower dielectric constant than ethanol (acetic acid, 6; ethanol, 24) (447). Furthermore, the $S_N 1$ heterolysis postulated by de la Mare and Vernon must involve charge separation akin to that involved in the isomerization. The solvolysis rates of LI and LII in acetic acid and in ethanol differ only slightly (table 37). The rate of the $S_N i'$ reaction would be expected also to be of similar magnitude in the two solvents. The fact that no isomerization occurs in ethanol renders the hypothesis of independent mechanisms untenable.

On the other hand, the results are readily explicable by the hypothesis of a common intermediate. The partition of the common intermediate between the "return" reactions and further solvolysis reactions will depend on the nucleophilicity and the ionizing power of the solvent. An increase in solvent nucleophilicity will increase the rates of reactions which involve bonding between the

TABLE 37

Solvolysis of α,α- and γ,γ-dimethylallyl chloride

$$LI \xrightarrow{k_i} LII$$

$$\downarrow k_T \qquad \downarrow k_p$$

Solvolysis products
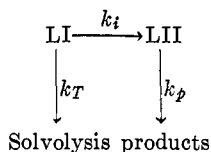
Rate Constant	$10^5 k$, sec.$^{-1}$ (200, 701)		
	Solvent		
	Acetic acid	75% Ethanol	Ethanol
k_T	1.5	380	1.8
k_p	0.22	115	0.65
k_i	4.0	180*	~0

* Calculated from the data of reference 200 by the method given in reference 701.

carbonium ion and the solvent. An increase in the solvation forces associated with the leaving group will tend also to facilitate further solvolysis and will relatively retard the return step. In acetic acid, the return as measured by k_i is high. The return step is relatively much slower than reaction with solvent in the more nucleophilic 75 per cent aqueous ethanol and cannot compete with reaction with solvent in pure ethanol. These facts are in complete accord with the above interpretation. The explanation is a valid one whether the intermediate is formulated as an ion-pair (LV) held together by purely electrostatic forces, or as LIII in which covalent bonding forces are important, or as a structure similar to LIII but modified to include one or more specific solvent molecules as in LVI.

carbonium ion and the solvent.

LV   LVI
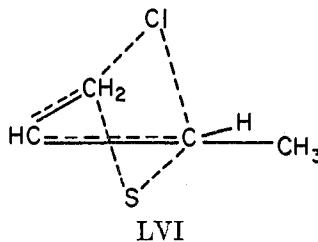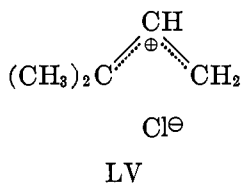
Internal return has also been investigated in the reactions of *cis*- and *trans*-3-chloro-5-methylcyclohexene (LVII and LVIII, respectively) (278), in which stereochemistry and geometric isomerism have been ingeniously combined to yield a maximum of information. In both ethanol and acetic acid, the rate of loss of optical activity of both LVII and LVIII exceeds the rate of solvolysis. Each chloride gradually racemizes as it solvolyzes *without cis–trans isomerism*. These results are readily interpretable as "internal return" phenomena. The first intermediates involved in each case, LIX and LX, are symmetrical; hence they are incapable of sustaining optical activity.

LIX   LX

The term "ion-pair", which has been used in connection with structures of these types, must not be taken in the literal sense of a pair of oppositely charged ions held in close juxtaposition by chiefly electrostatic forces. Since varying degrees of covalent bonding can, in principle, be involved, it is difficult rationally to define a dividing line between an ion-pair and an ordinary compound. If the bonding in LX were purely ionic, one would expect relatively free rotation of each of the ions and therefore facile *cis–trans* interconversion.

Because the carbonium ion which results from the ionization is of the disecondary allyl type, the halides LVII and LVIII are very reactive. The relative solvolysis rates in ethanol at 30°C. are as follows: *tert*-butyl chloride, 1.00 (298); LVII, 102 (278); LVIII, 75 (278); benzhydryl chloride, 480 (647). The high rates of solvolysis suggest that there is no significant nucleophilic contribution by solvent at the rear at the first transition state. This conclusion is supported by the fact that the rates of racemization of both isomeric allylic chlorides are slightly greater in acetic acid (278). Hence, LIX and LX are good representations of the first intermediates. Reactions with solvent (S) to form covalently solvated intermediates, such as LXI and LXII, are probably the subsequent steps.

LXI   LXII

The reaction sequence is written as follows (for LVII):

$$LVII \; \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} \; LIX \; \overset{k_s}{\longrightarrow} \; LXI \text{ and products}$$

If k_α is the rate constant obtained by measuring the loss of optical activity (polarimetric constant) and k_t is the rate constant obtained by measuring the development of acidity or of chloride ion (titrimetric constant), the ratio, k_{-1}/k_s, is given by $(k_\alpha/k_t) - 1$. Some measured values are given in table 38.

In each case, the amount of internal return is much greater for less nucleophilic solvents. Internal return for LVII and LVIII is greater for the *trans*

TABLE 38

Internal return in allylic systems

Compound	Conditions	k_{-1}/k_s	Reference
cis-5-Methyl-3-chlorocyclohexene...................	Ethanol	0.11 ± 0.07	(278)
	Acetic acid, 30°C.	2.03 ± 0.10	(278)
trans-5-Methyl-3-chlorocyclohexene................	Ethanol, 30°C.	0.63 ± 0.04	(278)
	Acetic acid, 30°C.	4.07 ± 0.13	(278)
Hydrogen *cis*-5-methyl-3-cyclohexenyl phthalate...	90% Acetone, 100°C.	0.74 ± 0.07	(279)
	80% Acetone, 100°C.	0.49 ± 0.09	(279)
	60% Acetone, 100°C.	0.29 ± 0.06	(279)
	50% Acetone, 100°C.	0.26 ± 0.08	(279)
Hydrogen *trans*-5-methyl-3-cyclohexenyl phthalate.	90% Acetone, 100°C.	0.69 ± 0.12	(279)
cis-5-Methyl-3-cyclohexenyl *p*-nitrobenzoate........	80% Acetone, 100°C.	0.74 ± 0.06	(280)
	80% Acetone, acid-catalyzed	0.00 ± 0.03	(280)
trans-5-Methyl-3-cyclohexenyl *p*-nitrobenzoate.....	80% Acetone, 100°C.	0.53 ± 0.02	(280)
	80% Acetone, acid-catalyzed	0.03 ± 0.02	(280)

isomer, perhaps because of steric hindrance to nucleophilic solvation by the methyl group which is on the same side of the ring as the incoming solvent molecule. With larger leaving groups, however, the trend is reversed.

The relative reactivities of LVII and LVIII have interesting consequences with regard to the solvolysis products. The relative rates of solvolysis imply that the stabilities of the intermediates are rather close to the stabilities of the corresponding intermediates formed during the solvolyses of benzhydryl systems. The stereochemical outcome of the solvolysis of a benzhydryl system is generally complete racemization. In a similar manner, the di-solvated species, LXII, would be expected to form from both LVII and LVIII before appreciable rehybridization of earlier intermediates to tetrahedral products had occurred. *The solvolysis rates of LVII and LVIII imply that both should give the same product mixture.* In ethanol both LVII and LVIII do in fact give the same mixture of isomeric 3-ethoxy-5-methylcyclohexenes (278).

Studies have also been made of the solvolyses of hydrogen *cis*- and *trans*-5-methylcyclohexenyl-3 phthalates in aqueous acetone (279) and in acetonitrile (277) solutions. The phenomenon of internal return was observed in both solvent systems. In agreement with the theory outlined above, the rate of the return step relative to further solvolysis, k_{-1}/k_s, decreases rapidly as the water content (and the ionizing power) is increased in aqueous acetone media (table 38). The rates of both the uncatalyzed and the acid-catalyzed solvolyses of *cis*- and *trans*-5-methylcyclohexenyl-3 *p*-nitrobenzoate have been examined titrimetrically and polarimetrically (280). In the uncatalyzed solvolysis a normal amount of internal return is found (table 38) from an intermediate which is probably best formulated as LXIII. In the acid-catalyzed solvolysis, in which the leaving group is undoubtedly *p*-nitrobenzoic acid, no internal return is found. Goering and Silversmith (280) interpreted these results to mean that the intermediate had to possess the electrostatic bonding of an "ion-pair" in order for the internal return phenomenon to be observable. Because structure LXIV is not an ion-pair, it was considered to be too unstable to represent an intermediate in the solvolysis.

LXIII   LXIV

Other systems which do not involve allylic rearrangement have been found to necessitate the postulation of charged intermediates which cannot be described as ion-pairs. It does not seem improbable that corresponding charged intermediates can be found in allylic systems which will show internal return. The nucleophilicity of the leaving group is certainly an important factor in determining the relative rate of the return step. A leaving carboxylic acid group is certainly far less nucleophilic than a leaving carboxylate ion and should show a much smaller tendency to return.

(d) Internal return in other systems

An isotopic labeling technique applied to some solvolyses of a tertiary carbinyl hydrogen phthalate failed to give evidence of internal return. Hydrogen 2,4-dimethylhexyl-4 phthalate-ether-O^{18} (LXV) was solvolyzed for approximately one half-life in acetonitrile and in aqueous sodium bicarbonate. In each case the

LXV   LXVI

unreacted ester was recovered and was found to be unchanged with respect to the position and amount of the heavy oxygen (214). In acetonitrile, the reaction is probably acid-catalyzed, and, in agreement with the related results of Goering and Silversmith (280), no internal return was found. Return from an intermediate such as LXVI should result in a redistribution of the heavy oxygen. In the aqueous solvolysis the leaving group is a singly or doubly charged phthalate ion, but the great solvating power of water is not conducive to internal return.

When allowed to stand at room temperature, optically active α-phenylethyl p-toluenesulfinate (LXVII) isomerizes to racemic α-phenylethyl p-tolyl sulfone

(389). Arcas, Balfe, and Kenyon (13) found that the formolysis of LXVII is accompanied by the formation of a small amount of optically active sulfone of

$$C_6H_5CHCH_3$$
$$|$$
$$OSOC_7H_7$$
LXVII
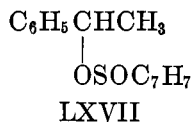
retained configuration. The results were explained by an internal rearrangement similar to a Hofmann rearrangement. The results could also be interpreted as a phenomenon of internal return.

Other examples of internal return are discussed in Sections V and VI.

D. SPECIAL EFFECTS

1. Steric effects

(a) Steric acceleration in tertiary halides

At the transition state for solvolysis of a tertiary carbinyl halide the angle between the alkyl group substituents is greater than in the ground state. Any congestion caused by bulky alkyl groups would be partially relieved at the transition state and would result in an acceleration in rate. This effect has been demonstrated but only for the most demanding systems (110, 112, 116). Most tertiary halides show a rather small variation in rate, plausibly ascribable to the electron-releasing inductive effect of alkyl groups (page 694), but dimethylneo-pentylcarbinyl chloride shows a rate effect too large to be due merely to an inductive effect (table 39). A Stuart model of dimethylneopentylcarbinyl chloride cannot be constructed without strain in the links. When the model is forced together, some of the methyl groups are not free to rotate. For most alkyldi-

TABLE 39

Relative solvolysis rates of tertiary halides

Compound	X = I; 76% Ethanol; 25°C. Relative Rate (569)	X = Cl; 80% Ethanol; 25°C.		X = Br; 85% n-Butyl Cellosolve; 25°C.	
		Relative rate (112, 116)	Per cent olefin (112, 117)	Relative rate (124, 126)	Per cent olefin (124, 126)
$CH_3CX(CH_3)_2$	0.49	0.59	16	—	—
$CH_3CH_2CX(CH_3)_2$	1.00	1.00	34	1.00	34
$CH_3CH_2CH_2CX(CH_3)_2$	0.92	0.94	33	0.77	39
$CH_3(CH_2)_3CX(CH_3)_2$	0.87	0.86	35	—	—
$CH_3(CH_2)_4CX(CH_3)_2$	0.76	—	—	—	—
$(CH_3)_2CHCX(CH_3)_2$	0.79	0.53	62	0.51	63
$(CH_3)_3CCX(CH_3)_2$	1.39	0.73	61	—	—
$(CH_3)_3CCH_2CX(CH_3)_2$	—	12.4	65	12.2	65
$(CH_3)_2CHCH_2CX(CH_3)_2$	—	—	—	1.81	53
$(C_2H_5)(CH_3)_2CCX(CH_3)_2$	—	3.38	—	—	—
$(C_2H_5)_2CXCH_3$	1.71	1.56	41	1.07	42
$[CH_3(CH_2)_4]_2CXCH_3$	—	0.94	—	—	—
$(CH_3)_3CCX(CH_3)C_2H_5$	—	4.13	—	—	—
$[(CH_3)_3CCH_2]_2CXCH_3$	—	322	100*	—	—

* In water.

methylcarbinyl chlorides the models can be easily constructed and allow free rotation of all of the alkyl groups. When two or more of the alkyl groups attached to the reacting carbon are larger than methyl, congestion and hindrance to rotation become more marked. An extreme example is methyldineopentylcarbinyl chloride, which is several hundred times as reactive as *tert*-butyl chloride. Hughes, Ingold, and Shiner (370), however, prefer an explanation based on hyperconjugation of a *tert*-butyl cation.

Since the spreading of congested alkyl groups ("B-strain") (116) gives stabilization over and above that due to the inherent stabilization provided by a planar carbonium ion, the transition state in such cases is expected to be closer to tetrahedral than is the transition state for, say, *tert*-butyl. Charge separation at the transition state for the congested cases would, therefore, be smaller and a smaller dependence on solvent ionizing power should be anticipated. The relative values of m in the Grunwald–Winstein correlation (equation 11) should provide an additional measure of the congestion. Experimentally, the following m values are found (table 24): *tert*-butyl chloride, 1.00; *tert*-amyl chloride, 0.96^{11}; neopentyldimethylcarbinyl chloride, 0.86; dineopentylmethylcarbinyl chloride, 0.70 (112).

In tertiary systems in which skeletal branching occurs next to the reactive carbon, rearrangement is known to occur in some systems with concomitant acceleration of rate (page 709). Rearrangement, however, has been shown to be absent in the solvolyses in aqueous media of neopentyldimethylcarbinyl chloride (112), 2-chloro-2,3,3-trimethylpentane (128), 3-chloro-2,2,3-trimethylpentane (128), and 2-chloro-2,3,3-trimethylbutane (540).

(b) Steric effects in elimination

It has been shown that another criterion of steric congestion (B-strain) (109) is the proportion of olefin in the total solvolysis product. The carbonium-ion intermediate can react with solvent to give a tetrahedral compound or it can eliminate a proton to give an olefin. If steric congestion is important in the tetrahedral system, it should be manifest to some degree in the transition state leading to such a system and the rate of this reaction will be decreased. In the competing elimination reaction, the hybridization of the central carbon is not changed and bulky substituents can have but a second-order effect on the rate. The net result is that systems in which B-strain is important will produce a larger proportion of olefinic products (table 39). The interpretation is complicated by the electronic factors which influence olefin stability; thus, a system which could yield a more highly substituted olefin will tend to form more olefin than a system which can form only less substituted ethylenes.[12] This electronic factor is probably the most important reason why *tert*-amyl chloride yields more

[11] The value for *tert*-amyl chloride was obtained from the bromide (table 24) by correcting for the difference between *tert*-butyl bromide and *tert*-butyl chloride. The value 0.87 quoted by Brown and Berneis (112) was apparently calculated from the rates in only two solvent mixtures (374).

[12] Compare references 370 and 125.

olefin than *tert*-butyl chloride (table 39). On the other hand, the B-strain argument undoubtedly applies to the following olefin percentages in the solvolysis products: *tert*-amyl chloride, 34 per cent in 80 per cent ethanol; neopentyldimethylcarbinyl chloride, 64 per cent in 80 per cent ethanol; dineopentylmethylcarbinyl chloride, 100 per cent in water (table 39).

(c) Steric hindrance to conjugation

The relative rates of solvolysis in 80 per cent ethanol at 45°C. of the compounds C_6H_5CHClR, for different R groups, are as follows: methyl, 540; ethyl, 125; isopropyl, 27; *tert*-butyl, 1 (20). The effect has been plausibly ascribed to the steric repulsions between the R group and the ortho hydrogens of the ring, which prevent the ring from achieving coplanarity with the developing carbonium ion (20). As the R group becomes larger, the angle between the plane of the carbonium ion and the plane of the ring becomes greater, overlap of the carbonium *p* orbital with the benzenoid *p* orbitals is decreased, and the stabilization of the cation is decreased. Such steric hindrance undoubtedly also provides the explanation for the lesser rate-enhancing effectiveness of a methyl group compared to a *p*-methyl group in the solvolyses of arylmethyl systems (table 20).

The π-overlap between two *p* orbitals is roughly proportional to the cosine of the angle between them. Hence, a carbonium ion may be twisted rather severely from the plane of an attached benzene ring and still be able to distribute a considerable amount of positive charge to the ring. In the α-mesitylethyl cation (LXVIII) the carbonium center must be far from coplanar with the ring; yet
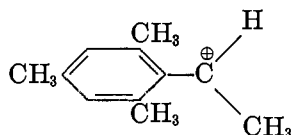
LXVIII

the ethanolysis of α-mesitylethyl chloride at 25°C. is 2000 times faster than that of α-phenylethyl chloride (19). The ability of the *o*- and *p*-methyl groups to further distribute positive charge far outweighs the effect of steric hindrance to coplanarity.

2. Effect of ring size
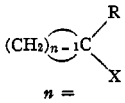
The facility with which direct displacement reactions and solvolyses occur with cycloalkane derivatives is markedly dependent on the size of the ring and on the nucleophilicity of the substituting group. Direct displacement reactions give a pattern of rates as a function of ring size different in detail from reactions which are more limiting in character (table 40).

(a) Cyclopropyl systems

Cyclopropyl halides and sulfonate esters are exceptionally slow in displacement reactions. The analogy to vinyl and phenyl groups has been made (532). Because the three-membered ring has bond angles much less than the normal

TABLE 40

Relative reactivities of cycloalkyl systems

$(CH_2)_{n-1}C$ with R and X, $n =$	Relative Rates				
	Solvolyses			Direct displacements	
	R = H, X = OTs CH$_3$COOH, 60°C. (325a, 532)	R = H, X = Cl 50% C$_2$H$_5$OH 95°C. (532)	R = CH$_3$, X = Cl 80% C$_2$H$_5$OH 25°C. (113)	R = H, X = Br LiI, acetone 25°C. (253, 254)	R = H, X = I NaI, C$_2$H$_5$OH 25°C. (441, 633)
(CH$_3$)$_2$CRX	1.00	1.00	1.00	1.00	1.00
3	2×10^{-5}	<0.005	—	<0.0001 [a]	—
4	12	15	0.074	0.0075	—
5	14	5.2	44	1.6	1.28
6	0.88	0.36	0.35	0.010	0.012
7	27 [b]	—	38	0.98	1.74
8	251 [b]	—	100	0.22	0.41
9	234 [b]	—	15.4	—	—
10	474 [b]	—	6.2	—	—
11	59 [b]	—	4.2	—	—
12	2.7 [b]	—	—	—	—
13	—	—	1.0	—	—
15	—	—	0.64	—	0.14
20	1.7 [b]	—	—	—	—

[a] This is an approximate upper limit. No reaction could be detected between potassium iodide and cyclopropyl bromide at 100°C. or with cyclopropyl chloride at 200°C. in acetone (532).

[b] At 50°C.

tetrahedral, the hybrid orbitals comprising the ring structure probably have considerably more p character than the normal sp^3 orbitals. The additional p requirements of these bonds render more difficult the partial localization of the p orbital required at the transition state for displacement. The term "I-strain" has been applied to the energetics of strained ring systems (120).
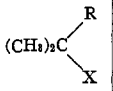
(b) Cyclobutyl systems

The considerations discussed with reference to cyclopropyl compounds will apply also to cyclobutyl systems, albeit to a lesser extent. Rates of displacement on the four-membered ring are expected to be low. The solvolysis of 1-chloro-1-methylcyclobutane and the displacement of cyclobutyl bromide by iodide ion are significantly slower than the corresponding reactions of acyclic compounds (table 40). However, the acetolysis of cyclobutyl tosylate and the solvolysis of cyclobutyl chloride in 50 per cent ethanol are *faster* than the corresponding reactions of isopropyl derivatives. Anchimeric assistance with rearrangement (page 712) is probably involved in these cases. Such rearrangement has been demonstrated not to occur in the case of 1-chloro-1-methylcyclobutane (113). The reason rearrangement does not occur in this case is undoubtedly because the primary or secondary carbonium ions which would result from rearrangement are much less stable than the original tertiary carbonium ion.

(c) Cyclopentyl systems

Since the bond angles in cyclopentane are constrained to values close to tetrahedral, rehybridization of one carbon to sp^2 with bond angles of 120° would

TABLE 41

Comparison of isopropyl, cyclopentyl, and cyclohexyl systems

Compound		Reaction Conditions	Relative Rates			References
R	X		$(CH_3)_2C\diagdown_X^{\diagup R}$	$\square\diagdown_X^{\diagup R}$	$\hexagon\diagdown_X^{\diagup R}$	
CH₃	Cl	80% Ethanol, 25°C.	1.00	44	0.35	(113)
i-C₃H₇	Cl	84% Ethanol, 30°C.	1.00[a]	14.9	0.45	(577a)
H	Cl	80% Ethanol, 85°C.	1.00	9.2	0.65[b]	(365, 375, 538)
H	Cl	50% Ethanol, 95°C.	1.00	5.2	0.36	(532)
H	OTs	Ethanol, 50°C.	1.00	6.1	0.17	(676, 684)
H	OTs	Methanol, 50°C.	1.00[c]	7.7	0.20	(349, 544)
H	OTs	Acetic acid, 50°C.	1.00[d]	18	0.88	(669, 676, 684)
H	OTs	HCOOH, 25°C.	1.00[d]	32	1.7	(676, 684)
H	Br	LiI, acetone, 25°C.	1.00	1.6	0.010	(253)

[a] For diethylisopropylcarbinyl chloride.

[b] At 125°C.

[c] $k_{ROTs}/k_{ROSO_2C_6H_5}$ taken as 0.63.

[d] k_{ROTs}/k_{ROBs} was assumed to be identical for isopropyl and for cyclohexyl.

be somewhat hindered. On the other hand, it has been pointed out (113, 119, 532) that such rehybridization is accompanied by a decrease in the number of carbon–hydrogen bond oppositions from ten to six with the consequent increase in stability associated with staggered bonds. As the nucleophilicity of the attacking group becomes more important, its bond to the central carbon is shorter at the transition state and bond opposition strains between this grouping and the neighboring hydrogens would be expected to become progressively more important. Direct displacement reactions on cyclopentyl systems are about as fast as on isopropyl systems. Solvolytic displacements are considerably faster, and, moreover, the relative rate increases with decreasing nucleophilic contribution at the transition state (table 41).

(d) Cyclohexyl systems

Since the puckered cyclohexane ring is strainless and without opposed bonds, a driving force for reaction analogous to the cyclopentyl case is absent. Furthermore, nucleophilic attack on a cyclohexyl ring carbon will invoke bond opposition strains between some of the ring hydrogen atoms and the entering and leaving groups. Solvolytic reactions proceed at about the same rate as in acyclic analogs, although the relative rate decreases with increasing nucleophilic contribution at the transition state (table 41). Direct displacement reactions in which nucleophilicity and close approach of the attacking reagent are of prime importance are only 0.01 as fast as those of acyclic analogs.

The recognition of axial and equatorial positions in cyclohexane ring systems (58, 312, 313) and the derived conformational analyses have substantially contributed to an understanding of the physical and chemical properties of ring structures (reviewed in references 10, 57, and 188a). The importance of the axial-equatorial concept in simple cyclohexyl systems has recently been quanti-

tatively evaluated by Winstein and Holness (676). The relative reactivities of cis- and trans-4-tert-butylcyclohexyl tosylates (LXIX and LXX, respectively), in which the tert-butyl group is constrained to an equatorial position because of its bulk, provide measures of the relative reactivities of axial and equatorial substituents in various reactions. These authors found that the difference in reactivity between axial and equatorial leaving groups is significant but rather small; the rate ratios, $k_{axial\ (cis)}/k_{equatorial\ (trans)}$, for tosylate solvolysis at 50°C. in ethanol, acetic acid, and formic acid are, respectively, 3.9, 3.2, and 3.6. LXIX (axial tosyl group) gave significantly more olefin among the products than did the trans isomer (LXX). If a common carbonium-ion intermediate were involved, each isomer would have given the same mixture of products. In each case, the non-olefinic component of the product showed almost complete inversion of configuration, although in some cases rearrangement products were encountered (page 715).

Closely similar results were obtained by Noyce and Weingarten (479), who found the relative acetolysis rates at 75°C. of trans-(axial) and cis-(equatorial) 3-carbomethoxycyclohexyl tosylates to be 4.8. The effect of the inductive influence of the ester grouping is likely to be closely the same in both isomers. The products again corresponded to complete inversion of configuration.

Complete inversion of configuration also results from the methanolyses of 3α- and 3β-cholestanyl tosylates (468) and from the acetolyses of 3α- and 3β-coprostanyl chlorides (104), although the acetolyses of 3α- and 3β-cholestanyl chlorides yield a mixture of epimeric acetates corresponding to partial racemization at the reacting carbon (566). Free carbonium ions in the classical sense are obviously not involved in these reactions.

(e) Larger ring systems

In the solvolyses of 1-chloro-1-methylcycloalkanes in aqueous ethanol the cycloheptyl through cycloundecyl compounds show enhanced rates compared to tert-butyl chloride (table 40). Brown, Fletcher, and Johannesen (119) suggest that the medium-sized rings possess considerable internal strain (I-strain), due primarily to carbon–hydrogen repulsions. These repulsions are then partially relieved in reactions which involve a change in the coordination number. The nucleophilic contribution at the transition state, however, is apparently of considerable importance. When this contribution is great, additional strain from the increased number of bond oppositions seems likely; e.g., 1-chloro-1-methylcyclooctane is 100 times more reactive than tert-butyl chloride in 80 per cent ethanol, whereas the reaction of iodide ion with cyclooctyl bromide is only one-fourth as rapid as with isopropyl bromide (table 40). The analysis of the situation is rather similar to the cyclopentyl cases.

The acetolysis rates of cycloalkyl tosylates with a nine-, ten-, or eleven-membered ring are not only much greater than that of isopropyl tosylate, but the rate enhancements are an order of magnitude greater than in the solvolysis of 1-chloro-1-methylcycloalkane (table 40). In these cases it seems probable that transannular anchimeric assistance is involved (page 716).

Although exceedingly little data is available, it seems likely that in large ring systems the neighborhood of the reactive center is essentially like that in acyclic systems and no important rate effects should be manifest.

(f) Benzcycloalkene systems

The rates of ethanolysis of α-o-tolylethyl chloride, 1-chloroindane (LXXI), 1-chlorotetralin (LXXII), and 3-chloro-1,2-benzcycloheptene (LXXIII) at 25°C. are, respectively, 1.0, 40, 11, and 0.42 (19). The rates of ethanolysis of LXXI and LXXII are faster than that of α-o-tolylethyl chloride, probably because of

LXXI   LXXII   LXXIII
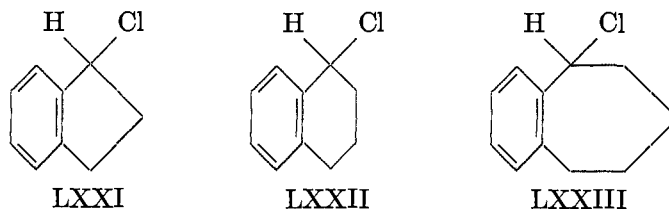
the absence of steric hindrance to coplanarity between the developing carbonium ion and the benzene ring. The relative slowness of the ethanolysis of LXXIII is probably due to an inability of the developing carbonium ion to achieve coplanarity with the benzene ring, because of the conformational requirements of the seven-membered ring. The use of molecular models then allows the prediction that the rate will remain relatively low for the eight- and nine-membered ring analogs. The relative rates of ethanolysis of LXXI, LXXII, LXXIII, and 3-chloro-1,2-benzcycloöctene at 40°C. are 1040, 264, 7.9, and 1.0, respectively (376b).
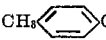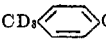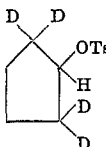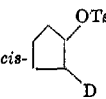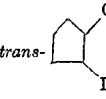
The relative rates of solvolysis of compounds LXXIV, LXXV, and LXXVI in 80 per cent aqueous acetone at 25°C. have been found to be, respectively, 1.93, 1.31, and 1.00 (15). In ethanol at 20°C. the relative rates are, respectively, 1.39, 1.18, and 1.00 (20a). This small rate effect has, nevertheless, been ascribed to steric inhibition of hyperconjugation of an alpha C—H bond with the benzene ring (15, 20a).

LXXIV   LXXV   LXXVI
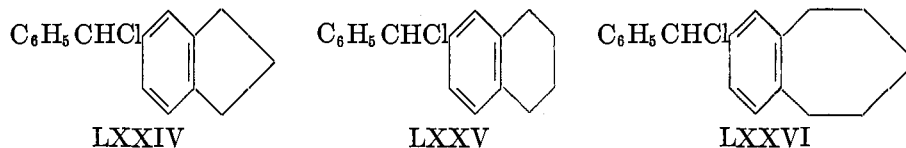
3. Deuterium isotope effects

In reactions in which the rate-determining step involves a breaking of a carbon–hydrogen bond, substitution of deuterium for hydrogen causes a sixfold decrease in rate (153, 563, 697). Solvolysis reactions of alkyl halides and sulfonates do not involve a breaking of a carbon–hydrogen bond in the rate-determining step; yet substitution of deuterium for hydrogen at the carbon adjacent to the reacting center causes a small but significant reduction in the rate of

TABLE 42

Deuterium isotope effects on solvolysis

Parent Compound	Deuterated Compound	Reaction Conditions	k_H/k_D	$\Delta\Delta F^{\ddagger(a)}$	Reference
Isopropyl bromide........	$(CD_3)_2CHBr$	C_2H_5ONa, C_2H_5OH, 25°C.	1.13	12	(563)
tert-Amyl chloride........	$(CD_3)_2CClCD_2CH_3$........	80% C_2H_5OH, 25°C.	2.36	64	(564)
	$(CH_3)_2CClCD_2CH_3$	80% C_2H_5OH, 25°C.	1.41	95	(564)
	$(CD_3)_2CClCH_2CH_3$	80% C_2H_5OH, 25°C.	1.78	56	(564)
Dimethylisopropyl-carbinyl chloride........	$(CH_3)_2CDCCl(CH_3)_2$	80% C_2H_5OH, 25°C.	1.28	156	(565)
2-Pentyl bromide........	$C_2H_5CD_2CHBrCD_3$	HCOOH, 98°C.	1.39	48	(424)
2-Pentyl OTs.............	$C_2H_5CD_2CHOTsCD_3$	HCOOH, 98°C.	1.56[b]	65	(424)
	$C_2H_5CD_2CHOTsCD_3$	HCOOH, 58°C.	1.64[b]	65	(424)
	$C_2H_5CD_2CHOTsCD_3$	CH_3COOH, 58°C.	1.64	65	(424)
	$C_2H_5CD_2CHOTsCD_3$	80% C_2H_5OH, 58°C.	1.40	44	(424)
α-(*p*-Tolyl)ethyl chloride.	CH_3⟨⟩$CHClCD_3$[c]	CH_3COOH, 50°C.	1.28	66	(425)
	CD_3⟨⟩$CHClCH_3$[d]	CH_3COOH, 50°C.	1.10	29	(425)
Cyclopentyl OTs.........		CH_3COOH, 50°C.	2.06	116	(593a)
		CH_3COOH, 50°C.	1.22	125	(593a)
		CH_3COOH, 50°C.	1.17	99	(593a)

[a] Average reduction in free energy of activation per deuterium atom in calories per mole.
[b] Extrapolated from lower temperatures.
[c] Contained 80 per cent of three deuterium atoms per mole.
[d] Contained 67 per cent of three deuterium atoms per mole.

solvolysis (table 42). In some cases, the decrease amounts to as much as a factor of two.

The source of isotope effects is well understood on the basis of statistical thermodynamics and absolute rate theory (87a, 452, 577b). A difference in zero-point energy is one of the factors which determines the effect of isotopic substitution on rate. A weakening of the carbon–hydrogen bond at the transition state implies a lower force constant for bond stretching and a lower zero-point energy for vibration. Since a carbon–deuterium bond has a lower zero-point energy initially, less zero-point energy is lost at the transition state; therefore, the total energy difference between the ground state and the transition state is greater (figure 19). This treatment is simple but somewhat naive; in particular, a more detailed treatment predicts a change in both the energy and the entropy of activation. The rate reductions in the solvolyses of 2,3-dimethyl-2-chlorobutane-
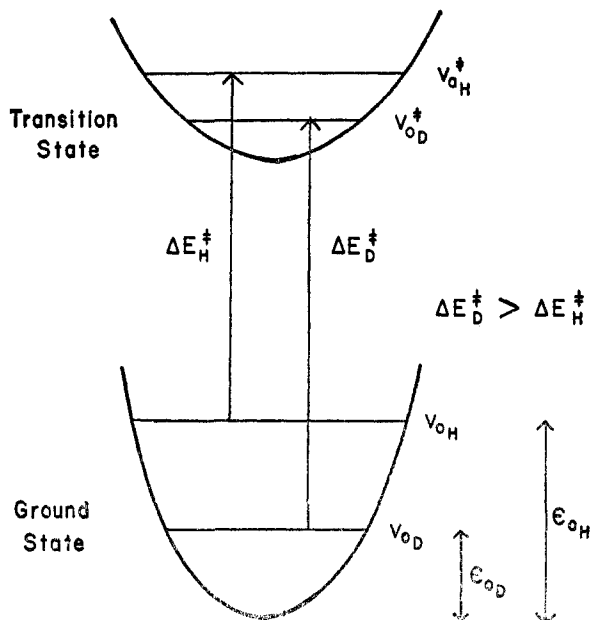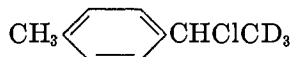
FIG. 19. Diagram showing the effect of deuterium substitution on reaction rates. v_0 is the first vibrational level.

3-d (LXXVII) (565) and 1-chloro-1-p-tolylethane-2,2,2-d_3 (LXXVIII) (425) have been shown to be due to changes in both the energy and entropy of activation.

$$(CH_3)_2CDCCl(CH_3)_2 \qquad CH_3 \langle\!\!\!\bigcirc\!\!\!\rangle CHClCD_3$$

LXXVII   LXXVIII

The magnitude of the isotope effect is dependent in part on the requirements of the developing carbonium ion for internal electron supply at the transition state. Since the tosyl group is a "better" leaving group than bromide (table 36), the reacting center has more of a positive charge to be distributed at the transition state; i.e., solvolysis of tosylates involves greater electron withdrawal from neighboring bonds than the corresponding solvolysis of bromides. The deuterium isotope effect, consequently, is greater for tosylates than for bromides; e.g., the rate ratio, k_H/k_D, for the formolysis of 2-pentyl-1,1,1,3,3-d_5 tosylate (LXXIX) compared to 2-pentyl tosylate is 1.56 at 98°C.; the ratio for the corresponding bromides under the same conditions is 1.39 (table 42).

$$CH_3CH_2CD_2CHOTsCD_3$$

LXXIX

The greater the solvent nucleophilicity, the greater the demand for electrons can be fulfilled by orbital overlap with a solvent molecule and the less the necessity for weakening neighboring bonds. The ratios k_H/k_D for the solvolyses

of LXXIX in 80 per cent ethanol, acetic acid, and formic acid are, respectively, 1.40, 1.64, and 1.64 at 58°C. (table 42). Because of the probable difference in the position of the transition state along the reaction coordinate in formolysis compared to acetolysis, one would have expected the isotopic rate reduction to be somewhat greater in the former case. The difference, however, could well lie within the experimental error. The difference between the aqueous ethanol and carboxylic acid solvents is probably significant.

In direct displacement reactions, nucleophilicity of the substituting group is of major importance and the amount of positive charge developed at the reacting center at the transition state is small (page 587); consequently, the deuterium isotope effect for such substitutions is rather small. Each substitution by deuterium of a β-hydrogen atom in isopropyl bromide decreases the rate of substitution by ethoxide ion by only 2 per cent (563).

Lewis, Boozer, and Coppinger (96, 98, 424, 425) have interpreted the deuterium isotope effect in substitution reactions as a manifestation of hyperconjugation. This interpretation is consistent with the results of Shiner (564, 565), who found that the effectiveness of a single substitution of deuterium for hydrogen in decreasing the solvolysis rate of tertiary halides depended on the nature of the hydrogen and increased along the series primary < secondary < tertiary. Based on the stabilities of the corresponding olefins the order of importance of hyperconjugation resonance structures in the stabilization of carbonium ions is expected to be LXXX > LXXXI > LXXXII.
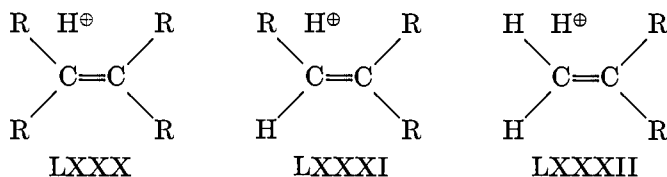
Shiner (564, 565) has suggested that solvation of the hydrogens which bear a partial positive charge is important and that the more readily a hydrogen atom tends to be eliminated as a proton to generate olefin, the greater will be its effectiveness in stabilizing the developing carbonium ion. Lewis and Coppinger (425) have demonstrated that deuterium substitution in the p-methyl group of α-(p-tolyl)ethyl chloride causes a significant albeit rather small reduction in the rate of acetolysis. In this case elimination of the substituted hydrogens to form an olefin does not occur.

Streitwieser, Jagow, and Suzuki (593a) have recently shown the absence of stereospecificity in such hyperconjugation; cis- and trans-cyclopentyl-2-d tosylate showed the same rate reduction in acetolysis compared with cyclopentyl tosylate. The rate reduction in each case was one-fourth the effect shown by cyclopentyl-2,2,5,5-d_4 tosylate (table 42). These results may be taken to indicate that although hydrogen no-bond structures (LXXX, LXXXI, and LXXXII) may be important in determining carbonium-ion stability, the hydrogens involved need not be specifically solvated; i.e., there need not be an analogy to elimination reactions.

TABLE 43

Effect of α-halogen substituents

Compound	Conditions	$\dfrac{k_{X = Cl}}{k_{X = H}}$	$\dfrac{k_{X = Br}}{k_{X = H}}$	$\dfrac{k_{X = F}}{k_{X = H}}$	References
(C₆H₅)₂CXCl.............	Ethanol, 25°C.	14			(7, 647)
	75% Acetone, 0°C.	57.5			(76a)
	85% Acetone, 25°C.	37.0			(76a)
C₆H₅CHXCl..............	50% Acetone, 30°C.	9.9			(333, 490)
C₆H₅CHXBr..............	50% Acetone, 30°C.	5.5	1.21		(7)
C₆H₅CX₂Cl..............	50% Acetone, 30°C.	497		0.187	(333, 334, 490)
C₆H₅CX₂Br..............	50% Acetone, 30°C.	374	203		(333)
C₆H₅CHXCl..............	Ethanol, 25°C.	7.9			(9, 485, 670)
C₆H₅CH=CHCHXCl......	Ethanol, 25°C.	7.6*			(9, 636)
CH₂=CHCHXCl..........	Formic acid, 44.6°C.	64			(635)
	50% Ethanol, 44.6°C.	1.3			(635)
C₆H₅CXClCH₃.............	Ethanol, 25°C.	32			(19, 619)
C₆H₅CXBrCH₃.............	Ethanol, 55°C.		9.7		(619)
	80% Ethanol, 55°C.		8.3		(619)

* Calculated from data at other temperatures, using the value of $\Delta E^{\ddagger}$ in 50 per cent ethanol (635).

4. α-Heteroatoms

(a) Halogens

A halogen atom bonded to the reacting carbon atom will tend to accelerate the rate of solvolysis by sharing the developing positive charge with p orbital π-overlap and will tend to retard the rate by inductively inducing greater electronegativity in the reacting carbon atom which renders it less able to support a positive charge. Electronegativity decreases along the series F > Cl > Br > I, but so also does the carbon–halogen π-bond overlap, since the higher p orbitals are effectively larger and more diffuse. The effect of electronegativity apparently predominates with α-fluorine substituents, for they generally decrease the rate of solvolysis (334). The resonance effect seems to predominate for α-chlorine substitution, which generally increases the rate of solvolysis (table 43). Bromine behaves much like chlorine but seems to be less effective in accelerating the rate of solvolysis.

This pattern of results for halogen atoms conjugated directly with the reacting center may be contrasted with that obtained for the solvolysis of p-halobenzyl chlorides. In this system conjugation with the reacting center is still effective, although the resonance effect must be transmitted through a benzene ring. The distance between the functional groups, however, substantially reduces the inductive effect of electronegativity. The relative rates in 50 per cent acetone at 70°C. for fluorine, chlorine, bromine, and iodine substituents are, respectively, 1.00, 0.35, 0.27, and 0.25 (75). The fluorine group imparts the greatest reactivity in this system.

The shorter and stronger the bond between the central carbon atom and the nucleophilic solvent molecule, the greater will be the extent of the repulsive neighboring orbital overlap (page 598). Conversely, as the solvolysis system becomes more limiting, α-chlorine substitution is more effective in accelerating the rate. The acceleration provided by an α-chlorine atom in allyl chloride is

64-fold in formic acid but only 1.3-fold in 50 per cent aqueous ethanol. The acceleration of ethanolysis rate by an α-chlorine atom substituted into benzhydryl chloride is double that of the same change in benzyl chloride (table 43). In aqueous acetone the effect is even greater.

(b) Oxygen

Despite the high electronegativity of oxygen, the great stability of the carbon–oxygen π-bond is reflected in the high reactivities of α-halo ethers. The relative solvolysis rates in 36 per cent aqueous dioxane at 100°C. of ethyl chloromethyl ether, butyl chloride, and ethyl β-chloroethyl ether are, respectively, 10^9, 1, and 0.2 (91, 92). In ethanol, methyl chloromethyl ether solvolyzes about 10^{13} times faster than n-propyl chloride (38a). The relative energies of resonance structures LXXXIII and LXXXIV imply that the intermediate in the hydrolysis of ethyl chloromethyl ether should be regarded more as an oxonium salt than as a carbonium ion.

$$CH_3CH_2\overset{+}{O}{=}CH_2 \quad \leftrightarrow \quad CH_3CH_2OCH_2^+$$
$$\text{LXXXIII} \qquad\qquad \text{LXXXIV}$$
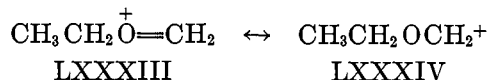
The reactions of α-chloro ethers in dioxane with small amounts of an alcohol are catalyzed by hydrochloric acid. In pure alcohol the reactions are not acid-catalyzed (414, 415). In dioxane, which has a low dielectric constant, the results mean that hydrogen chloride is probably required to help solvate the leaving halide with the formation of an ion-pair (LXXXV).

$$ROCH_2Cl \; + \; HCl \; \rightleftarrows \; ROCH_2^+ \; HCl_2^-$$
$$\text{LXXXV}$$
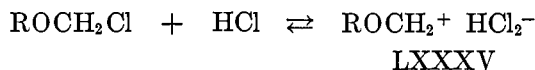
V. Intramolecular Displacements

In the displacement reactions described in Sections III and IV the required electron supply was realized from the carbon system itself and frequently from an attacking nucleophilic molecule. In a large class of systems, the role of the latter group is assumed in whole or in part by a nucleophilic function which is a part of the organic molecule undergoing displacement. As in the displacement reactions by external agents, the varying fraction of the required electrons supplied by this internal function depends on the nucleophilicity of the function and on the requirements of the reacting center for electrons; thus, the driving force associated with the intramolecular attack by the function may range from very large to insignificantly small. The term "neighboring group" has been associated with the internal nucleophilic function. The term "anchimeric assistance" has been used to denote the driving force provided by participation by the neighboring group (679).

In general, the transition state for neighboring group displacement may be represented by LXXXVI. The central carbon may but need not necessarily have the planar sp^2 configuration. The role of neighboring groups on a β-carbon atom has been studied with particular intensity. The results have been summarized

in a general theory by Winstein and Grunwald (667), who discuss the chemistry
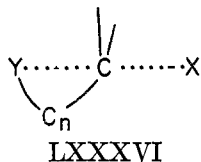
LXXXVI

of the intermediate in terms of the contributing resonance structures LXXXVII, LXXXVIII, and LXXXIX. In brief, an increase in the stability of LXXXVII generally decreases anchimeric assistance; an increase in the stability of LXXXVIII or LXXXIX increases anchimeric assistance.

LXXXVII   LXXXVIII   LXXXIX
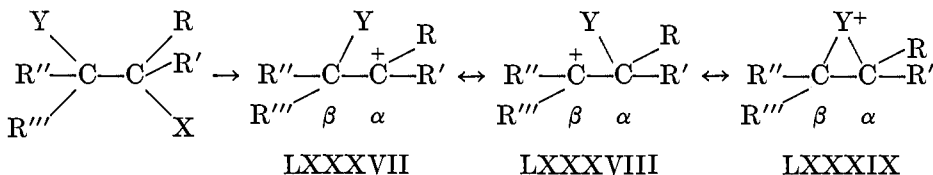
Three principal methods have been used to detect neighboring group participation. *If anchimeric assistance is significant in a given system, the rate of reaction must be greater than the rate of solvolysis in the absence of such participation.* A rate enhancement, consequently, is one criterion for participation, but only if the participation is significant at the transition state of the rate-determining step. The application of this criterion obviously requires some means of estimating the expected rate in the absence of participation.

Subsequent reaction of the intermediate can frequently give rise to isomeric products in which rearrangement is apparent. From the intermediate formulated as the resonance hybrid of structures LXXXVII, LXXXVIII, and LXXXIX, for example, reaction could give XC or XCI as the final products, in which S is frequently a solvent moiety. The isolation of rearranged products constitutes another criterion for the involvement of intermediates which result from participation. Finally, neighboring group participation often has stereochemical consequences which determine a further mechanistic criterion. Both of these latter criteria can sometimes be applied to cases in which participation occurs *after* the rate-determining step.
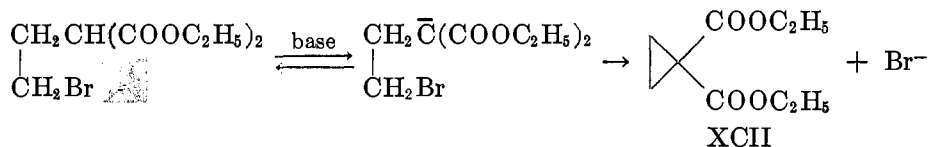

XC   XCI
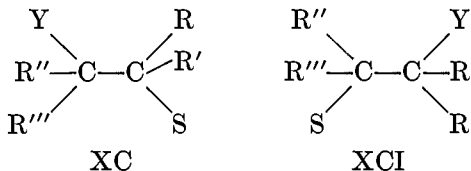
The various neighboring nucleophilic functions will be individually discussed.

A. NEIGHBORING CARBANION

Important synthetic methods for preparing cycloalkane systems include those reactions in which a halide ion is displaced by a neighboring carbanion.

An example is the preparation of diethyl 1,1-cyclopropanedicarboxylate (XCII) (517).

$$CH_2CH(COOC_2H_5)_2 \xrightleftharpoons{\text{base}} CH_2\bar{C}(COOC_2H_5)_2 \rightarrow \begin{array}{c} \diagup COOC_2H_5 \\ \diagdown COOC_2H_5 \end{array} + Br^-$$
$$| \qquad\qquad\qquad\qquad |$$
$$CH_2Br \qquad\qquad\qquad CH_2Br$$

XCII

Such reactions may be looked upon as intramolecular direct displacement reactions. The driving force for these reactions stems almost entirely from the nucleophilicity of the carbanion group.

B. NEIGHBORING NITROGEN

An extensive study has been made of the rates of cyclization of various ω-bromoalkylamines (264, 265, 266, 267, 268, 269, 550, 551, 552, 553). Salomon (553) has pointed out the complications which occur in these systems. Cyclization is frequently accompanied by reaction with solvent and by polymerization. By a combination of kinetic and preparative experiments data leading to the relative rates in table 44 were obtained.

It is appropriate to compare the rates of ring formation with the rate of solvolysis. Definite driving forces for the formation of three-, five- and six-membered rings are apparent from the rates relative to solvolysis, 10^3, 10, and 10^4, respectively (table 44). There is some driving force for formation of a seven-membered ring (rate relative to solvolysis = 10^2), but there is virtually no anchimeric assistance for the formation of a four-membered ring.

The formation of small rings, three- and four-membered, is not energetically favorable, since these rings involve a certain amount of bond strain. The formation of such rings somewhat restricts the motions of a few atoms, but the consequent entropy decrease is far less than that involved in a bimolecular displacement reaction in which the translational motions of two separate molecules are reduced to the motions of one "activated complex" molecule. The formation of a three-membered ring involves the restriction of fewer atoms than the closure of a four-membered ring; hence it is more rapid (by 100-fold).

TABLE 44

Cyclization of ω-bromoalkylamines

$$Br(CH_2)_{n-1}NH_2 \rightarrow \overparen{(CH_2)_{n-1}NH}\cdot HBr$$

n (Ring Size)	Relative Rate (553)	n (Ring Size)	Relative Rate (553)
3	0.12[a]	12	10^{-5}
4	0.002[a]	14	3×10^{-4}
5	100	15	3×10^{-4}
6	1.7[a]	17	6×10^{-4}
7	0.028[a]	Solvolysis[b]	10^{-4}
10	10^{-3}	Dimerization[c]	10^{-2}

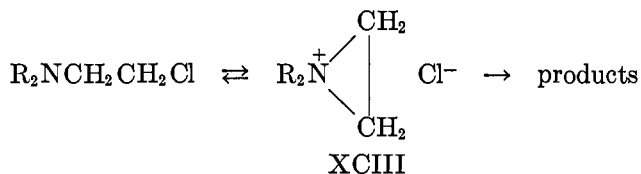[a] At 25°C. in water; others at 73°C. in 30 per cent aqueous 2-propanol.
[b] For reaction with water without participation.
[c] At 1 M concentration.

Five-membered rings are generally rather stable systems, i.e., the bond strengths are normal. In addition, sufficiently few atoms are involved that the entropy requirements are not large. Thus, five-membered rings are readily formed. Six-membered rings have the same order of stability as five-membered rings, but their formation requires the restriction of more atomic motions; hence, they are formed less rapidly than five-membered rings. In intermediate rings of from seven to eleven members, the vibrational modes of all of the atoms between the nucleophilic center and the reaction center are restricted and the entropy demands are high. These rings are relatively difficult to form. Larger rings, however, are sufficiently loose and flexible that sizable segments of the rings behave essentially like similar segments of open-chain analogs. The entropy of such a segment will be essentially the same in the ground state and in the transition state for ring formation. The rates of formation of such rings are not unlike the rates of analogous bimolecular displacement reactions (table 44, dimerization).

Because the entropy changes which accompany the formation of small rings are generally less than the changes involved in bimolecular displacements, steric hindrance effects are not as important for such intramolecular displacements. Consequently, polar effects become more important. The relative rates of cyclization of 1-amino-2-chloroethane, 1-amino-2-chloropropane, and 2-amino-1-chloro-1-phenylethane are, respectively, 1, 4, and 800 (269). The fact that the secondary chloride reacts somewhat more rapidly than the primary is consistent with the proposition that the polar effect of alkyl groups is generally to increase the rate of displacement (page 587).

The chemistry of 2-dialkylaminoethyl chlorides was extensively studied during the last war because of their relationship to mustard gas. Aqueous solvolysis of these compounds has been abundantly shown to involve a reactive though isolable ethylenimonium ion intermediate, XCIII (44, 52, 53, 150, 271, 283, 284, 306, 323, 572, 573, 574, 625).

$$R_2NCH_2CH_2Cl \ \rightleftarrows \ R_2\overset{+}{N}\underset{CH_2}{\overset{CH_2}{<\!\!|}} \ \ Cl^- \ \rightarrow \ products$$

XCIII

Consideration of the cyclization process as an intramolecular direct displacement reaction is consistent with the observed increase in rate with an increase in the basicity of the amino group (53, 150, 547).

The courses of further reaction open to the intermediate (XCIII) are several. XCIII can react with halide ion to regenerate the original chloroamine, with solvent water to form an ethanolamine, with the chloroamine to form ultimately the piperazinium dichloride (XCIV), or with other nucleophilic materials to yield the corresponding displacement products (44, 52, 53, 151, 152, 183, 271, 271a, 282, 283, 284, 306, 308, 323, 547a, 572, 573, 574, 625). The ability of a

nucleophilic agent to compete with solvent water for the intermediate is known as the competition factor, F (484). F values for a number of ions and amines are

XCIV
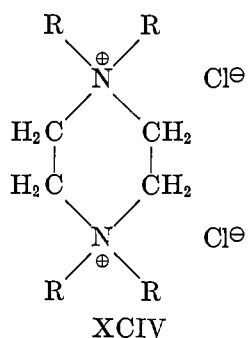
listed in table 45. The relative values parallel the nucleophilicities as determined by other means, although the parallelism is not exact. In particular, the order of the halide ions, $I > Cl > Br > F$, is not the expected order, $I > Br > Cl > F$ (table 2), although the discrepancy might be due to the relatively large experimental error.

If the system produces an unsymmetrical imonium ion such as XCVII, subsequent reaction can occur at center (a) or (b) or both. Basic hydrolysis

TABLE 45

Competition factors of nucleophiles towards ethylenimonium and ethylenesulfonium ions

Reagent	F Values	
	β-Naphthyl-bis(2-chloroethyl)amine, 50% acetone, 37°C. (547a)	Mustard gas, water, 25°C. (211)
$PO_2S_2^{---}$	—	130,000
$S_2O_3^{--}$	1680	27,000
OH^-	—	8,000
$CH_3CS_2^-$	—	5,200
HS^-	—	1,050
SCN^-	—	670
I^-	760	660
p-Anisidine	670	—
p-Toluidine	570	—
Aniline	360	760
Methylamine	—	390
Thiourea	—	150
Pyridine	—	54
Cl^-	250	21
Br^-	125	—
$C_6H_5COO^-$	120	—
CH_3COO^-	100	8.5
Triethylamine	—	6.7
SO_4^{--}	70	7.3
$HCOO^-$	65	3.0
$HOCH_2COO^-$	60	—
p-Chloroaniline	43	—
$ClCH_2COO^-$	40	3.0
F^-	20	—
NO_3^-	4	0.2

of 1-diethylamino-2-chloropropane (XCV: R $=$ C$_2$H$_5$, R$'$ $=$ CH$_3$) yields 2-diethylamino-1-propanol (XCVIII; R $=$ C$_2$H$_5$, R$'$ $=$ CH$_3$) (546), although the neutral hydrolysis of 2-dibenzylamino-1-chlorobutane (XCVI: R $=$ C$_6$H$_5$CH$_2$, R$'$ $=$ C$_2$H$_5$) yields 1-dibenzylamino-2-butanol (XCIX: R $=$ C$_6$H$_5$CH$_2$, R$'$ $=$ C$_2$H$_5$) (393).
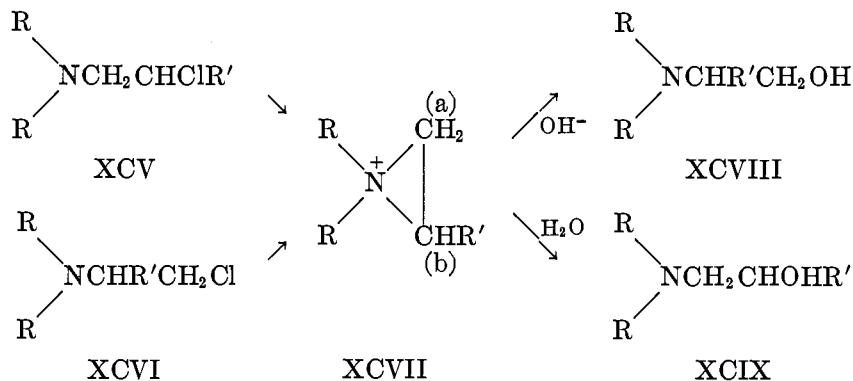
Both reactions undoubtedly proceed through the same analogous intermediate (XCVII), which reacts with hydroxide ion at (a) but with water at (b). The oxygen atom in water is effectively more electronegative than in hydroxide ion; hence the central carbon atom has more of a positive charge in solvolysis and reaction at the secondary position is favored. The more facile attack at the primary position by hydroxide ion is in common with analogous direct displacement reactions. Similarly, solvolysis of 2,2-dimethylethylenimine in aqueous hydrochloric acid gives a mixture of 1-amino-2-methyl-2-propanol and 1-chloro-2-methyl-2-propylamine (553a).

Other examples of similar rearrangements are known (105, 273, 393). However, rearrangement is absent in reactions of 8-chloromethylpyrrolizidine (C), presumably because the required intermediate tricyclic imonium ion (CI) is too highly strained (416).
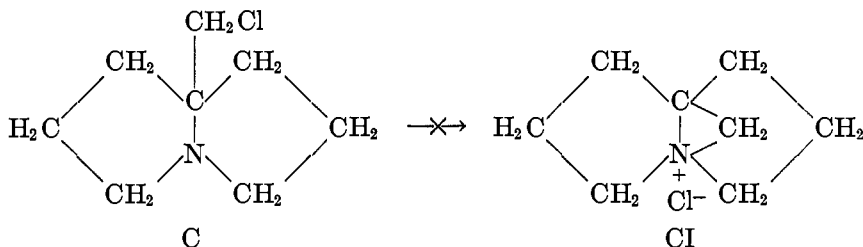
C. NEIGHBORING SULFUR

The importance of ring size in solvolytic reactions of halosulfides is shown in table 46. Those chlorides which on cyclization would give rise to three-, five-, or six-membered sulfonium rings show decided rate enhancements. Chlorides which on cyclization would form four-membered rings are no more reactive
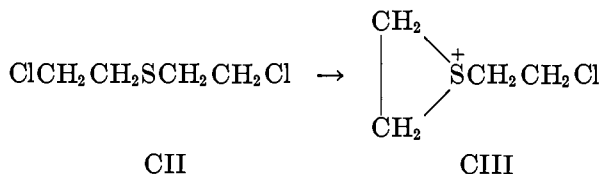
TABLE 46

Solvolysis of chloroethers and chlorosulfides

Relative rates: *n*-hexyl chloride = 1

R	R'	R—O—R' Aqueous Dioxane, 100°C. (92)	R—S—R' Aqueous Dioxane, 100°C. (92)	R—S—R' 50% Acetone, 80°C. (74, 76, 489)
C_2H_5	$(CH_2)_2Cl$	0.21	3200	—
C_2H_5	$(CH_2)_3Cl$	0.91	1.2	—
C_2H_5	$(CH_2)_4Cl$	—	—	334
C_2H_5	$(CH_2)_5Cl$	—	—	3.5
C_6H_5	$(CH_2)_2Cl$	0.11	104	—
C_6H_5	$(CH_2)_3Cl$	0.43	0.55	—
C_6H_5	$(CH_2)_4Cl$	0.98	21	1900
C_6H_5	$(CH_2)_5Cl$	—	—	25

than *n*-hexyl chloride. Ring formation is probably not important in these cases. That five-, six-, and seven-membered sulfonium rings are formed has been demonstrated by the isolation of the corresponding cyclic sulfonium chloroplatinates (74, 76).

The reactions of the phenyl sulfides are considerably slower than those of the corresponding ethyl sulfides. This phenomenon is probably a manifestation of the intrinsic electron-attracting ability of the benzene ring, which inductively destabilizes a neighboring positive charge. An investigation of the solvolysis rates of substituted phenyl β-chloroethyl sulfides has shown that the rate is increased by electron-donating substituents and is decreased by electron-withdrawing substituents (73). Electron-donating substituents render the sulfur atom more nucleophilic.

Because of the use of β,β'-bischloroethyl sulfide (mustard gas) (CII) as a war gas, the chemistry of β-chlorosulfides has been studied more than that of its homologs. Kinetic studies (55, 484) of the relatively rapid aqueous hydrolysis of CII are consistent with a rate-determining cyclization step to form the ethylenesulfonium ion (CIII). Unlike the analogous ethylenimonium ions, CIII is too reactive to permit isolation. Reaction occurs rapidly with any available nucleophilic species.

$$ClCH_2CH_2SCH_2CH_2Cl \rightarrow \begin{array}{c} CH_2 \\ | \quad \diagdown \\ | \quad \overset{+}{S}CH_2CH_2Cl \\ | \quad \diagup \\ CH_2 \end{array}$$

CII   CIII

Values of the competition factors (*F* values (484)) for a number of nucleophilic materials towards CIII have been determined in various war research projects. Some of these values are listed in table 45 for comparison with competition factors towards ethylenimonium ions. Where comparison is possible the ethylenimonium ion in all but two cases ($S_2O_3^-$ and aniline) is the more selective, undoubtedly in consequence of its greater stability (compare page 627).

Reaction of either 2-ethylthio-1-propanol (CIV) or 1-ethylthio-2-propanol (CV) with hydrochloric acid yields ethyl 2-chloro-1-propyl sulfide (CVI) (272).

$$C_2H_5SCH(CH_3)CH_2OH$$
$$CIV$$

$$\xrightarrow{HCl} \quad C_2H_5SCH_2CHClCH_3$$
$$CVI$$

$$C_2H_5SCH_2CHOHCH_3$$
$$CV$$
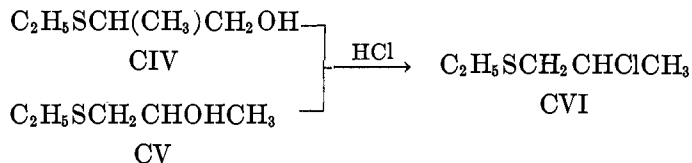
Both systems probably involve the same cyclic sulfonium intermediate (CVII). The formation of CVI as the product requires attack by chloride ion at the *secondary* carbon atom in preference to the primary. This result suggests that the cyclic sulfonium intermediates have real carbonium-ion character; i.e., structures such as CVIII are important resonance contributors. At the transition state for reaction of CVII, the central carbon atom must possess more of a positive charge than is usual in direct displacement reactions or in the subsequent reactions of the ethylenimonium analog (page 680). The distinction is undoubtedly one of degree rather than of kind.

CVII   CVIII
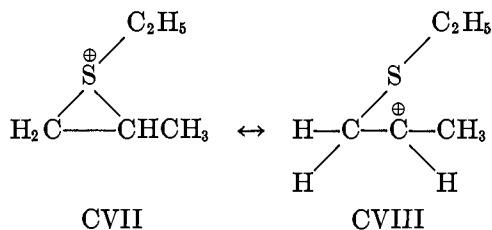
D. NEIGHBORING OXYGEN

1. Neighboring oxide ion

The reaction of ethylene chlorohydrin with ethoxide ion in ethanol at 30°C. is 5100 times faster than the corresponding reaction of ethyl chloride (287, 586). If both reactions were direct displacements by ethoxide ion, the rate ratio would be expected to be of the order of 0.1 (page 588). The product of the reaction with ethylene chlorohydrin, moreover, is ethylene oxide (586). The ring closure has been interpreted by Winstein and Lucas (680) by the following reaction sequence:

$$HOCH_2CH_2Cl + B^- \rightleftarrows BH + {}^-OCH_2CH_2Cl \rightarrow H_2C\overset{\displaystyle O}{\overline{\quad\quad}}CH_2 + Cl^-$$
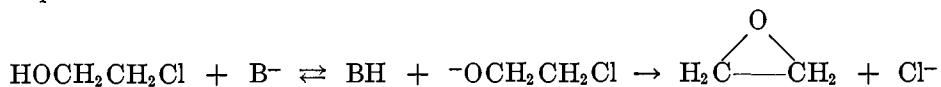
The chemistry of the oxirane ring and its formation has been reviewed by Winstein and Henderson (673). The evidence for the reaction mechanisms involved has been summarized more recently by Frost and Pearson (270). Kinetic investigations of the ring-closure reaction are completely consistent with the Winstein–Lucas mechanism; e.g., stereochemical results show that the reactive carbon undergoes an inversion of configuration in the formation of the oxide ring.

TABLE 47

Relative rates of chlorohydrins with aqueous sodium hydroxide

Chlorohydrin	Relative Rate at 18°C. (474)	Chlorohydrin	Relative Rate at 18°C. (484)
CH₂OHCH₂Cl......................	1.0	(CH₃)₂COHCHClCH₃.................	1370
CH₃CHOHCH₂Cl...................	21	CH₃CHOHC(CH₃)₂Cl.................	1960
CH₂OHCHClCH₃..................	5.5	(CH₃)₂COHC(CH₃)₂Cl...............	11600
(CH₃)₂COHCH₂Cl.................	252	(C₂H₅)₂COHCH₂Cl..................	577
CH₂OHC(CH₃)₂Cl.................	248*	CH₂OHC(C₂H₅)₂Cl..................	1150

* The product from this compound is isobutyraldehyde.
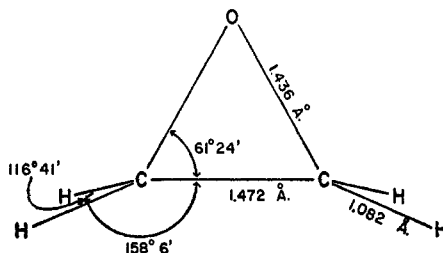
FIG. 20. Structure of ethylene oxide (187)

Substituted ethylene chlorohydrins undergo more facile reaction with base, as shown by the data in table 47. The ring closure of tetramethylethylene chlorohydrin, for example, is almost 12,000 times faster than that of ethylene chlorohydrin. The rate constants in table 47 are products of the equilibrium constant for the formation of the chloroalkoxide ion and the specific rate constant for intramolecular cyclization of the chloroalkoxide ion. Since the presence of alkyl substituents is expected to decrease the equilibrium constant, the observed increases in overall rates must be due to a more facile ring-closure step. A plausible explanation for the large rate acceleration produced by α- or β-alkyl substitution is to be found in the structure of ethylene oxide (figure 20). The angle which separates geminal hydrogen atoms, 116° 41′, is significantly greater than the tetrahedral angle, 109° 28′. The spreading of the bond angle suggests that geminal alkyl groups will suffer lesser hindrances to motion and will contribute greater entropy in the transition state leading to three-membered rings. This increase in entropy could constitute a major driving force for the formation of highly substituted three-membered rings.

3-Bromo-2,2-dimethyl-1-pentanol (CIX) has recently been reported to form the four-membered oxide with base at a rate faster than trimethylene bromo-

$$BrCH_2C(CH_3)_2CH_2OH$$

CIX

hydrin itself (430). The explanation for the acceleration in rate may well be similar to that given above for substituted three-membered rings. The H—C—H bond angle in trimethylene oxide has the value 112°, which is somewhat greater than the tetrahedral angle (251).
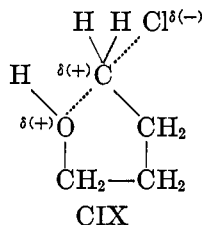
The reaction of tetramethylene chlorohydrin with base yields tetrahydrofuran at an overall rate only 0.15 that of the analogous reaction of ethylene chlorohydrin (328), although by analogy with neighboring sulfur and nitrogen, the five-membered ring would be expected to form more rapidly than the three-membered ring. This apparently anomalous result has been plausibly explained on the basis that ethylene chlorohydrin is a stronger acid than tetramethylene chlorohydrin, in which the electron-attracting chlorine atom is farther removed from the hydroxyl function (328). At any given concentration of hydroxide ion, the concentration of 2-chloroethoxide ion is greater than that of 4-chloro-1-butoxide ion. The specific rate of cyclization of the latter could be faster, yet still give a smaller overall rate.

2. Neighboring hydroxyl

The aqueous solvolysis of ethylene chlorohydrin under neutral or acidic conditions is ~1000 times faster than the calculated rate for the ring-closure reaction (270):

$$HOCH_2CH_2Cl \rightarrow H_2\overset{\displaystyle O}{\overset{\displaystyle /\quad\backslash}{C\text{------}CH_2}} + H^+ + Cl^-$$
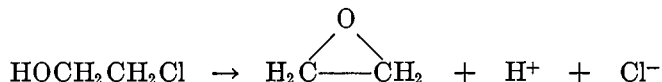
The product of the solvolysis is almost exclusively ethylene glycol (116). It may be inferred that internal displacement by the hydroxyl group cannot compete with normal solvolytic displacement in this case. As a consequence of the proximity of the electronegative oxygen function to the reacting center, the rate of the aqueous solvolysis of ethylene iodohydrin is only 0.022 that of ethyl iodide at 60°C. (116, 459). Similarly, aqueous solvolysis of trimethylene chlorohydrin does not yield any trimethylene oxide (327). The rate is about four times that of ethylene chlorohydrin (327, 516), presumably because of the greater distance of separation of the hydroxyl group. On the other hand, the solvolysis of tetramethylene chlorohydrin is about 1000 times as rapid as that of ethylene chlorohydrin and yields tetrahydrofuran (327). Anchimeric assistance by the hydroxyl group undoubtedly occurs in this case because of the ease of formation of the five-membered ring transition state (CIX).

$$
\begin{array}{c}
\overset{H\ H}{\diagdown\diagup}\ Cl^{\delta(-)} \\
H\ \overset{\delta(+)}{\diagdown}\ C \\
\overset{\delta(+)}{\diagup}O\ \diagdown CH_2 \\
|\qquad\quad| \\
CH_2\text{---}CH_2 \\
CIX
\end{array}
$$

The rate retardation due to a neighboring hydroxyl group is far greater in the solvolyses of tertiary halides in which the amount of charge separation at the transition state is greater. The inductive withdrawal of electrons by the oxygen atom decreases the ability of the system to support a positive charge. By a simplified electrostatic treatment, Winstein and Grunwald (667) have calcu-
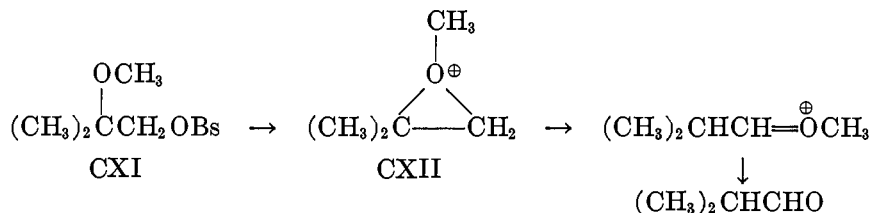
lated that the effect of a neighboring hydroxy dipole on the dipole generated at the reactive center at the transition state should produce a rate retardation factor of $\sim 10^{-2}$. This value is close to the observed rate retardations in table 52.

3. Neighboring alkoxy group

The rate of aqueous solvolysis of 2-methoxyethyl iodide (CX) is 0.28 that of ethylene iodohydrin and 0.0064 that of ethyl iodide at 60°C. (399). The data of Klemperer, McCabe, and Sindler (399) for the solvolysis of CX in aqueous ethanol mixtures at 91°C. yield a value of m in the Grunwald–Winstein correlation (equation 11) of 0.20, close to the values of this parameter given by other primary halides. The solvolysis of CX is probably similar in type to direct displacement by solvent with no participation by the neighboring methoxyl group.

The solvolysis of 2-ethoxyethyl chloride in aqueous dioxane at 100°C. is 0.2 as rapid as that of n-hexyl chloride (table 46). The rate retardation in this case is not as great as that observed for CX in water but could be due to the differences in the ionizing powers of the solvents. The relative rate of alcoholysis of 2-ethoxyethyl tosylate compared to butyl tosylate, 0.30, is about the value expected in the absence of participation (page 696). The data of tables 46 and 53 also demonstrate that an alkoxy group more than two carbons away from the reacting center has little effect on the rate. This observation is not unexpected, since the extent of inductive electron-withdrawal by the oxygen atom should fall off rapidly with distance.

2-Methoxy-2-methyl-1-propyl brosylate (CXI) is rather comparable to neopentyl brosylate as far as steric bulk close to the reacting center is concerned. The rate of acetolysis of CXI is *faster* than that of the neopentyl system by fifteenfold and suggests participation by the methoxyl group. Winstein, Lindegren, and Ingraham (678) have estimated that the observed rate of acetolysis of CXI is approximately 1500 times greater than the value expected in the absence of participation. The solvolysis of CXI in aqueous dioxane yields predominantly isobutyraldehyde (678), an expected product of the further solvolysis of the intermediate ion (CXII) which would result from participation by the adjacent methoxyl group. Scrutiny of the reaction products similarly suggests that

$$(CH_3)_2 \overset{\overset{\displaystyle OCH_3}{|}}{C} CH_2 OBs \quad \rightarrow \quad (CH_3)_2 \overset{\overset{\displaystyle \overset{\displaystyle CH_3}{|}}{\overset{\displaystyle O^{\oplus}}{\diagup \diagdown}}}{C}{-}{-}{-}CH_2 \quad \rightarrow \quad (CH_3)_2 CHCH{=}\overset{\oplus}{O}CH_3$$

$$CXI \qquad\qquad CXII \qquad\qquad \downarrow$$

$$(CH_3)_2 CHCHO$$

methoxyl group participation occurs in the solvolysis of 3-bromo-2-methoxy-2-methylbutane.

The greater tendency for participation to occur in the substituted cases may be due to the same relief of steric interactions of geminal groups in substituted three-membered rings which was suggested to explain the rates of formation of

ethylene oxides (page 683). Winstein and Grunwald (667) have interpreted the tendency in terms of the greater importance of the contributing resonance structure, CXIII, compared to cases in which the β-carbon atom is less highly substituted.


CXII   CXIII
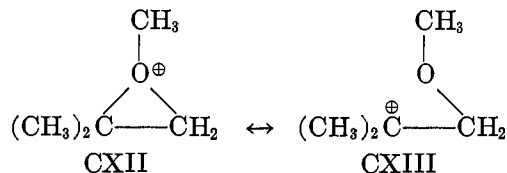
The rate of acetolysis of *trans*-2-methoxycyclohexyl brosylate relative to cyclohexyl brosylate is 0.057 at 75°C. From figure 21 the relative rate in the absence of participation is estimated to be 0.008; hence there is but little driving force for participation in this case. One reason may be that the reaction with participation requires that both groups be in the axial conformation (CXIV) rather than the presumably more stable diequatorial conformation (CXV). The importance of this factor, however, is difficult to estimate. Despite the absence of a large driving force, participation probably does occur, because the reaction of *trans*-1-bromo-2-methoxycyclohexane with silver acetate in acetic acid yields *trans*-2-methoxycyclohexyl acetate (672). The overall stereochemical result is a net retention of configuration. Similarly, the reactions of *threo*- and *erythro*-2-bromo-3-methoxybutane with silver acetate in acetic acid yield 3-methoxy-2-butyl acetate with retention of configuration in both cases (672). In the case of the *threo* compound, for example, configurational retention would result from the bridged-ion, CXVI. The normal silver-ion-assisted solvolyses of these systems involve but little nucleophilic overlap with solvent. The neigh-

CXIV   CXV

CXVI
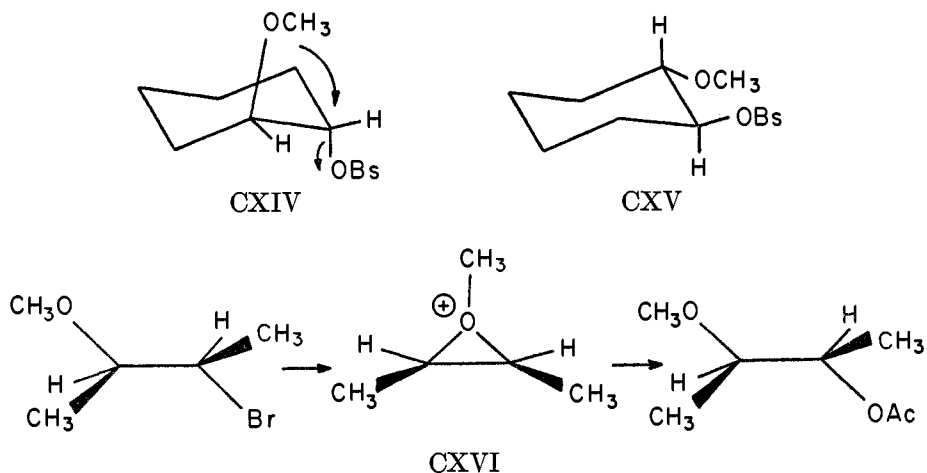
boring methoxyl group, which replaces the solvent, need participate only slightly at the first transition state to predominate over the normal solvolysis.

4. Neighboring ester

The rate of acetolysis of *cis*-2-acetoxycyclohexyl brosylate (CXVII) is slower than that of cyclohexyl brosylate by a factor of 3.8×10^{-4} (668, 669), undoubtedly because of electron withdrawal by the neighboring acetoxyl group. However, the acetolysis of *trans*-2-acetoxycyclohexyl brosylate (CXVIII) is only a little slower than that of the parent system; the relative rate is 0.24 (668, 669). The cause of the 630-fold rate difference between CXVII and CXVIII is to be ascribed to participation by the neighboring acetoxyl group in the latter. Such participation involves an internal displacement at the rear and probably requires a *trans* orientation of the neighboring and the leaving groups. The 630-fold rate difference is only a crude measure of the driving force for participation in CXVIII, because the effects due to conformational differences are neglected. The magnitude of the conformational differences is difficult to estimate because, in addition to the mere bulk of substituent groups, dipole–dipole interactions are involved.

CXVIII   CXIX
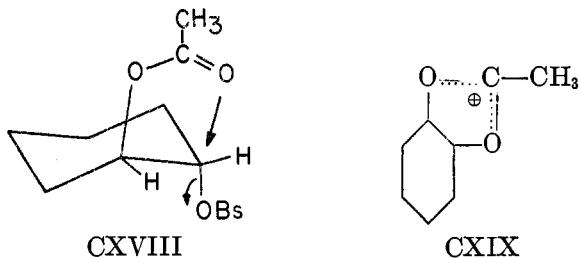
The product of the solvolysis of CXVIII in dry acetic acid containing acetate ion is *trans*-1,2-diacetoxycyclohexane. This result amounts to an overall *retention* of configuration. Racemic product is obtained from optically active CXVIII. These results are consistent with the postulate that an intermediate having structure CXIX is formed (661, 662, 674). Subsequent reaction of this intermediate with acetate ion with inversion yields the observed product. Structure CXIX is symmetrical and must lead to racemic products.

Solvolysis of CXVIII in *wet* acetic acid yields a mixture of mono- and diacetates of *cis* configuration. This result has been plausibly interpreted as a reaction of CXIX with water to form an orthodiacetate (CXX), which subsequently opens to give *cis*-2-acetoxycyclohexanol (674). Much the same result is obtained

CXX   CXXI
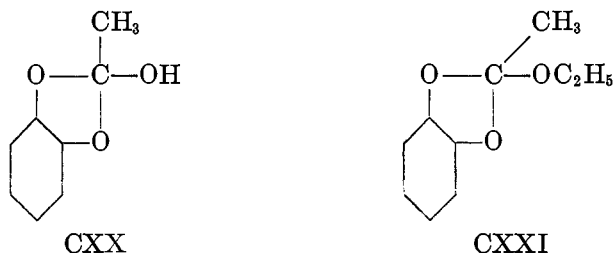
by the solvolysis of CXVIII in dry acetic acid without added acetate ion. The reaction of CXIX in this case yields the acetate of CXX, which subsequently isomerizes to cis-1,2-diacetoxycyclohexane (671, 674). The isolation by Winstein and Buckles (663) of cyclohexene ethyl orthoacetate (CXXI) from the solvolysis of CXVIII in dry ethanol has provided strong confirmation of these mechanistic sequences.

The structural and stereochemical consequences of neighboring group participation by the acetoxyl group have been reproduced in a number of systems which include reactions of 2-acetoxycyclohexyl bromide (661, 662), 2-acetoxy-3-bromobutane (661, 662), 3-acetoxy-2-butyl tosylate (438), and cyclopentane and indane derivatives (686). Neighboring acetoxy participation has been suggested to explain some reactions in the carbohydrate series (347, 498).

On the other hand, the solvolysis products of the isomeric 2,3-butaneditosylates indicate that sulfonate esters show no significant tendency towards participation (438).
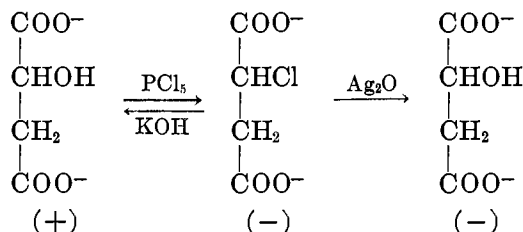
5. Neighboring carboxylate ion

It has long been known that aqueous solutions of salts of γ-halocarboxylic acids rapidly produce the corresponding γ-lactone (255, 256, 257, 258). In a weakly basic solution, optically active γ-chlorovaleric acid yields an optically active γ-lactone (420). As in other cases, these examples may be considered as internal direct displacements; the ease of formation of five-membered rings renders this kind of participation very important.

Although one preparation of the six-membered ring δ-lactones involves the dry distillation of the sodium salts of δ-halocarboxylic acids (343), the reaction of the salts in aqueous solution has apparently never been investigated. The importance of the participation of carboxylate ion in these cases is an open question.
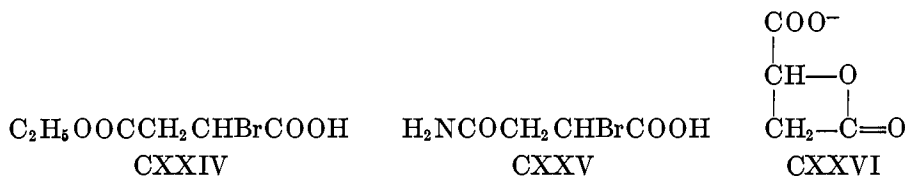
Few product studies have been made of the solvolytic reactions of salts of the higher halo acids. The reaction of ϵ-bromocaproic acid (CXXII) with silver oxide and water has been reported to give a mixture of the corresponding lactone and hydroxy acid (446). The solvolysis of ξ-bromoenanthic acid (CXXIII) in boiling water yields only the hydroxy acid (103). Apparently, formation of the seven-membered lactone ring can compete with ordinary solvolysis but the formation of the eight-membered ring cannot.

$$Br(CH_2)_5COOH \qquad Br(CH_2)_6COOH$$
$$CXXII \qquad\qquad CXXIII$$
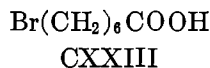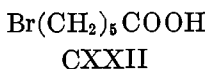
Treatment of β-halocarboxylate salts with hot water yields a mixture of the corresponding hydroxy acid and α,β-unsaturated acid (259, 434). The stereochemistry of these solvolyses has been intensively investigated and is of great historical significance; the reactions of optically active chlorosuccinic acid were involved in the first complete Walden inversion cycle (641; summarized in 642, 643):

$$\begin{array}{ccc}
\text{COO}^- & \text{COO}^- & \text{COO}^- \\
| & | & | \\
\text{CHOH} \xrightarrow[\text{KOH}]{\text{PCl}_5} & \text{CHCl} \xrightarrow{\text{Ag}_2\text{O}} & \text{CHOH} \\
| & | & | \\
\text{CH}_2 & \text{CH}_2 & \text{CH}_2 \\
| & | & | \\
\text{COO}^- & \text{COO}^- & \text{COO}^- \\
(+) & (-) & (-)
\end{array}$$

In the hydrolysis of chlorosuccinate ion Holmberg (339, 340, 341) demonstrated the presence of a halogen-free intermediate by kinetic techniques. The reactions were not given by ethyl hydrogen 3-bromosuccinate (CXXIV) or by bromo-succinamic acid (CXXV) (341). In these compounds there is no free carboxylate

$$\begin{array}{c}
\text{COO}^- \\
| \\
\text{CH}\!-\!\text{O} \\
| \quad | \\
\text{CH}_2\!-\!\text{C}\!=\!\text{O}
\end{array}$$

$$\text{C}_2\text{H}_5\text{OOCCH}_2\text{CHBrCOOH} \qquad \text{H}_2\text{NCOCH}_2\text{CHBrCOOH}$$
$$\text{CXXIV} \qquad\qquad\qquad \text{CXXV} \qquad\qquad\qquad \text{CXXVI}$$

group in the β-position; hence the intermediate was formulated as a β-lactone (CXXVI). Johannson (382, 383) was able to isolate the β-lactone intermediates of the solvolyses of β-bromocarboxylate salts.

By analogy with a set of related reactions, the formation of the β-lactone should be considered as a displacement reaction accompanied by complete inversion of configuration. The subsequent reactions of the lactone depend on the reaction conditions. In acid or basic media reaction occurs at the carbonyl group with acyl–oxygen fission (342, 493, 496). Since this step retains configuration, the net result from the halo acid is a single inversion. In neutral solution, reaction occurs at the reacting carbon with alkyl–oxygen fission and with inversion of configuration (493, 496). The overall result from halo acid is a net retention of configuration. This particular case differs from many other examples of neighboring group participation only in that the intermediate is isolable.

No intermediate has been isolated in the solvolyses of salts of α-halocarboxylic acids, but their existence has been demonstrated stereochemically. The reaction of α-bromopropionate ion with methoxide ion follows second-order kinetics and yields α-methoxypropionate ion with inversion of configuration (167). The methanolysis of the salt itself in weakly basic solutions follows first-order kinetics and yields α-methoxypropionate ion with *retention* of configuration (167). Similarly, the reaction of α-tosyloxypropionic acid with aqueous silver oxide yields lactic acid with retention of configuration (392).

Intramolecular nucleophilic participation is also indicated by the lack of a significant steric effect on the rate. α-Bromopropionate ion solvolyzes only 2.5 times as fast as α-bromo-*tert*-butylacetate ion in water at 25°C. (292, 406).

The implicated intermediate has been variously considered to be a zwitterion (CXXVII) (168), an α-lactone (CXXVIII) (301), and an α-lactone with much ionic character (CXXIX) (297, 672). In the absence of more definitive evidence

$$\underset{\text{CXXVII}}{\overset{\ominus O}{\underset{\oplus}{R\overset{}{C}H}}\text{———}C\text{=}O} \qquad \underset{\text{CXXVIII}}{\overset{O}{R\overset{}{C}H}\text{———}C\text{=}O} \qquad \underset{\text{CXXIX}}{\overset{\overset{\delta -}{O}}{\underset{\delta +}{R\overset{}{C}H}}\text{———}C\text{=}O}$$
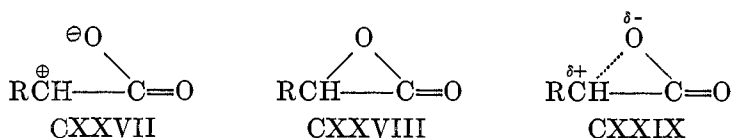
there would seem to be little justification in introducing a special symbolism for this three-membered ring system alone. Accordingly, there would seem to be little reason for not regarding the intermediate simply as an α-lactone. The tendency of β-lactones to react by alkyl–oxygen fission is undoubtedly due in large part to ring strain. It would seem plausible that the greater ring strain of an α-lactone should facilitate alkyl–oxygen fission to the complete exclusion of reaction at the carbonyl group.

One approach to the electronic structure of the α-lactone *as it exists at the transition state* depends on the effect of ionic strength on solvolysis rate. A basic postulate is that an increase in rate with increase in ionic strength means that the transition state has more charge or a more concentrated charge than the ground state (59, 352, 356). An attempt to apply this criterion to solvolyses of halo-acetates is difficult because of the complicating side reactions demonstrated for these salts (106, 192, 193, 559, 561). Three separate studies have shown that the rate of the first-order solvolysis of α-bromopropionate ion increases slightly with increasing ionic strength (141, 297, 549). The only study which led to the contrary result (167) has been demonstrated to have been incorrectly interpreted (297).

The magnitude of the ionic strength effect is consistent with the generation of but a small amount of additional charge at the transition state. This conclusion is in good agreement with the effect on rate of a change in solvent. The change from water to methanol involves a large decrease in ionizing power, yet the decrease in solvolysis rate of α- or β-halocarboxylate ions is small ($<$ tenfold) (table 48).

A study has been made of the effect on solvolysis rate of the position of the halogen relative to the carboxylate group (326, 406). Because of the presence of the negative charge, estimates of the solvolysis rate in the absence of participation have not been attempted. γ-Bromocarboxylate salts are by far the most reactive of the bromocarboxylates. The high velocities of the compounds which lead to five-membered rings are in line with rate studies in other systems,

TABLE 48

Effect of solvent on halocarboxylate-ion solvolysis

Compound	Temperature	$\dfrac{k_{H_2O}}{k_{CH_3OH}}$ (297)	Compound	Temperature	$\dfrac{k_{H_2O}}{k_{CH_3OH}}$ (297)
	°C.			°C.	
⁻OOCCHBrCH₂COO⁻	25.8	1.14	CH₃CHBrCOO⁻.........	64	2.4
CH₃CHBrCH₂COO⁻..............	45	4.4	(CH₃)₂CHBr.............	50	270*
(CH₃)₂CBrCOO⁻................	44.3	8.2	(CH₃)₃CBr..............	25	17000*

* Estimated with the Grunwald–Winstein correlation (equation 11).

TABLE 49

Effect of substitution on halocarboxylate-ion solvolysis

Compounds Compared	Temperature	Rate Ratio	References
	°C.		
CH₃CHBr(CH₂)₂COO⁻: Br(CH₂)₃COO⁻...............	0	1.07	(138, 406)
CH₃CHBrCH₂COO⁻: Br(CH₂)₂COO⁻..................	38	5.15	(382, 406)
CH₃CHBrCOO⁻: BrCH₂COO⁻.........................	25	11	(192, 297, 406)
(CH₃)₂CBrCOO⁻: CH₃CHBrCOO⁻....................	25	260	(297, 406, 576)
C₆H₅CHBrCOO⁻: CH₃CHBrCOO⁻....................	25	600	(292, 406, 560)
(CH₃)₃CBr: (CH₃)₂CHBr...............................	25	∼10⁵	

The effect of ring size on the nucleophilicity of the neighboring carboxylate ion is also demonstrated by the data in table 49 in which related primary, secondary, and tertiary systems are compared. As ring size decreases and ring strain increases, the effective nucleophilicity of the carboxylate group decreases and the reacting carbon itself must bear more positive charge. Additional substitution at the reacting center is therefore expected to increase the rate. Except for the cases in which tertiary or benzylic systems are involved, the rate changes are rather small and indicate again that the amount of charge actually generated at the transition state is small.

The high values of the energies of activation (27–30 kcal./mole) and entropies of activation (10–13 e.u.) in the solvolysis of α- and β-halocarboxylate ions have been ascribed to solvation effects (292, 326). Since the ionic charge is less concentrated at the transition state compared to the ground state, the extent of solvation is decreased. The decrease in bonding to the solvent at the transition state results in a higher energy of activation; however, the increase in mobility of some solvent molecules also results in a compensating increase in the entropy of activation. The aqueous solvolysis of γ-bromovalerate ion has an energy of activation of only 22 kcal./mole (326), presumably because of the greater bonding inherent in the relatively strain-free five-membered ring lactone character of the transition state.

6. Neighboring carboxylic acid and ester

The solvolysis in water at 50°C. of isopropyl bromide is about 100 times as fast as that of α-bromopropionic acid (411, 670). α-Bromophenylacetic acid is about five powers of ten less reactive than α-phenylethyl bromide in water at 50°C. (560, 619). In the absence of participation such rate differences would be expected, because of the added difficulty of generating a positive change next to the already electron-deficient carbon atom of a carbonyl group.

The solvolysis rate of methyl *trans*-3-tosyloxycyclohexanecarboxylate relative to the *cis* isomer is 4.5 in acetic acid at 75°C. and 4.3 in formic acid at 40°C. (479). These values are close to the corresponding ratio of 3.3 found by comparing the rates of acetolysis of the isomeric *trans*- and *cis*-3-*tert*-butylcyclohexyl tosylates (676). The differences in rate are very probably due to the conformational differences. There is no evidence in these rates for any participation by the carbomethoxyl group.

The methanolysis of methyl α-bromopropionate is accompanied by complete inversion of configuration (167). By analogy with other neighboring groups, if participation were to occur in this system, a retention of configuration would be expected.

These limited data indicate the absence of any significant neighboring group participation by a carboxylic acid or ester function in solvolytic reactions.

### 7. Neighboring benzamido group

trans-2-Benzamidocyclohexyl tosylate (CXXX) solvolyzes ~10^3 more rapidly than the cis isomer (CXXXI) and yields as an isolable product cis-2-phenyl-4,5-tetramethyleneoxazolinium tosylate (CXXXII) (659, 666). Solvolysis of CXXXI is reported to proceed in a more complex manner (659), but the products have not been described. Neighboring group participation is clearly important for the amido function in cases permitted by geometry.
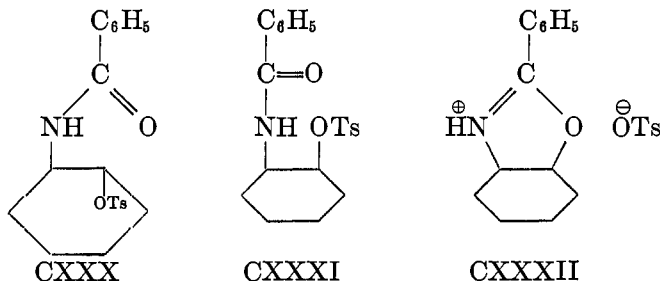
Winstein and Boschan (659) have reviewed a number of related examples which indicate the generality of neighboring group participation or displacement by amido and similar functions.

E. NEIGHBORING HALOGEN

The reaction of dl-2,3-dibromobutane (CXXXIII) with silver acetate in acetic acid yields dl-2,3-diacetoxybutane. meso-2,3-Dibromobutane similarly treated yields meso-2,3-diacetoxybutane (661). The acetolyses of the 2-acetoxy-3-bromobutanes presumably involved as intermediates in the above reactions are known to proceed with an overall retention of configuration (page 688). Consequently, the replacement of the first bromine by acetoxy in each of the above cases must have involved an overall retention of configuration. These results are taken to indicate participation by neighboring bromine. The first intermediate in the reaction of CXXXIII is written as a cyclic bromonium ion, CXXXIV.
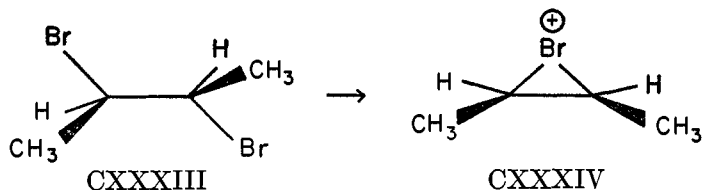
Evidence for the existence of cyclic bromonium ions has accumulated in some related reactions (526, 656, 657, 680, 681). In like manner, cyclic iodonium (436) and chloronium (437) ion intermediates have been demonstrated.

Qualitatively, the driving force for chloronium-ion formation appears to be small. Both *meso-* and *dl*-stilbene dichloride with silver acetate in acetic acid yield predominantly *meso*-1,2-diacetoxy-1,2-diphenylethane. One interpretation of these results, which is not unique, is that a cyclic chloronium ion (CXXXV) is involved in the *meso* case but not with the *dl* isomer. The chloronium ion (CXXXVI) in the latter case would have a *cis*-stilbene configuration. The steric repulsions involved in such a configuration are sufficient to prevent formation of the cyclic ion.

CXXXV   CXXXVI
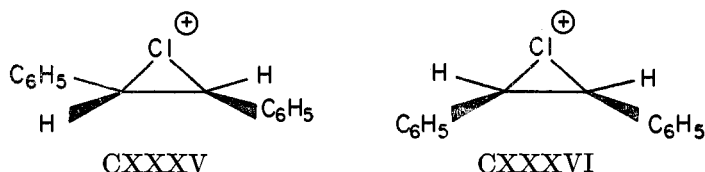
Solvolysis rates can be used to provide more quantitative measures of the driving forces for participation provided an estimate can be made of the rate in the absence of participation. The presence of a substituent function by its inductive effect alone will alter the ability of a nearby carbon atom to bear a positive charge. Winstein, Grunwald, and Ingraham (294, 669) have elegantly solved this problem by measuring the rates of acetolysis of *cis-* and *trans*-2-substituted cyclohexyl brosylates. For the *cis* isomers, intramolecular rearward attack is geometrically precluded as a significant mode of reaction. In the absence of participation, *cis* and *trans* isomers would be expected to react at roughly the same rate. The important distinction between the isomers is a conformational difference, the magnitude of which is difficult to assess because of the presence of strong dipole–dipole interactions. This factor may well be small; the rates of acetolysis of *cis-* and *trans*-1,2-dibrosyloxycyclohexane differ by a factor of only 1.12 (669). The actual rate ratio of a *trans* isomer relative to the *cis* isomer is then a rough measure of the driving force for participation by the substituent group. The values for halogen substituents are given in table 50. The value, 3.8, found for chlorine, indicates an exceedingly small driving force for partici-

TABLE 50

Acetolysis rate ratios for cis- and trans-2-halocyclohexyl brosylates

2-Substituent	k_{trans}/k_{cis} CH$_3$COOH, 75°C. (294, 669)	$k_{trans}/k_{no\ participation}$ Calculated using the electrostatic approach (669)
Cl............................	3.8	(1.0)[a]
Br............................	810	120
I.............................	2,700,000[b]	1,100,000

[a] This value was assumed in order to calculate the one disposable parameter required by the method used.
[b] From figure 21.

pation. The rate factors for bromine and for iodine, 810 and 2,700,000, respectively, constitute sizable driving forces for participation.

Values of the effects of inductive forces have been calculated by a simplified electrostatic treatment (294, 669). Quantitatively different though qualitatively similar driving forces result from this procedure. Because of the approximations inherent in the electrostatic treatment, the method offers little advantage over the simple assumption that the rates of the *cis* and *trans* isomers would be the same in the absence of participation, although the agreement of the results of the two methods supports the assumptions required in both. The electrostatic calculation procedure is of use in estimating solvolysis rates in the absence of participation for those cases in which both the *cis* and the *trans* isomers have not been kinetically investigated.

An attractive alternative procedure is suggested by the success of Taft's polar substituent constants, σ^*, in correlating many diverse reactions (613, 614, 615). The acetolysis rates of aliphatic secondary carbinyl brosylates relative to isopropyl brosylate and of *cis*-2-substituted cyclohexyl brosylates relative to cyclohexyl brosylate as presented in table 51 are plotted in figure 21 against the appropriate polar substituent constant. The linear correlation obtained is reasonably good and may be used as a standard of comparison for determining the magnitude of participation and other effects. It is interesting to observe in figure 21 that the inductive effects of alkyl groups are adequately represented in this scheme considering the small differences involved and the relative importance of other effects.

TABLE 51

Polar effects in acetolyses of secondary brosylates

Letter in Figure 21	Compound	Rate Relative to		σ^* (615)	References
		Isopropyl brosylate at 70°C.	Cyclohexyl brosylate at 75°C.		
A..........	CH₃CHOBsCH₃	1.00		0.000	(298)
B..........	CH₃CH₂CHOBsCH₃	1.83		−0.100	(127, 684)
C..........	CH₃(CH₂)₂CHOBsCH₃	1.78		−0.115	(127)
D..........	(CH₃)₂CHCH₂CHOBsCH₃	1.64		−0.125	(127)
E..........	(CH₃)₂CHCHOBsCH₃	5.83		−0.200	(684)
F..........	(CH₃)₃CCHOBsCH₃	3.96		−0.320	(684)
G..........	(CH₃)₃CCH₂CHOBsCH₃	3.82		−0.165[(a)]	(127)
A..........	Cyclohexyl brosylate		1.00	0.000	(669)
H..........	*cis*-4-*tert*-Butylcyclohexyl tosylate		2.39[(b)]	−0.04[(a)]	(676)
I..........	*trans*-4-*tert*-Butylcyclohexyl tosylate		0.88[(b)]	−0.04[(a)]	(676)
J..........	*cis*-3-*tert*-Butylcyclohexyl tosylate		0.78[(b)]	−0.114[(a)]	(676)
K..........	*trans*-3-*tert*-Butylcyclohexyl tosylate		2.56[(b)]	−0.114[(a)]	(676)
L..........	*cis*-2-Chlorocyclohexyl brosylate		1.27×10^{-4}	+1.050	(294)
M..........	*cis*-2-Bromocyclohexyl brosylate		1.24×10^{-4}	+1.030	(294)
N..........	*cis*-2-Acetoxycyclohexyl brosylate		3.79×10^{-4}	+0.85	(669)
O..........	*trans*-2-Chlorocyclohexyl brosylate		4.80×10^{-4}	+1.050	(294)
P..........	*trans*-2-Bromocyclohexyl brosylate		0.101	+1.030	(669)
Q..........	*trans*-2-Acetoxycyclohexyl brosylate		0.240	0.85	(669)
R..........	*trans*-2-Methoxycyclohexyl brosylate		0.057	+0.52	(669)
	trans-2-Iodocyclohexyl tosylate		1170[(b)(c)]	+0.85	(669)

[(a)] Calculated using the inductive parameter of 2.8 (615).
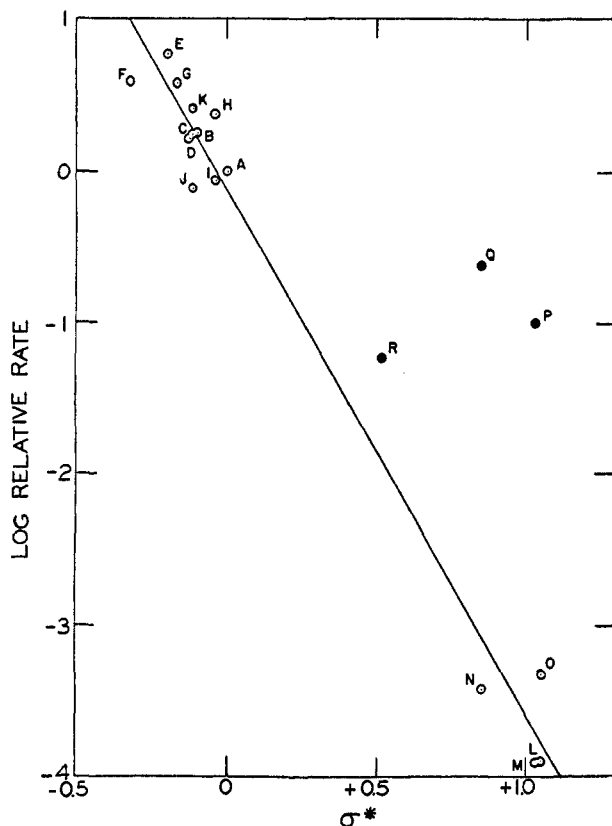[(b)] Rates relative to cyclohexyl tosylate.
[(c)] At 23.6°C.

FIG. 21. Correlation of the rates of acetolysis of secondary carbinyl tosylates and p-bromobenzenesulfonates with σ^*. The letters refer to the compounds listed in table 51.

Winstein and Grunwald (667) have pointed out that, *as substitution about the reacting center is increased, participation becomes less important as a means of distributing the positive charge.* Since neighboring chlorine participation is at best small for secondary sulfonates, it should be negligible in correspondingly substituted tertiary carbinyl halides. The reactivities of such systems can then be used to construct a correlation curve with Taft's σ^* values. The curve so defined may then be used to estimate driving forces of other functions in tertiary systems. The available data are given in table 52 and have been used to construct figure 22.

The points belonging to neighboring chlorine in figure 22 are all close to the correlation line. To the extent that resonance among structures LXXXVII, LXXXVIII, and LXXXIX is important in the electronic structure of the cyclic halonium ion, substitution at the β-carbon atom should stabilize the intermediate by increasing the contribution of structure LXXXVIII (667). Yet, even 2,3-dichloro-2,3-dimethylbutane, in which the β-carbon atom is fully substituted, shows no evidence of participation.

The importance of β-substitution is demonstrated by neighboring bromine. When this function is primary, there is no rate effect ascribable to participation.

TABLE 52

Polar effects in solvolyses of substituted tertiary carbinyl halides

Letter in Figure 22	Compound	Relative Rate 80% Ethanol, 25°C.	σ^* (615)	References
A...........	$(CH_3)_3CCl$	1.00	0.000	(116, 119, 350, 370)
B...........	$(CH_3)_2CCICH_2CH_3$	1.65	−0.100	(116, 370, 564)
C...........	$(CH_3)_2CCICH_2CH_2CH_3$	1.58	−0.115	(116)
D...........	$(CH_3)_2CCl(CH_2)_3CH_3$	1.43	−0.130	(116)
E...........	$CH_3CCl(C_2H_5)_2$	2.58	−0.200	(116, 370)
F...........	$(CH_3)_2CCICH(CH_3)_2$	0.95	−0.190	(565)
G...........	$(CH_3)_2CCIC(CH_3)_3$	1.21	−0.300	(116)
H...........	$(C_2H_5)_3CCl$	3.02	−0.300	(116, 370)
I...........	$[(CH_3)_2CH]_2CClCH_3$	14.2	−0.38	(118)
	$(CH_3)_2CCICH_2C(CH_3)_3$	21.6	−0.165	(116, 370)
	$CH_3CCl[CH_2C(CH_3)_3]_2$	574	−0.330	(112)
J...........	$(C_2H_5)_2CCICH_2OH$	$0.045^{(f)}$	+0.365	(402, 474, 608)
K...........	$(CH_3)_2CCICH_2OH$	$6.6 \times 10^{-3\,(f)}$	+0.555	(402, 474, 608)
L...........	$(CH_3)_2CCICOH(CH_3)_2$	$6.0 \times 10^{-2\,(f)}$	+0.365	(402, 474, 608)
M...........	$(CH_3)_2CCICHOHCH_3$	$3.4 \times 10^{-3\,(f)}$	+0.455	(402, 474, 608)
N...........	$CH_3CH_2C(CH_3)ClCH_2Cl$	$4.71 \times 10^{-4\,(e)}$	+0.950	(122)
O...........	$(CH_3)_2CCICH_2Cl$	$2.53 \times 10^{-4\,(e)}$	+1.050	(122)
P...........	$(CH_3)_2CCICCl(CH_3)_2$	$5.8 \times 10^{-4\,(c)(d)}$	+0.860	(626, 667)
Q...........	$(CH_3)_2CBrCH_2Br$	$1.6 \times 10^{-4\,(a)}$	+1.030	(667)
R...........	$(CH_3)_2CBrCHBrCH_3$	$2.1 \times 10^{-2\,(a)}$	+0.930	(596)
S...........	$(CH_3)_2CBrCBr(CH_3)_2$	$0.0325^{(b)(c)}$	+0.840	(503)
T...........	$(CH_3)_2CCICH_2I$	0.486	+0.85	(667)

[a] Rate relative to *tert*-butyl bromide.
[b] Rate relative to *tert*-butyl bromide in 76 per cent ethanol at 18.5°C.
[c] Rate divided by the statistical factor of two.
[d] At 100°C.
[e] At 79°C.
[f] In water at 18°C. The rate of *tert*-butyl chloride was extrapolated from 25°C., using $E^\ddagger = 22.5$ kcal./mole.

A neighboring secondary bromine exhibits a barely significant rate acceleration of fourfold. A neighboring tertiary bromine, however, has a solvolysis rate 32 times the expected rate in the absence of participation. A neighboring iodine, even in a primary position, shows a large rate acceleration which can be ascribed to participation.

The success of this sort of polarity correlation invites examination of other neighboring functions. Hydroxyl groups adjacent to a tertiary reactive center apparently do not participate. The poor fit of two of the points in figure 22 may indicate the limitations of the method or may merely point out the approximations inherent in an extrapolation from a different solvent and a different temperature.

Most of the alkyl substituents fall rather close to the correlation line. In particular, according to this scheme, the relatively high reactivity of methyldiisopropylcarbinyl chloride is explicable wholly as a polar effect; steric acceleration of rate need not be invoked (118). On the other hand, there can be little question that neopentyl groups introduce a decided rate acceleration; the solvolysis rates of dimethylneopentylcarbinyl chloride and methyldineopentylcarbinyl chloride are, respectively, 10- and 76-fold greater than predicted on the basis of polar effects alone. These rate accelerations can be plausibly ascribed to steric congestion of the ground state (page 664).

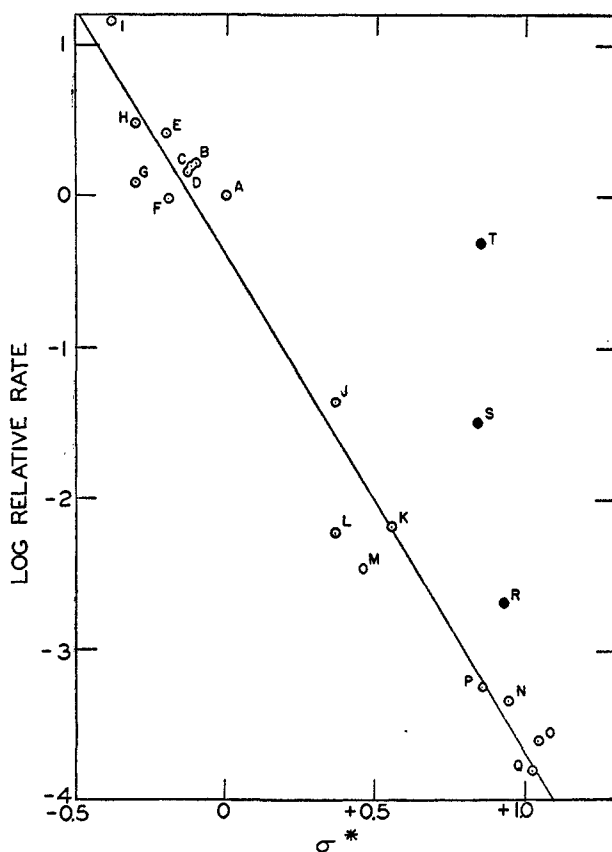The recent data of Laughton and Robertson (410) have been used to establish

FIG. 22. Correlation of the rates of solvolysis of tertiary carbinyl chlorides in 80 per cent aqueous ethanol with σ^*. The letters refer to the compounds listed in table 52.

TABLE 53

Relative rates of substituted primary tosylates in ethanol

ROTs	Relative Rate (410) 100°C.	σ^* (615)	ROTs	Relative Rate (410) 100°C.	σ^* (615)
CH₃CH₂OTs.................	1.00	0.000	C₂H₅OCH₂CH₂OTs........	0.18	+0.52[b]
CH₃CH₂CH₂OSO₂C₆H₅......	0.64[a]	−0.100	C₂H₅OCH₂CH₂CH₂OTs.....	0.40	+0.185[c]
CH₃(CH₂)₂OSO₂C₆H₅........	0.61[a]	−0.115	C₂H₅OOCCH₂CH₂OTs......	0.29	+0.71[d]
CH₃(CH₂)₄OSO₂C₆H₅........	0.65[a]	−0.130	NCCH₂CH₂OTs............	0.059	+1.30

[a] Rate relative to ethyl benzenesulfonate.
[b] Value for CH₃OCH₂— substituent used.
[c] Calculated from value for CH₃OCH₂— substituent, using the inductive parameter of 2.8 (615).
[d] Derived from the value for CH₃OOC— substituent, using the inductive parameter of 2.8. The σ^* value for CH₃OOC— is based on only one compound (615).

a correlation plot for primary sulfonate esters in ethanol (table 53; figure 23). Only two points fall off the line. Because of the importance of nucleophilic character in the solvolyses of primary systems, ethyl tosylate is faster than is indicated by the curve probably because of its lower steric hindrance to rearward
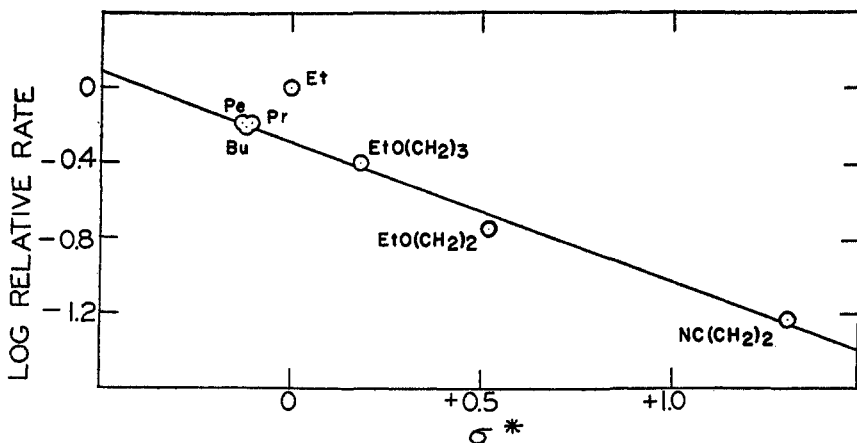
FIG. 23. Correlation of the rates of ethanolysis of primary tosylates and benzene-sulfonates with σ^*.

attack. The deviation of ethyl β-tosyloxypropionate from the line could well be due to an error in the σ^* value approximated for this substituent. The slope of the correlation line (-0.74) is less than that for tertiary halide solvolysis (figure 22: slope $= -3.29$). The difference may be taken as a reflection of the difference in the amounts of positive charge developed at the reactive center at the transition state.

F. NEIGHBORING CARBON AND HYDROGEN

1. Neighboring saturated carbon: Wagner–Meerwein rearrangements

(a) The bicyclo[2.2.1]heptyl system

Meerwein and van Emster (450, 451) have made a detailed investigation of the rearrangement of camphene hydrochloride (CXXXVII) to isobornyl chloride (CXXXVIII). The reaction yields an equilibrium mixture the composition of which is solvent-dependent. In a variety of solvents the rate of the camphene

CXXXVII   CXXXVIII
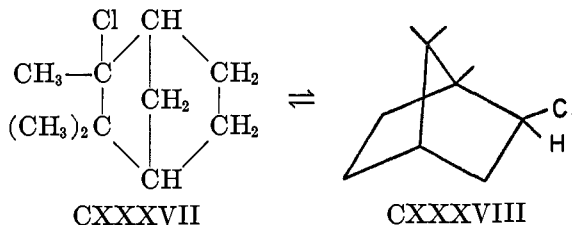
hydrochloride rearrangement was found to parallel roughly the dielectric constant of the solvent. A better parallelism was found in the solvolysis rates of triphenylmethyl chloride in similar solvent mixtures. Camphene hydrochloride rearranges faster in those solvents in which triphenylmethyl chloride solvolyzes more readily. Furthermore, the isomerization rate is profoundly catalyzed by Lewis acids, such as stannic chloride and ferric chloride.

Meerwein and van Emster suggested (451) that the reaction occurs by ionization followed by rearrangement of the intermediate carbonium ion. One difficulty with this proposal was recognized: namely, that the carbonium ion formed in
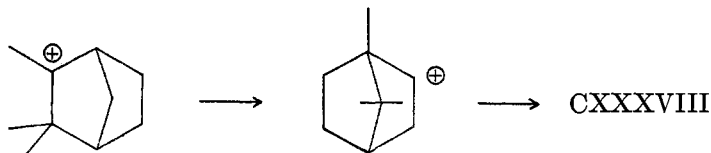
the rearrangement would presumably be the same as that formed by the analogous rearrangement of pinene hydrochloride (CXXXIX). Yet the product of the latter reaction is the epimeric bornyl chloride (CXL). The lower thermodynamic stability of isobornyl chloride is shown by its slow isomerization to bornyl chlo-

CXXXIX   CXL
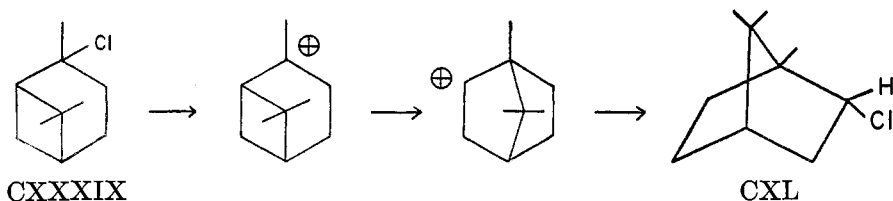
ride at ordinary temperatures. These results clearly indicate that although an electron-deficient intermediate of some sort is involved in the rearrangement of camphene hydrochloride, the bornyl (isobornyl) cation is precluded as an important intermediate.

Bartlett and Pöckel (49, 50) showed that the rearrangement of camphene hydrochloride in non-hydroxylic solvents is strongly catalyzed by hydrogen chloride; i.e., the rate law for the reaction is

$$\text{Rate} = k[\text{CXXXVII}][\text{HCl}]$$

They further pointed out that the stereochemistry of isobornyl chloride requires a Walden inversion at the new active center. Initially, they suggested that attack occurred at the bornyl center by hydrogen chloride with a concerted rearrangement and elimination of chloride ion. This hypothesis was discarded when camphene hydrochloride was found not to rearrange with the more nucleophilic chloride ion in acetone solution.

That the function of the hydrogen chloride is to help pull off chloride ion is indicated by the catalytic effect of phenols on the rearrangement rate. With substituted phenols, the order of catalytic activity towards camphene hydrochloride is the same as the order of increase of the acid strength of hydrogen chloride which the phenols promote in dioxane. Both phenomena are presumably due to hydrogen bonding between the phenolic hydroxyl group and the leaving chloride (43, 45).

The hypothesis was advanced by Nevell, de Salas, and Wilson (472) that a mesomeric ion such as that formulated as CXLI was involved. The hydrogen-

chloride-catalyzed reaction in the inert solvents used would then produce an ion-pair, the anionic part of which could be represented as HCl_2^-. The mesomeric
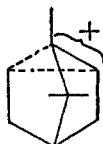
CXLI

cation could react with HCl_2^- at the tertiary center to regenerate camphene hydrochloride or at the secondary center to produce isobornyl chloride. A number of the consequences of this interpretation are capable of experimental verification.

The rate of isotopic chlorine exchange between hydrogen radiochloride and camphene hydrochloride has been found to be fifteen times faster than the rate of the rearrangement to isobornyl chloride (472).[13] Hence the rate-determining step of the rearrangement of CXXXVII must be the reaction of the bridged-ion with HCl_2^- at the secondary position. Conversely, from the principle of microscopic reversibility, the rate-determining step of the rearrangement of isobornyl chloride back to CXXXVII must be the reaction with hydrogen chloride (or other catalyst) to produce the bridged-ion pair directly.

If the proposed bridged-ion is an intermediate not only for the rearrangement in inert solvent but also for solvolytic reactions of camphene hydrochloride and of isobornyl chloride, both isomers must give the same products. In cold methanol, camphene hydrochloride gives first the tertiary methyl ether and, on long standing, isobornyl methyl ether. The reaction of isobornyl chloride is slower and yields isobornyl methyl ether (451). These results are undoubtedly caused by the presence of the liberated hydrogen chloride which would make the solvolyses reversible. In dilute aqueous base both chlorides yield camphene hydrate (16, 17, 450, 451).

The aqueous hydrolysis of isobornyl chloride is greatly catalyzed by phenol but not by alkali (451).

The postulate that a bridged-ion is formed as the first intermediate implies a transition state of like structure and necessitates a *faster* rate for reactions of camphene hydrochloride than the rate which would obtain if the first intermediate were of the normal solvolysis type. In actual fact, the ethanolysis of camphene hydrochloride is 6000 times faster at 0°C. than the corresponding reaction of *tert*-butyl chloride (108); hence, camphene hydrochloride is 370 times more reactive than the closely related 1-chloro-1-methylcyclopentane (113, 350), although from considerations of ring strain, it should be less reactive in the absence of participation.

The argument applies as well to the reactivities of isobornyl systems. The

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[13] Some of the other isotopic results of Nevell, de Salas, and Wilson (472) in this system have not been interpreted in any consistent fashion. A reinvestigation of these results would certainly be desirable.

reaction rates of these systems may be compared with cyclopentyl systems or perhaps better to bornyl systems. At ordinary temperatures the equilibrium position for the isobornyl–bornyl chloride epimerization contains significant quantities of isobornyl chloride (451). In fact, at high temperatures the equilibrium position favors isobornyl chloride (443). Consequently, under ordinary reaction conditions, bornyl chloride cannot be a great deal more stable than isobornyl chloride; yet the isomerization reaction is exceedingly slow compared with the camphene hydrochloride–isobornyl chloride rearrangement. *The rate-determining step of the epimerization of bornyl chloride cannot lead to the bridged-ion.* This conclusion should also apply with high probability to the solvolytic reactions of bornyl chloride. Because of the structural similarities of the two epimers, the rates of solvolyses of bornyl chloride are probably good measures of what the rates of the corresponding solvolyses of isobornyl chloride would be if the bridged-ion were not involved.

In brief, the relative rates of solvolysis of cyclopentyl chloride, bornyl chloride, and isobornyl chloride in 80 per cent ethanol at 85°C. are, respectively, 9.4, 1.0, and 36,000 (538, 684). The difference in the rates of bornyl and isobornyl chlorides is far too great to be plausibly associated only with a difference in steric effects (684). The reason why bornyl chloride is significantly less reactive than cyclopentyl chloride may well be due to the greater rigidity of the bicyclic system. The fact that camphene hydrochloride itself shows definite rate enhancement argues against Doering's suggestion (207) that isobornyl chloride rearranges directly to the hydrocamphyl cation as the first intermediate.

The results are completely consistent with the effects of neighboring group participation found in other systems; in the bicyclic case, the neighboring group is a saturated carbon function. In isobornyl chloride the methylene bridge and the leaving chloride are constrained *trans* to one another—an ideal situation for participation. The high reactivity of isobornyl chloride is evidence that such participation is important. In bornyl chloride the neighboring methylene group and the chloride group are *cis*-related and no neighboring group participation should occur; the *gem*-dimethyl bridge, of course, is *trans* to the leaving chloride, but if it were to participate a structure containing a four-membered ring would result. Such participation is not expected.

In principle, various representations are possible for the bridged-ion intermediate. A simple consistent structure written in orbital terms is depicted in figure 24. An equivalent dotted-line version is shown in formula CXLII (684).
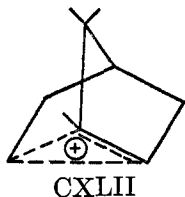
CXLII

This interpretation, however, cannot be distinguished from one in which there are two intermediates, CXLIIIa and CXLIIIb. These intermediates could be
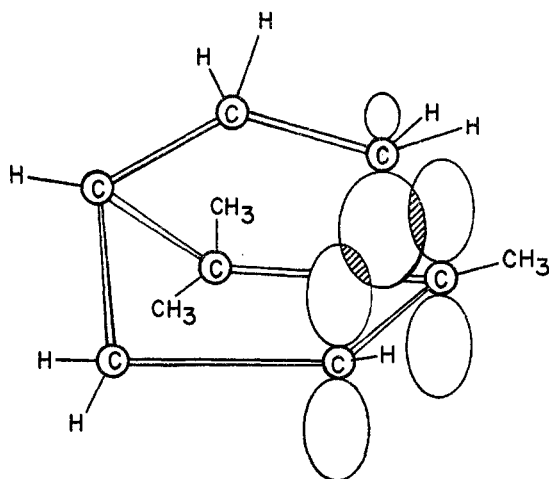
Fɪɢ. 24. Orbital diagram of the hydrocamphyl-isobornyl bridged cation

considered as ordinary carbonium ions in which the positive charge is somewhat relieved by overlap with the electron charge cloud of the neighboring carbon–carbon bond. CXLII would then be the structure of the transition state separating these intermediates. This explanation will give the same answers as the
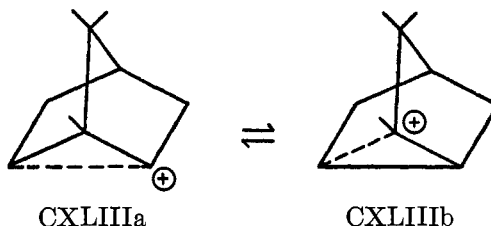

CXLIIIa   CXLIIIb

preceding interpretation if CXLIIIa and CXLIIIb are rapidly interconvertible. The former interpretation, however, is conceptually simpler.

A question which is still unanswered on the basis of the data so far discussed concerns the nature of the bonding between the ions in the ion-pair involved in the camphene hydrochloride rearrangement in inert solvents.

A rather similar system exists in the fenchyl series. The ethanolysis of β-fenchyl tosylate (CXLIV) at 30°C. is 710 times faster than that of α-fenchyl tosylate (CXLV) (349). Neighboring group participation with the formation of a bridged-ion (CXLVI) also serves to interpret the rate enhancement in CXLIV.

CXLIV   CXLV   CXLVI
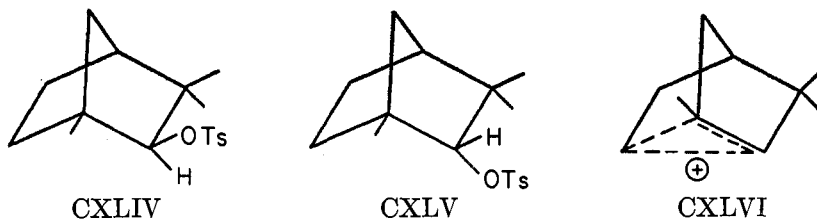
In recent years, the parent norbornyl system has been intensively studied. Rate differences between *exo* and *endo* isomers (CXLVII and CXLVIII, respectively) are also apparent in this system. The rates of solvolysis of *exo* isomers relative to the *endo* isomers are ~70 for the chlorides in 80 per cent ethanol at

CXLVII   CXLVIII
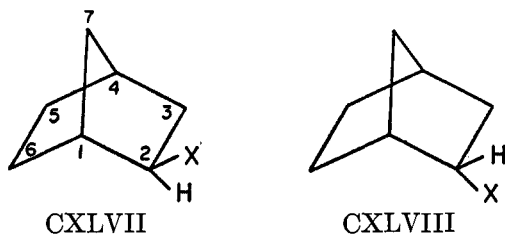
85°C. (529, 530), 350 for the brosylates in acetic acid at 25°C. (692, 693), and 310 for the brosylates in 75 per cent aqueous acetone at 45°C. (534). The large relative rates of the *exo* isomer are again explicable in terms of neighboring group interaction with the formation of a bridged-ion, CXLIX (684, 691).

CXLIX   CL
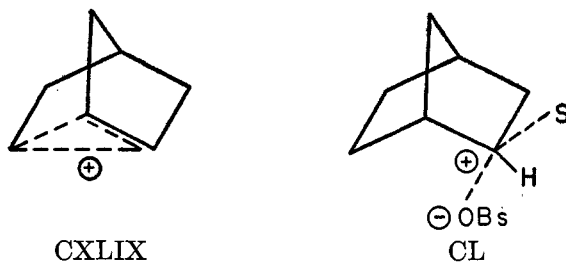
Some implications of CXLIX are clear. Unlike the intermediate in the camphene hydrochloride–isobornyl chloride system, CXLIX has a plane of symmetry and is optically inactive. Furthermore, subsequent reaction of CXLIX with solvent with the usual inversion of configuration should yield *exo* products. The solvolysis of *exo*-norbornyl brosylate in aqueous acetone, ethanol, or acetic acid yields, in fact, only *exo* products. When optically active starting material is used, the products are completely racemic (693).

The acetolysis of *endo*-norbornyl brosylate at 25°C. is 0.045 times as fast as that of cyclopentyl brosylate and 1.5 times as fast as that of cyclohexyl brosylate (684). This relative rate is about what one might expect for such a rigid system (684). The solvolysis products in acetic acid, aqueous acetone, and aqueous dioxane are wholly *exo*. Although in normal solvolyses a predominant inversion of configuration is indeed general, the solvolysis products are almost completely racemic. Only 7–8 per cent of the optical activity is retained. These results have been interpreted to mean that the first intermediate in the solvolysis of *endo*-norbornyl brosylate has the "normal" structure, CL. This intermediate either rehybridizes to give an *exo* product which is optically active or it rearranges to the bridged-ion (CXLIX), which produces racemic *exo* products (692). Winstein
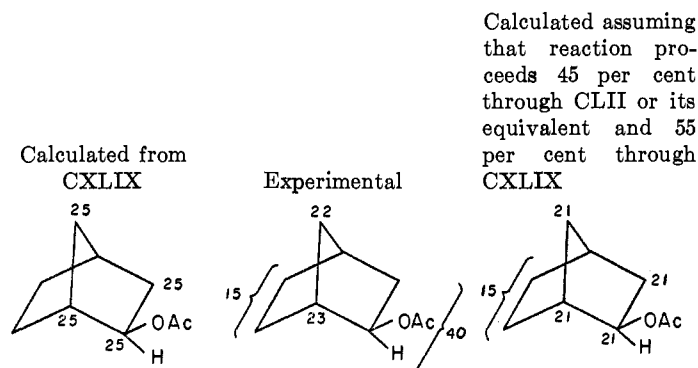
Calculated from
CXLIX

Experimental

Calculated assuming
that reaction pro-
ceeds 45 per cent
through CLII or its
equivalent and 55
per cent through
CXLIX

FIG. 25. Distribution of radioactivity in the acetolysis of *exo*-norbornyl 2,3-C_2^{14} brosylates (533).

and Trifan (692) were able to logically exclude a number of alternative mechanistic hypotheses.

The skeletal rearrangement implied by structure CXLIX has been investigated by C^{14} tracer methods (533). The norbornyl derivatives used were labeled equally in the 2- and 3-positions. If the formation of CXLIX and its reaction with solvent are the only reactions which occur, the products should be labeled equally in the 1-, 2-, 3-, and 7-positions. The results demonstrated that rearrangement did occur but that it was somewhat more extensive than the simple reactions involving CXLIX would indicate. In particular, during the acetolysis of the labeled *exo*-norbornyl brosylates, some 15 per cent of the radioactivity found its way to positions 5 and 6 (figure 25). The results can be readily explained on the basis of the type of 1,3-hydride shift known in the fenchyl series (215) (page 715). The interpretation of the net reactions in figure 26 may be made in
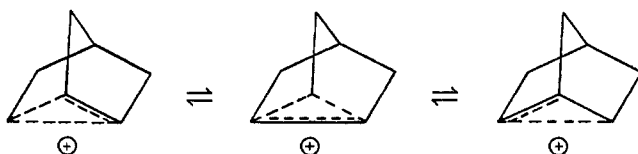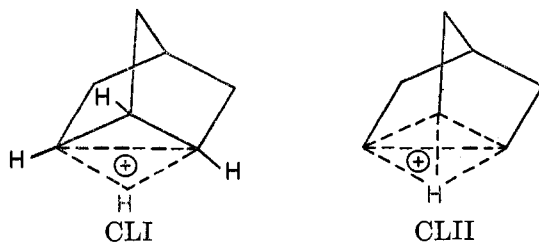

FIG. 26. Rearrangement equilibria among bridged norbornyl cations

terms of structures such as CLI and CLII acting as intermediates or as transition states (532, 693). As yet, the experimental distinction between the various possibilities has not been made.

CLI   CLII

The amount of extra rearrangement is less in aqueous acetone solutions. The rate of reaction of CXLIX with solvent compared to the rate of hydride migration would be expected to be greater in the more nucleophilic solvent.

The *endo* isomers were found to show 5–10 per cent less skeletal rearrangement than the *exo* isomers, in agreement with the comparable degree of optical activity retained in the former solvolyses (692).

Winstein and Trifan (693) made the important observation that during the solvolysis of optically active *exo*-norbornyl brosylate, the rate of loss of optical activity exceeded the rate of formation of *p*-bromobenzenesulfonic acid. Both rates were accurately of first order. The results are interpretable as an internal return phenomenon. As with the allylic systems (page 658), the results can be described kinetically in terms of equation 17 in which the initial intermediate is described as a *p*-complex "ion-pair" (CLIII). The values for the rate ratio,


$$\text{products} \quad (17)$$

CLIII
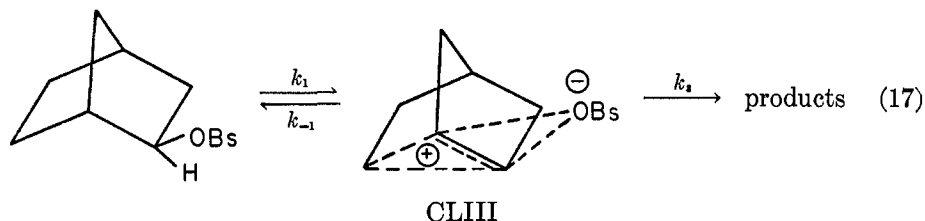
k_{-1}/k_s, at 25°C. in various solvents are: acetic acid, 2.46; ethanol, 1.94; 75 per cent aqueous acetone, 0.40 (688). These figures are not corrected for the complication which the fact of hydride migration introduces. As expected, the return step is relatively less favored in the more nucleophilic solvents.

It is pertinent that the polarimetric and titrimetric rates of solvolysis of *endo*-norbornyl brosylate are identical within experimental error (692).

(b) Other bicyclic systems

Doering and Farber (208) observed that treatment of 2-bromobicyclo[2.2.2]-octane (CLIV) with silver bromide in carbon tetrachloride produced the skeletal rearrangement product, 2-bromobicyclo[3.2.1]octane (CLV). This result establishes the greater thermodynamic stability of CLV compared with CLIV.
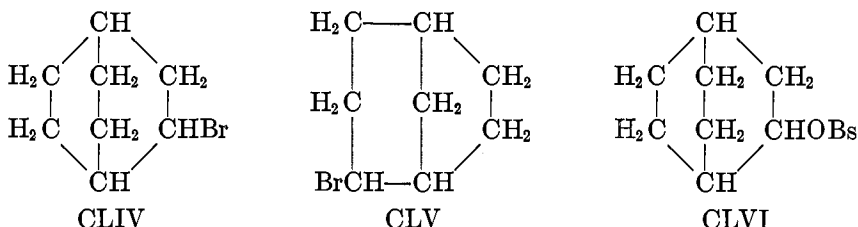
The solvolysis of bicyclo[2.2.2]octyl-2 brosylate (CLVI) in aqueous lithium carbonate yields the unrearranged alcohol (638). A bridged-ion is probably not formed in this case, since at least some of the more stable rearranged isomer would be expected to result. The acetolysis rate at 25°C. is 43 times the rate of acetolysis of cyclohexyl brosylate and 1.3 times that of cyclopentyl brosylate (639). Bi-

cyclo[2.2.2]octane consists of fused cyclohexane rings constrained to the boat conformation. The resulting non-bonded hydrogen–hydrogen interactions undoubtedly account for the lower stability compared to bicyclo[3.2.1]octane, in which the cyclohexane ring can assume the chair conformation. Solvolysis of CLVI brings about a reduction in the number of carbon–hydrogen bond oppositions at the transition state; hence the rate is enhanced compared with cyclohexyl systems (639). The rate is very close to that of the cyclopentyl system for which an identical explanation has been offered earlier (page 667). The product and rate studies in this system are fully explicable without recourse to bridged-ion intermediates; however, stereochemical data would be desirable.

Rearrangement of 2-bicyclo[2.2.2]octyl systems, consequently, must be rather slow compared with other reactions which the intermediates involved may undergo. Rearrangement occurs only when the intermediates are repeatedly formed; e.g., the reaction of the bromide with silver bromide.

The fact that, by contrast, 2-bicyclo[2.2.1]heptyl systems form bridged-ion intermediates rather readily must indicate in such systems a high degree of internal strain which is partially relieved in the bridged-ion. In several such systems, Bartlett (41, 42a) has found that the driving force is associated with a more favorable entropy of activation and has accounted for these results on the basis that less fixation of solvent molecules is required in cases in which positive charge can be distributed internally. Another entropy-increasing factor is undoubtedly the relief of structural rigidity in the formation of the bridged-ion.

Changes in structure with the introduction of suitable electronic inductive effects suffice to counteract the tendency towards rearrangement. The extreme unreactivity reported for dimethyl *trans*-4,5-dibromo-*exo-cis*-3,6-endoxohexahydrophthalate (CLVII) (85) indicates both the absence of rate enhancement due to neighboring bromine participation in this system, probably because the
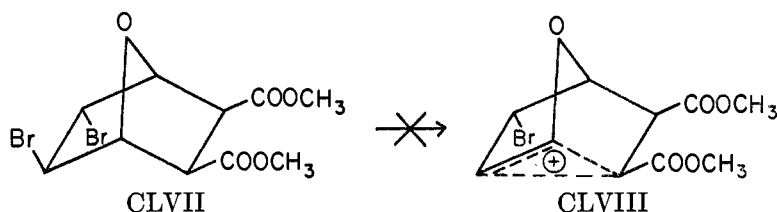
CLVII   CLVIII

intermediate bromonium ion would be highly strained, and the absence of rate enhancement due to rearrangement to a bridged-ion (CLVIII). The inductive effect of the oxygen would tend to destabilize the ion and the unshared electron pairs on the oxygen are geometrically unable to contribute to the positive centers.
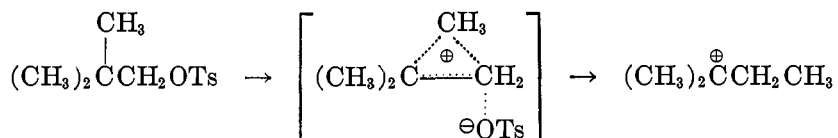
(c) Neighboring alkyl group

The reaction of neopentyl iodide with aqueous silver nitrate yields *tert*-amyl alcohol, obviously the product of a rearrangement (652). In fact, a number of solvolyses of neopentyl systems are known to result in rearrangement of a methyl

group (220, 652). The reaction has long been considered to be an example of a general class of rearrangement reactions which includes the camphene hydrochloride rearrangement and the pinacol rearrangement (650).

Bridged structures have been written as *intermediates* for many such reactions (12, 201, 202, 247, 513, 645, 648). The original carbonium ion, the bridged-ion, and the rearranged carbonium ion may possess, in principle, varying degrees of stability. In particular cases some of the ions, if present at all along the reaction coordinate, may exist only as transition states or as very unstable intermediates (slight dips in the free energy curve); i.e., the properties of many systems can be fully interpreted without reference to bridged-ion *intermediates*. Among the types of facts which have been used to determine the relative energetics of intermediates in reactions which involve rearrangement are the existence or absence of rate enhancements, product studies, and evidence from stereochemical and chemical isotope procedures.

The fact that the formolysis of neopentyl tosylate is as rapid as that of ethyl tosylate despite the appreciable nucleophilic contribution at the rear in the latter case has been interpreted as a rate enhancement due to rearrangement (page 646) (591, 682). A rate enhancement could result if the first intermediate were the *tert*-amyl cation. If the neighboring methyl group were to assume the role of the nucleophilic solvent molecule at the rear, the transition state would have a bridged-ion structure and the neopentyl cation would play no role at all:

$$(CH_3)_2 \overset{\overset{\displaystyle CH_3}{\displaystyle |}}{C} CH_2 OTs \;\;\rightarrow\;\; \left[(CH_3)_2 C \overset{\overset{\displaystyle CH_3}{\diagup \overset{\oplus}{} \diagdown}}{-\!\!-\!\!-\!\!-} CH_2 \atop \overset{\vdots}{\ominus OTs} \right] \;\;\rightarrow\;\; (CH_3)_2 \overset{\oplus}{C} CH_2 CH_3$$

Some increase in the rate of neopentyl systems compared with ethyl systems should be expected, however, simply from the inductive effect of the additional methyl groups.

On the basis of general neighboring group behavior, *substitution at the α-position should decrease the driving force for anchimeric assistance;* i.e., α-substitution stabilizes the developing positive charge, hence the system has less need for a further electron supply. The formolysis of pinacolyl brosylate does show a small rate enhancement (table 54); however, significant rate enhancement is absent in the acetolysis of pinacolyl brosylate or in the aqueous ethanol solvolysis of pinacolyl chloride. In some of these cases rearrangement products do result

TABLE 54

Rate enhancements in secondary carbinyl systems

Reaction	Relative Rates				
	Isopropyl	2-Butyl	3-Methyl-2-butyl	3,3-Dimethyl-2-butyl	References
RCl, 80% C$_2$H$_5$OH, 80°C............	1.0	—	—	0.60	(108, 376)
ROBs, CH$_3$COOH, 25°C.............	1.0	2.3	6.0	2.9	(682)
ROBs, HCOOH, 25°C................	1.0	2.5	14.4	14.4	(682)

(685). In all of these cases the bridged-ion certainly cannot be credited with appreciable stability.
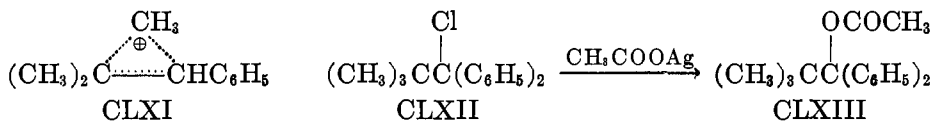
Closely analogous are the acetolyses of *cis*- and *trans*-9-decalylcarbinyl tosylates (CLIX and CLX, respectively). These compounds solvolyze at the same rate at 90°C. and some five times faster than neopentyl tosylate, corresponding to a slight rate enhancement. The product is predominantly the rearranged olefin (CLXI) (189).

CLIX   CLX   CLXI
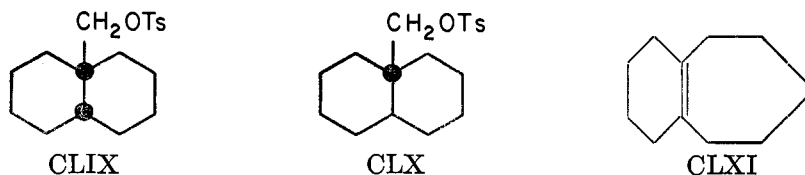
In cases in which the reactive carbon is tertiary, the tendency to form a bridged-ion is apparently very small, unless further driving forces are involved; e.g., relief from steric strain. The solvolysis of dimethyl-*tert*-butylcarbinyl chloride in 80 per cent ethanol is only 20 per cent faster than that of *tert*-butyl chloride (116). An even faster rate would have been expected solely from the inductive electron release of the additional methyl groups (figure 22). By labeling one methyl group with C^{14}, Roberts and Yancey (540) found that aqueous solvolysis gave no rearrangement. Treatment of the chloride with hydrochloric acid and zinc chloride gives complete equilibration of the radiocarbon label among the five methyl groups. The conditions serve to form and re-form the carbonium ion a number of times. Even a small relative rate for rearrangement of the carbonium ion compared with reaction with chloride ion would suffice to explain these results.

Brown and Okamoto (128) have found that solvolyses of 2-chloro-2,3,3-trimethylpentane and 3-chloro-2,2,3-trimethylpentane are unattended by rearrangement. For these systems also, bridged-ion intermediates have yet to be demonstrated.

Rearrangement also does not occur in the α-phenylneopentyl system. Solvolyses of the chloride or bromide under a variety of conditions yield unrearranged products (224, 577, 683). Also significant is the fact that the use of optically active material results in products which show a small amount of *inversion* of configuration (683). If a bridged-ion intermediate such as CLXI were involved, *retention* of configuration would be expected. The failure of these

$$(CH_3)_2\overset{\overset{CH_3}{\underset{\oplus}{\diagup}}}{C}\text{------}\overset{}{C}HC_6H_5 \qquad (CH_3)_3C\overset{\overset{Cl}{|}}{C}(C_6H_5)_2 \xrightarrow{CH_3COOAg} (CH_3)_3C\overset{\overset{OCOCH_3}{|}}{C}(C_6H_5)_2$$

CLXI   CLXII   CLXIII

systems to form bridged-ions renders rearrangement improbable in α,α-diphenylneopentyl systems. In fact, 1-chloro-2,2-dimethyl-1,1-diphenylpropane (CLXII) yields the unrearranged acetate (CLXIII) on treatment with silver acetate (516a).

Rearrangements occur more readily in strained systems. Methyl group migration in the camphene series, for example, is known to occur (page 715). Highly branched carbinyl chlorides can be exceedingly reactive. Alcohols such as methyl-di-*tert*-butylcarbinol, isopropyl-di-*tert*-butylcarbinol, and tri-*tert*-butyl-carbinol react with hydrochloric acid to give mixtures of chlorides, some components of which have solvolysis rates as much as 50,000 times greater than that of *tert*-butyl chloride (56).[14] Because the chlorides could not be prepared from the alcohols without rearrangement, esters were studied and were found to possess decided rate enhancements.

The rates of the acid-catalyzed solvolyses in 75 per cent aqueous methanol of the *p*-nitrobenzoates of tri-*tert*-butylcarbinol (CLXIV) and *tert*-butyl alcohol are in the ratio 50,000:1 (47). Tri-*tert*-butylcarbinyl derivatives are very strained; the strain is readily apparent in Stuart models of the compounds by the ease with which the models tend to fall apart. In addition to the strain of compression energies, the compounds must possess low entropies because of the restriction of rotation of the methyl groups. Relief of steric strain is undoubtedly an important source of the rate enhancement.

The product obtained in high yields from the solvolysis of CLXIV in aqueous dioxane was *asym-tert*-butyltriptylethylene (CLXV) (54). Two rearrangements are involved in the reaction sequence:
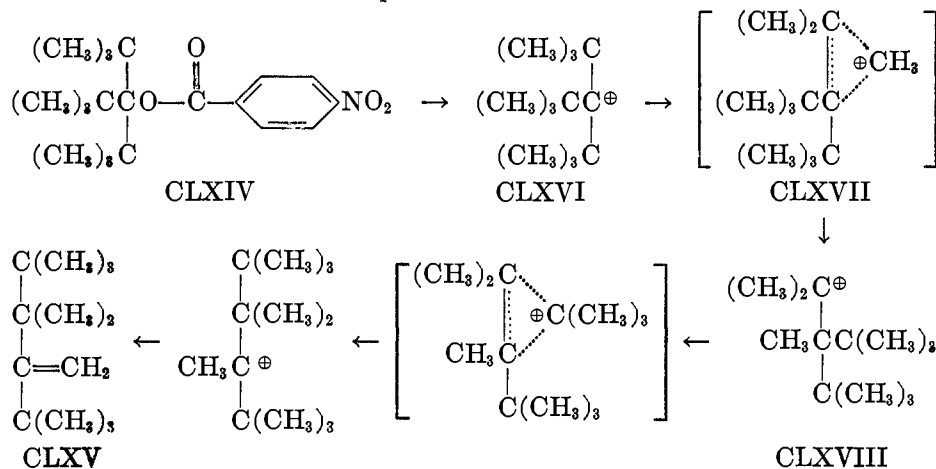
The pronounced rate enhancement in the solvolysis strongly suggests that rearrangement occurs simultaneously with ionization; i.e., the first intermediate is not CLXVI but CLXVII or CLXVIII. It has been suggested (685) that "participation may provide a mechanism for the relief of steric strain."

Some homologs of CLXIV are also much more reactive than *tert*-butyl systems. Relative rates of solvolysis of the *p*-nitrobenzoates of triisopropylcarbinol, di-

[14] The solvolysis rate of tri-*tert*-butylcarbinyl chloride has been reported to be only 600 times faster than that of *tert*-butyl chloride, although no experimental details were given (107). The results of Bartlett, Swain, Lefferts, and Stiles (47, 54, 56) render probable the proposition that this chloride has not in fact yet been prepared.

tert-butylisopropylcarbinol, *tert*-butyldiisopropylcarbinol, and tri-*tert*-butyl-carbinol in aqueous dioxane are, respectively, 1.0, 8.3, 8.5, and 30.8 (54).

The results discussed in this section suggest the following generalization: alkyl group migration is not accompanied by a large rate enhancement unless the rearrangement is accompanied by a decrease in steric strain.

(d) Neighboring small rings

The ethanolysis of cyclopropylcarbinyl benzenesulfonate at 20°C. is 14 times as rapid as that of allyl benzenesulfonate and 500 times as rapid as that of ethyl benzenesulfonate (83, 84, 628). The pronounced rate enhancement is undoubtedly due to participation of some sort by the adjacent cyclopropyl group. Rate enhancement is also found in the solvolysis of cyclopropylcarbinyl chloride in 50 per cent aqueous ethanol (535).

Although the product of the ethanolysis of cyclopropylcarbinyl benzene-sulfonate is chiefly ethyl cyclopropylcarbinyl ether (82), the sulfonate readily rearranges in chloroform to a mixture of cyclobutyl benzenesulfonate and 3-buten-1-yl benzenesulfonate (83). The aqueous solvolysis of cyclopropyl-carbinyl chloride when not carried to completion yielded a mixture of carbinols consisting of 48 per cent cyclopropylcarbinol, 47 per cent cyclobutanol, and 5 per cent of allylcarbinol and a mixture of unreacted chlorides which contained both cyclobutyl chloride and allylcarbinyl chloride (535). Under the conditions used, the isomeric chlorides would not have reacted significantly. The rearranged carbinols are, therefore, products of cyclopropylcarbinyl chloride. Aqueous solvolysis of cyclobutyl chloride resulted in a closely similar mixture of carbinols (535). Acetolysis of cyclobutyl tosylate or cyclopropylcarbinyl chloride resulted in a mixture of acetates which contained roughly the same proportions of cyclo-butyl acetate and cyclopropylcarbinyl acetate (532, 535). Isomerization of these systems occurs, consequently, to give not only rearranged products but also rearranged starting materials. Formation of the less reactive rearranged halides was also shown by the drifting instantaneous rate constants obtained in kinetic measurements of cyclopropylcarbinyl chloride in aqueous ethanol (535). It is pertinent that the solvolysis of cyclopropylcarbinyl benzenesulfonate in absolute ethanol gives good first-order rate constants without drift (83).

The reactions can be explained by assuming an interconversion of the car-bonium ions, CLXIX and CLXX, with a slow and essentially irreversible reaction to allylcarbinyl derivatives. Treatment of any of the isomeric chlorides with zinc chloride and hydrochloric acid, for example, results in conversion to essentially pure allylcarbinyl chloride. Formation of rearranged starting materials implies internal return from "ion-pair" intermediates.

The stability of the cyclopropylmethyl cation has been attributed to resonance among the structures CLXIXa and CLXXI (535) and among the structures CLXIXa, b, and c (83). CLXXI and CLXIXb (and c) are not resonance structures of the same resonance hybrid. Resonance among structures CLXIXa and CLXXI is equivalent to orbital interactions of the type in figure 27A. Such interaction is not unlike that assumed to occur in hyperconjugation. Resonance
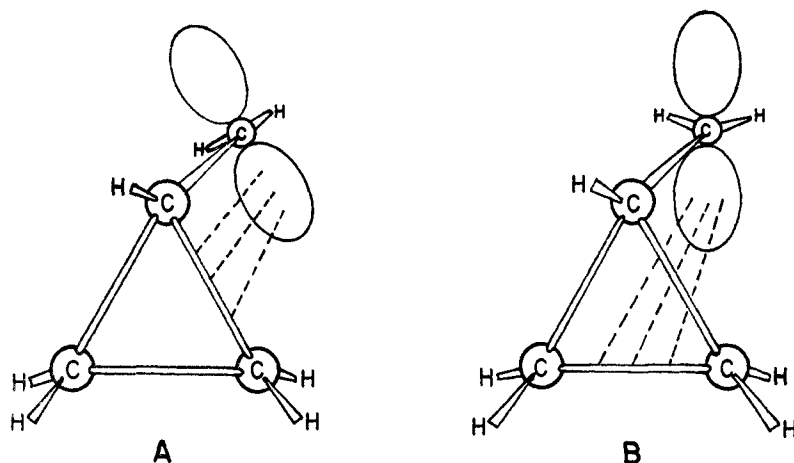
FIG. 27. Orbital representations of two of the possible cyclopropylmethyl cations

among structures CLXIXa, b, and c is equivalent to molecular orbital inter-
actions, as in figure 27B. *Interconversion of A and B in figure 27 requires a move-
ment of atoms.*
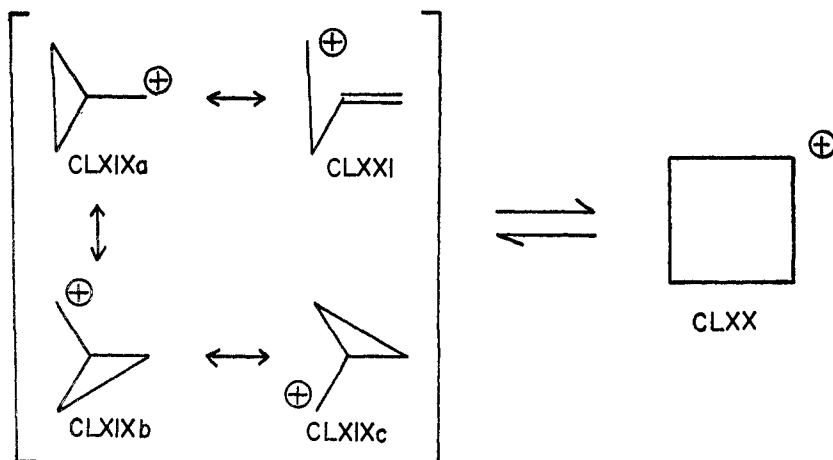
Structure B in figure 27 is equivalent to the "non-classical" cation CLXXII,
which has been suggested as an intermediate. Justification for structure CLXXII

CLXXII
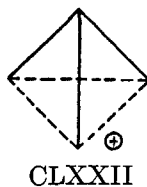
depends on the threefold symmetry required for maximum resonance among
structures CLXIXa, b, and c (83) and on the extensive rearrangement of the

radiocarbon label found in the reaction of cyclopropylcarbinylamine-1-C^{14} with nitrous acid (536). This reaction yields a mixture of carbinols identical to that obtained from the halide solvolysis. In the cyclobutanol product, the C^{14} was effectively equilibrated among three carbon atoms. Formation of CLXXII cannot be the only reaction whi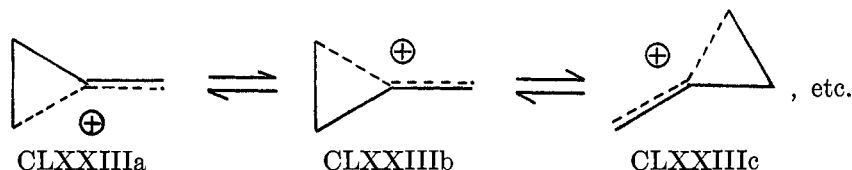ch takes place, however, because the C^{14} was not equally distributed among three carbons in the cyclopropylcarbinol product. The results can also be explained by the assumption of interconversion of cations of the structure CLXXIII.


CLXXIIIa   CLXXIIIb   CLXXIIIc

The acetolysis of nortricyclyl brosylate (CLXXIV) at 25°C. is about 200 times as fast as that of endo-norbornyl brosylate (CXLVIII: X = OBs) (694). The latter compound is used as a standard because it does not manifest a rate enhancement attributable to participation and because both systems are analogously strained. Because of the added bond-angle strain involved in the trigonal carbonium-ion configuration, CLXXIV would be expected to be less reactive in the absence of participation. The rate difference for the solvolysis of the chlorides in 80 per cent aqueous ethanol appears to be somewhat smaller (529).

CLXXIV
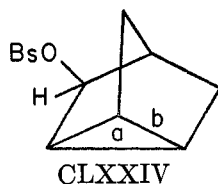
If interaction of the type in figure 27A is important, some rate enhancement in the nortricyclyl system is to be expected because the geometry permits appreciably such interaction between the developing p orbital at the reacting center and bond a in CLXXIV. Interaction with bond b in CLXXIV, on the other hand, is effectively prevented by the geometry.

The ability of the cyclobutyl cation to rearrange undoubtedly accounts for the rate enhancement observed in the solvolyses of some cyclobutyl systems (page 667). A unique example of a synthetic use for such rearrangement is the preparation of cycloheptatriene (CLXXVI) in 50 per cent yield from the acetolysis of 6-bicyclo[3.2.0]-2-heptenyl methanesulfonate (CLXXV) (225).

CLXXV   CLXXVI
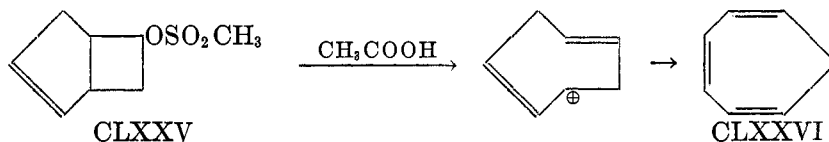
Rate enhancement for a neighboring cyclobutyl group has also been reported; e.g., acetolysis rates at 25°C. for dicyclobutylcarbinyl brosylate, methylcyclobutylcarbinyl brosylate, and isopropyl brosylate are in the ratio 220:510:1 (675, 682). The rate enhancements in the bicyclic systems α- and β-nopinyl brosylates (CLXXVII and CLXXVIII) are apparently very small; however, acetolysis of these compounds yields a mixture of rearranged compounds comprised mostly of apoisobornyl acetate (CLXXIX) and β-fenchoisocamphoryl acetate (CLXXX) (675).

CLXXVII   CLXXVIII

CLXXIX   CLXXX
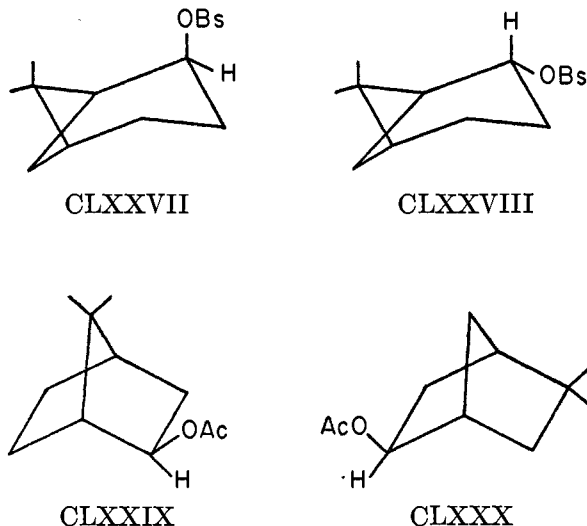
2. Neighboring hydrogen

Rearrangements of isobutyl systems into tert-butyl systems have long been recognized; for example, in 1872 Linnemann (431) discovered that the reaction of isobutyl iodide with silver acetate in acetic acid gave predominantly tert-butyl acetate. The reaction apparently occurs by way of a rearrangement of the tertiary hydrogen atom. The formolysis rate of isobutyl tosylate is only slightly greater than that of ethyl tosylate (table 31) and perhaps slightly larger than the expected rate in the absence of rearrangement. The acetolysis rate of 3-methyl-2-butyl brosylate, in which a tertiary hydrogen is adjacent to a secondary center, is greater than that of isopropyl brosylate by no more than a factor plausibly ascribable to the inductive effect of the methyl groups (table 54 and figure 21). The solvolysis rate of dimethylisopropylcarbinyl chloride, in which the tertiary hydrogen is adjacent to a tertiary center, is actually less than that of tert-butyl chloride in 80 per cent ethanol at 25°C. (table 38). In all of these cases a significant driving force for neighboring hydrogen participation is clearly absent. More precisely, for these cases, a transition state structure involving a hydrogen bridge (CLXXXI) is not significantly more stable than one involving only hyperconjugation (CLXXXII). Acetolysis of 3-phenyl-2-butyl tosylate

yields only a small amount of the rearranged ester, 2-phenyl-2-butyl acetate (174).

CLXXXI   CLXXXII
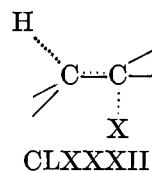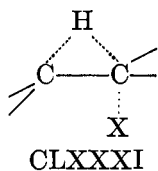
Participation by a neighboring secondary hydrogen with consequent rearrangement is slight. Equilibration of 2- and 3-pentyl bromides does occur slowly when treated with hydrobromic acid and sulfuric acid (562). Under these conditions the functional center undergoes repeated reaction. Only a small fraction of the individual reactions need result in rearrangement to accommodate these results. As much as 8 per cent rearrangement has been reported to accompany the acetolysis of 2-butyl-1-C^{14} tosylate under conditions in which each molecule reacts but once (531). Less than 2 per cent rearrangement was found in the acetolyses of 2-pentyl brosylate, 4-methyl-2-pentyl brosylate, and 4,4-dimethyl-2-pentyl brosylate (127).

The menthyl–neomenthyl system is particularly interesting. The acetolysis of neomenthyl tosylate (CLXXXIII) is 77 times faster than that of menthyl tosylate (CLXXXIV) at 50°C. (684). The corresponding ratio for the chlorides in 80 per cent ethanol at 125°C. is 41 (365). It has been suggested that the rate difference is due to bimolecular displacement by solvent in the neomenthyl case (365). This view, however, is inconsistent with the fact that the rate of solvolysis of neomenthyl tosylate in acetic acid is *more rapid* than in ethanol at 50°C.

CLXXXIII   CLXXXIV
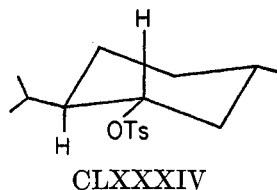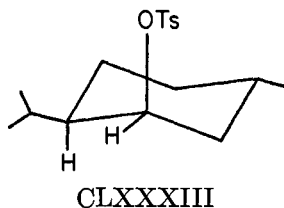
In neomenthyl tosylate, both the leaving group and the neighboring tertiary hydrogen occupy axial positions and are ideally disposed for neighboring hydrogen participation. Of the total rate difference between neomenthyl and menthyl systems, a factor of ~3 is ascribable to the fact that the axial leaving group of the former is being compared with the equatorial leaving group in the latter (676). Neighboring hydrogen participation, even in this almost ideally suited case, leads, then, to a rate enhancement of only ~ twentyfold. In the analogous open-chain system, hydrogen participation requires an additional restriction of atomic motions relative to the ground state. The resulting decrease in entropy can counter the rather small stabilization obtained by hydrogen bridging.

The initial ethanolysis product of optically active neomenthyl chloride is predominantly optically active 3-menthene (CLXXXV) and some 2-menthene

(CLXXXVI) (365). The formolysis product of optically active neomenthyl tosylate is *racemic* 3-menthene, although under the solvolysis conditions used, 3-menthene is optically stable (690). No 2-menthene is formed (684, 690). These results suggest that the formolysis involves the rearranged cation (CLXXXVII) as a symmetrical intermediate. An interpretation could be made based on possible subsequent reactions of a hydrogen-bridged *intermediate* but additional data would be desirable.

CH₃ CH₃

CH(CH₃)₂   CH(CH₃)₂
CLXXXV   CLXXXVI   CLXXXVII
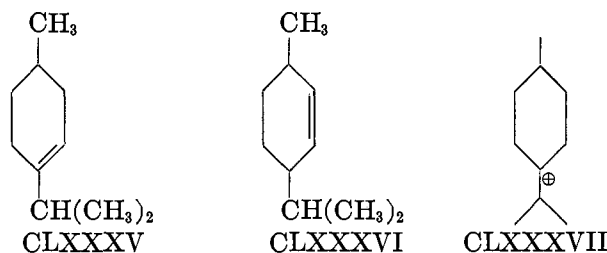
The tendency for participation by an axial hydrogen adjacent to an axial leaving group appears to be general. *cis*-2-Methylcyclohexyl tosylate (CLXXXVIII) is 71 times as reactive as the *trans* isomer in ethanol at 50°C. (349). In CLXXXVIII, the tosyl-axial conformation (CLXXXVIIIa) is highly populated. Solvolyses of *cis*-4-*tert*-butylcyclohexyl tosylate, in which the leaving group is constrained to an axial position, have been found to yield small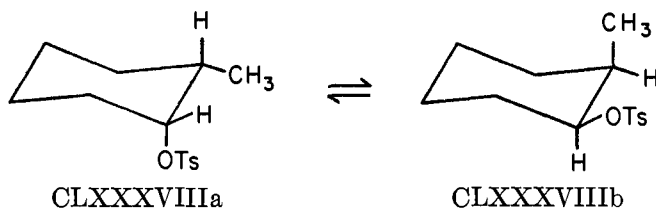 amounts of rearrangement products. In this system, the neighboring hydrogen which shows a small but definite tendency to rearrange is a secondary hydrogen. The *trans* isomer with an equatorial tosyl group gives no rearranged products (676).

H   CH₃
              CH₃   H
         H   OTs
OTs   H
CLXXXVIIIa   CLXXXVIIIb

A 1,3-hydrogen rearrangement is frequently encountered in bicyclo[2.2.1]-heptyl systems (page 704). The rearrangement has been demonstrated in some reactions in the fenchyl series which probably involve carbonium-ion intermediates (215). The rearrangement also seems required to explain the formation of β-fenchoisocamphorol in solvolysis of the nopinyl brosylates (page 713) (675).

The occurrence of the rearrangement in the camphene series is particularly interesting. Racemization of compounds in this series has long been recognized (575). Both a methyl migration (a) in the hydrocamphyl cation, CLXXXIX, and a 1,3-hydrogen shift (b) in the bridged-ion, CXLII, yield the enantiomer cation. When one of the methyl groups is labeled with C¹⁴ it is found that the label is equally distributed among all three methyl groups (634). Methyl migration therefore must occur. Furthermore, if the rearrangement were only to occur in the bridged-ion through structure CXC as a transition state or intermediate,

only the *exo*-methyl would be expected to migrate. If this were the only reaction which occurred, the radiocarbon label would be equally distributed between *two* methyl groups. An examination of the partially racemized material, however, demonstrates that the racemization is much faster than the radiocarbon exchange (539); hence, reaction (b) is more rapid than reaction (a). Since reaction (b) converts an *exo*-methyl group to an *endo*- and vice versa, the results are compatible with process (c) and the involvement of the hydrocamphyl cation is not necessary. It was previously shown that this cation is less stable than the bridged-ion (page 700).

CLXXXIXa   CXLIIa   CXC

CLXXXIXb   CXLIIb
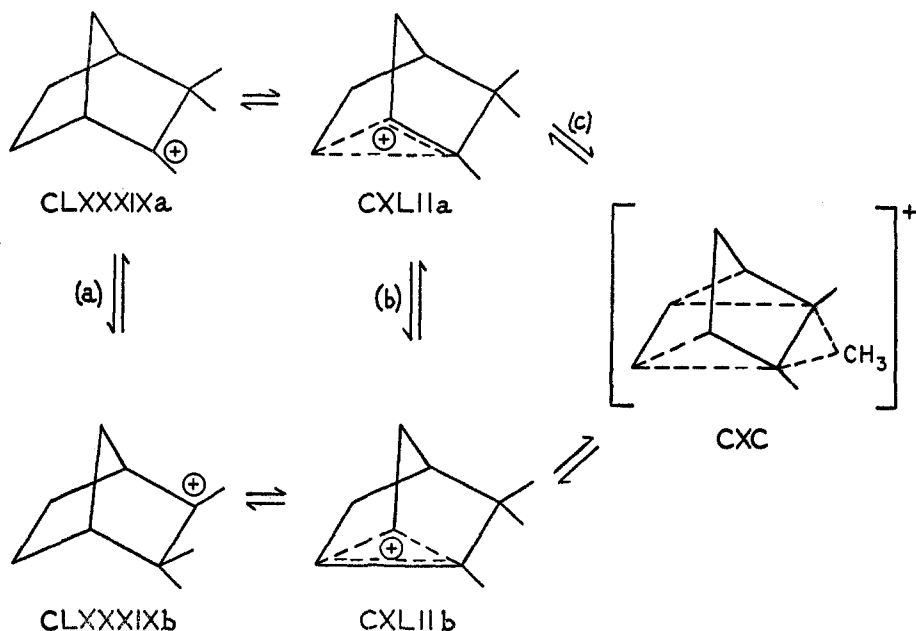
The relatively high acetolysis rates of cyclononyl, cyclodecyl, and cycloundecyl tosylates (table 40) suggest the involvement of transannular hydrogen participation in these cases.

3. Neighboring unsaturated groups

(a) Neighboring aryl group

i. The 3-phenyl-2-butyl and homologous systems

In 1949, Cram (171) reported his important results regarding the solvolyses of *erythro*- and *threo*-3-phenyl-2-butyl tosylates (CXCI and CXCII, respectively). The acetolysis of optically active CXCI gave *erythro*-3-phenyl-2-butyl acetate (CXCV) of about 94 per cent optical purity (175). The results correspond to a *retention* of configuration and of optical activity. On the other hand, acetolysis of optically active CXCII afforded the racemic *threo*-acetate (CXCVI). These results correspond to *retention* of configuration but with loss of optical activity.

The observations compare directly with the similar results obtained in solvolyses of the 3-acetoxy-2-butyl tosylates (438) and the 2,3-dibromobutanes (page 692) (661). The analogous interpretation involves the neighboring group participation of a phenyl function with the formation of a bridged-ion intermediate. Such an ion (CXCIII), formed from CXCI, is capable of sustaining optical activity. Attack at either positive center by solvent would yield the same product. The intermediate CXCIV, formed from CXCII, is a *meso* compound; hence, any reaction which proceeds through such an intermediate must yield racemic products.
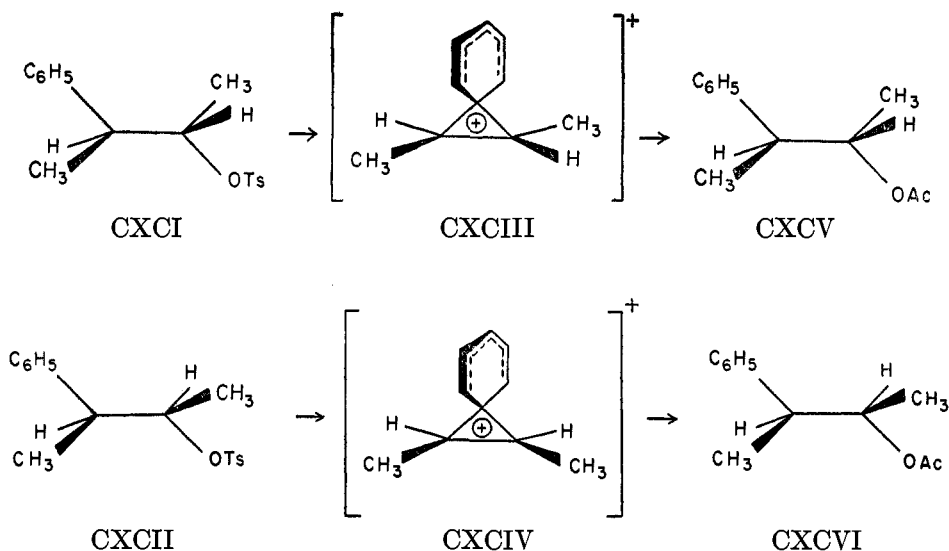
Rather than the symmetrical bridged structures such as CXCIII and CXCIV, the intermediates could perhaps be formulated as CXCVII (for the *threo* case) (537, 685). In this case, CXCIV could represent a transition state for interconversion of the ions.

An alternative explanation *which is not valid* is the postulate that "classical" carbonium ions (CXCVIIIa and CXCVIIIb) are in rapid equilibrium. The existence of such an equilibrium would not negate the additional rapid equilibrium of rotation about the central C—C bond. *Unless bonding interaction of some*

sort is maintained between the benzene ring and both active carbon centers, interconversion of erythro and threo isomers should occur.

Recent experimental results, to be discussed in the sequel (page 720), have provided substantiation for the hypothesis that bridged-ion intermediates such as CXCIII and CXCIV are important discrete *intermediates* in the reactions.

As with other neighboring functions which participate significantly, involvement of a neighboring phenyl group at the transition state of the rate-determining step implies a rate acceleration. The problem arises as to the rate to expect in the absence of participation. A rate-retarding effect of tenfold has been assigned to the normal inductive electron attraction of a benzene ring (685). Another estimate can be made with the use of Taft's polar substituent constants (page 695). Using the correlation previously established for the acetolyses of secondary alkyl brosylates (figure 21), the actual acetolysis rates of CXCI and CXCII are found to be about fivefold greater than the rates expected in the absence of participation. Increased substitution at the carbon atom bearing the phenyl group increases the driving force for participation; 2-methyl-2-phenyl-3-butyl brosylate shows an acetolysis rate enhancement of 106-fold (table 55). On the other hand, increased substitution at the carbon atom bearing the leaving group decreases the driving force for anchimeric assistance; the solvolysis rate

TABLE 55

Rate enhancements of neighboring phenyl systems

Compound	Relative Rate CH_3COOH 50°C.	Calculated Relative Rate Without Participation from Figure 21 at 70°C.[a]	Rate Enhancement[b]	References
2-Butyl brosylate	1.00	1.00	1.00	(685)
3-Phenyl-2-butyl brosylate (*erythro*)	0.58[c]	0.12	3.5	(685)
(*threo*)	0.66[c]	0.12	4.0	(685)
3-Methyl-3-phenyl-2-butyl brosylate	36	0.34	94	(685)
1,1-Diphenyl-2-propyl brosylate	0.91	0.012	57	(685)
1-Phenyl-2-propyl brosylate	0.16	0.065	2.2	(660)
1-*p*-Anisyl-2-propyl brosylate	3.6[d]	0.18[e]	23	(660)
3-*p*-Anisyl-2-butyl brosylate	45[c]	0.45[e]	130	(660)
4-Phenyl-3-hexyl brosylate	2.3	1.0	6.3	(180)

[a] Calculated with $\sigma^* = +0.215$ for $C_6H_5CH_2$ and $+0.405$ for $(C_6H_5)_2CH$ (615).

[b] These figures are qualitatively similar to those listed in references 660 and 685, but differ quantitatively.

[c] ROTs/ROBs rate ratio assumed to be 0.32.

[d] ROTs/ROBs rate ratio assumed to be 0.28.

[e] σ^* for *p*-anisyl-CH_2 taken as $+0.12$.

of 1-methyl-2-phenyl-2-butyl chloride in 80 per cent ethanol at 50°C. relative to *tert*-amyl chloride, 0.12 (565, 683), does not differ significantly from the value 0.15, the unassisted rate, which may be calculated from figure 22.

Some recent results of Huisgen (376a) are pertinent. The relative formolysis rates of benzcyclooctenyl-3,4,and 5 tosylates are, respectively, 602, 1080, and 1.0. The high rate of formolysis of the 3-tosylate is ascribed to conjugation with the benzene ring. The high rate of formolysis of the 4-tosylate is ascribed to phenyl group participation with the formation of a phenonium ion. The relative formolysis rates of benzcycloalkenyl-4 tosylates for different cycloalkenyl ring sizes are in the order $6 < 7 < 8$. As the ring size is increased, neighboring phenyl participation is sterically more feasible.

When the acetolysis of CXCII is stopped after one solvolytic half-life, the recovered tosylate is found to be pure but 94 per cent racemized. Recovered CXCI from an interrupted acetolysis is unchanged (173). Cram has demonstrated that the results are not due to a competition of tosylate ion with solvent for a free carbonium ion (external return) by running acetolyses of the corresponding brosylates in the presence of a tenfold excess of p-toluenesulfonic acid. The recovered sulfonates from the interrupted solvolyses were found in both cases to contain only relatively small amounts of the tosyl esters (173). These results provide evidence for the same type of internal return which was demonstrated for α,α-dimethylallyl chloride (page 658) and for *exo*-norbornyl brosylate (page 705). By analogy with the other phenomena of internal return, in acetic acid the first intermediate is the "ion-pair" CIC, which can either revert back to starting material or solvolyze.

CIC
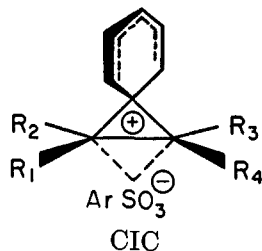
When the starting material is CXCII, the "phenonium" (173) intermediate, CIC ($R_1 = R_4 = CH_3$; $R_2 = R_3 = H$), is *meso*. CXCII regenerated from this intermediate is racemic. The results have been confirmed by kinetic analysis by Winstein and Schreiber (688), who were able to discard a number of alternative hypotheses.
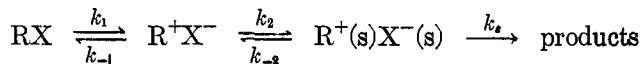
Comparison of the titrimetric and polarimetric rate constants for solvolysis of CXCII yields the following values of k_{-1}/k_s (page 661) for various solvents: ethanol, 1.11 at 75°C; acetic acid, 3.6 at 50°C.; formic acid, 0.2 at 25°C. (688). Compared to acetic acid, internal return is less, as expected, in the more nucleophilic ethanol and in the more highly ionizing formic acid.

The intermediate phenonium ion has been formulated as CC, and has been described in terms of the resonance structures CCIa, b, and c (171).

CC

CCIa   CCIb   CCIc
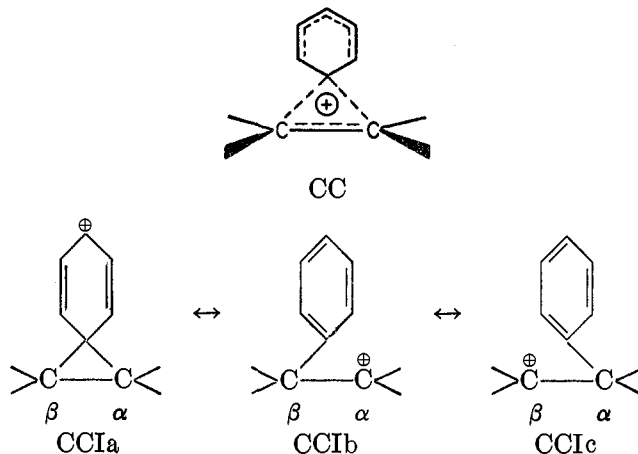
The contribution of structure CCIa indicates that electron-donating substituents on the benzene ring should stabilize the intermediate and provide greater rate enhancement. 3-p-Anisyl-2-butyl brosylate shows an acetolysis rate 130-fold in excess of that expected in the absence of participation (table 55).

Addition of lithium perchlorate to the solvolysis system of CXCII in acetic acid causes a linear increase in the rate, explicable as a normal salt effect phenomenon (665). In the acetolysis of either *erythro-* or *threo-*3-p-anisyl-2-butyl brosylate, addition of small amounts of lithium perchlorate causes a rather large increase in the rate, although larger quantities of lithium perchlorate produce only the small additional rate increase characteristic of the normal salt effect (545, 665). This result has been interpreted by an extension of the ion-pair concept in the reaction sequence (663a):

$$\text{RX} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \text{R}^+\text{X}^- \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} \text{R}^+(s)\text{X}^-(s) \overset{k_s}{\longrightarrow} \text{products}$$

In this sequence R^+X^- represents the type of ion-pair as in CIC, which has been called an "internal" or "intimate" ion-pair. $R^+(s)X^-(s)$ represents the type of ion-pair frequently encountered in inorganic solution chemistry, a pair of solvated ions of opposite charge held together by coulombic attraction, and has been called an "external," "loose", or "solvent-separated" ion-pair. Lithium perchlorate is thought to act as an efficient trap for "external" ion-pairs by way of a rapid and irreversible ion-pair–ion-pair reaction:

$$\text{R}^+(s)\text{X}^-(s) + \text{Li}^+(s)\text{ClO}_4^-(s) \rightarrow \text{R}^+(s)\text{ClO}_4^-(s) + \text{Li}^+(s)\text{X}^-(s)$$
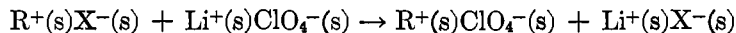
Formation of $R^+(s)\text{ClO}_4^-(s)$, which leads to the final solvolysis products, prevents the return step, k_{-2}, and results in a higher overall rate (545).

The mechanism requires that reaction of the intermediates with solvent to yield solvolysis products be slow compared to the interconversion of the intermediates in order for the unusual salt effects to be observed. This requirement is met only with relatively stable carbonium-ion intermediates. Apparently the

intermediates from CXCII are too unstable for "solvent-separated" ion-pair formation to be significant, although such stability is obtained with the corresponding anisyl compounds. The concepts involved in this interpretation and the techniques which led to them will doubtless be of great significance in organic chemistry. However, complete experimental details are not yet available and many corollaries are still being explored.

Many of the kinetic and stereochemical results observed in the solvolyses of CXCI and CXCII have been reproduced in the 4-phenyl-3-hexyl tosylate system (180). The closely similar results in the 2-phenyl-3-pentyl and 3-phenyl-2-pentyl series provide an additional feature in that rearrangement in these systems is not merely a deduction from stereochemical observations but is accompanied by a structural isomerization (172, 176).
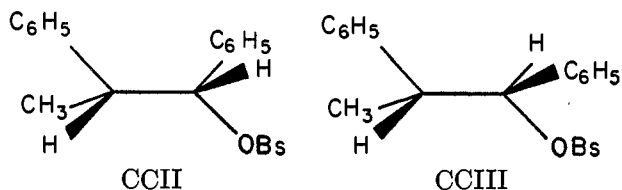
ii. Phenylpropyl and diphenylpropyl systems

Neighboring phenyl participation and internal return have also been demonstrated in the isomeric 1-phenyl-2-propyl and 2-phenyl-1-propyl systems. Acetolysis of 2-phenyl-1-propyl brosylate is accompanied by rearrangement to 1-phenyl-2-propyl brosylate (689). The rate of the rearrangement is independent of the amount of external p-bromobenzenesulfonate ion present; hence the rearrangement is intramolecular. The results are consistent with the chemistry of the supposed intermediate, CIC ($R_1 = R_2 = R_3 = H$; $R_4 = CH_3$).

Kinetic study (689) indicates that internal return is unimportant in ethanol (high nucleophilicity) and in formic acid (high ionizing power). The ethanolysis rate shows no appreciable enhancement when compared with the sterically similar isobutyl tosylate after correction is made for the greater reactivity of brosylate esters (682, 689). In acetic acid the rate enhancement over the expected rate in the absence of participation seems to be small. In formic acid the rate of ethanolysis of 2-phenyl-1-propyl brosylate is $\sim$15 times faster than that of ethyl brosylate (682, 689). Participation exerts an appreciable driving force in this case. The acetolysis rate of 2-p-anisyl-1-propyl brosylate is 112 times the rate of the unsubstituted compound (682). Introduction of the p-methoxy group greatly increases the driving force for participation.

In agreement with the general theory of the effect of substitution on participation driving force, the primary phenyl group in 1-phenyl-2-propyl brosylate produces a smaller enhancement of the acetolysis rate (twofold) and less of a tendency towards participation than the secondary phenyl group in 3-phenyl-2-butyl brosylate (fourfold) in which the driving force for such participation, although rather small, produces the familiar stereochemical consequences (table 55). A structural rearrangement in the 1-phenyl-2-propyl system has not been observed. Ethanolysis of the tosylate yields the corresponding ethyl ether with complete *inversion* of configuration (504). Acetolysis yields the unrearranged 1-phenyl-2-propyl acetate with 29 per cent inversion and 71 per cent racemization (660). These results are directly comparable with the solvolysis stereochemistry of ordinary secondary carbinyl systems in the absence of neighboring group participation (page 632). In formic acid, however, the formate is

obtained with as much as 70 per cent net *retention* of configuration (660). This result is difficult to explain in any other reasonable manner but that neighboring phenyl interaction occurs to give some sort of bridged-ion intermediate with inversion, followed by reaction with solvent with a second inversion. In the poorly nucleophilic, highly dielectric formic acid, nucleophilic participation by the neighboring phenyl group competes very well with participation by solvent at the rear.

Replacement of the α-methyl group in CXCI and CXCII by a benzene ring should be equivalent in effect to increasing the substitution at the α-position. The electron-deficient intermediate which would arise from normal solvolysis of *erythro-* and *threo*-1,2-diphenyl-1-propyl tosylates (CCII and CCIII, respec-

tively) would be of the benzyl cation type and would be more stable than the analogous intermediates from CXCI and CXCII. Hence the system has less to gain from neighboring phenyl participation and the driving force for such participation is expected to be smaller. Since the driving force is relatively small even for CXCI and CXCII (table 55), it is not surprising that the formation of bridged-ion intermediates is almost absent in some solvolyses of CCII and CCIII. Acetolysis and formolysis of CCII and CCIII give mixtures of the *erythro-* and *threo*-1,2-diphenyl-1-propyl acetates. The mixtures are different for the two isomers and do not correspond to the equilibrium mixture (229). If reaction occurred exclusively through bridged-ions, an overall retention of configuration would be expected. If reaction occurred exclusively through "normal" carbonium ions, closely similar product mixtures would be expected from both isomers. The observed results are consistent with the simultaneous operation of both modes of reaction.

On the other hand, in the structurally isomeric 1,1-diphenyl-2-propyl system, phenyl group participation is pronounced. The rate enhancement shown by the acetolysis of the brosylate, 57-fold, is rather large (table 55). The stereochemical results of Cram and Elhafez (181) are completely consistent with such participation.

iii. Phenylethyl, diphenylethyl, and triphenylethyl systems

Using figure 23 as a calibration curve, β-phenylethyl tosylate (CCIV) may be calculated to solvolyze in ethanol at 100°C. in the absence of anchimeric assistance at a rate 0.58 that of *n*-propyl tosylate. The observed relative rate at 75°C. is 0.40 (410, 679). Similarly, the calculated and observed relative rates for β-*o*-anisylethyl tosylate (CCV) and β-*p*-anisylethyl tosylate (CCVI) are,

respectively, 0.72, 0.47 and 0.69, 0.77. There does not seem to be any significant rate enhancement.

As the solvent is made less nucleophilic and more ionizing, the nucleophilic contribution of the aryl group becomes more important. The relative rates at 75°C. in ethanol, acetic acid, and formic acid are, respectively: ethyl tosylate: 1, 0.026, 0.64; CCIV: 1, 0.041, 5.3; CCV: 1, 0.83, 212; CCVI: 1, 0.62, 132 (679). Winstein, Lindegren, Marshall, and Ingraham (679) have interpreted these data to mean that β-aryl participation occurs in formic acid and probably also in acetic acid. In formic acid, for example, the relative rates of ethyl tosylate, CCIV, CCV, and CCVI at 75°C. are, respectively, 1, 2, 93, and 94 (679). Calibration curves such as that for ethanol (figure 21) are not available for primary systems in acetic acid and in formic acid and the participation driving forces in these systems cannot be quantitatively evaluated. The rate-retarding factor of 10 for each phenyl group used by Winstein (679) to estimate the unassisted solvolysis rates is probably high. The high relative rates of the anisyl compounds, however, are certainly indicative of substantial anchimeric assistance.

Unfortunately, these conclusions have not yet been confirmed by stereochemical or isotopic tracer studies. The only related experiments are the C^{14} results of Lee and Spinks (413), who showed that some phenyl group migration occurs when β-phenylethanol is treated with hydrobromic or hydriodic acid and of Roberts and Regan (537), who demonstrated partial rearrangement in the reaction of β-phenylethylamine with nitrous acid. Nevertheless, in the acetolysis of β-2,4-dimethoxyphenylethyl brosylate, there would seem little question but that a bridged-ion *intermediate* of relatively great stability is involved. This system manifests the unusual salt effects of "internal" and "external" ion-pairs characteristic of other relatively stable carbonium ions (page 720) (665).

In solvolyses of β,β-diphenylethyl tosylate (CCVII) phenyl group participation is clearly important. Despite the inductively electron-attracting effect of two phenyl groups, CCVII acetylizes 4.5-fold *faster* than ethyl tosylate at 100°C. (682, 685). The acetolysis product is stilbene, which must arise from a rearrangement (137, 685). Burr (137) has investigated the acetolysis of β-phenyl-β-p-tolylethyl tosylate by C^{14} tracer techniques and has established that tolyl migration occurs about three times as readily as phenyl migration. It is interesting that hydrogen participation apparently does not take place, even though such migration would yield the relatively stable α-methylbenzhydryl cation.

The acetolysis of β,β,β-triphenylethyl tosylate is 4000 times faster than that of neopentyl tosylate (685). The rate ratio of the corresponding chlorides in formic acid is 60,000 (144a). The high relative rate is reasonably attributable only to anchimeric assistance by a neighboring phenyl group. Nevertheless, in both this case and for CCVII, there is no compelling evidence that the bridged-ion structures formed by such participation are *intermediates* rather than *transition states*. These systems have much to gain by rearrangement, for relatively stable cations of the benzhydryl and benzyl type, respectively, result from phenyl group migration.

By analogy with similar systems previously discussed, the driving force for

phenyl participation in the acetolysis of α,β,β-triphenylethyl tosylate is expected to be rather small. Collins and Bonner (94, 156) have shown by C^{14} tracer techniques that phenyl group rearrangement is incomplete in the solvolyses of this compound in aqueous acetone and in acetic acid. They compared the extents of rearrangement of aliphatic C^{14} label with the rearrangement of ring-labeled phenyl groups under the same conditions and were able to account for their results wholly on the basis of "classical" carbonium ions (95, 156). The bridged phenonium ion does not have appreciably greater stability in this system than the "normal" solvolysis intermediates. Kinetic data have not been reported for this system; no rate enhancement is expected. Similar isotope labeling experiments with the acid-catalyzed rearrangement in acetic acid of 1,2,2-triphenylethyl acetate demonstrated the equality of the rates of radiochemical equilibration of ring-labeled and chain-labeled acetate and the loss of the labeled acetoxyl group (95). The results can be explained rather simply on the basis that "classical" carbonium ions are formed of sufficient stability that subsequent rearrangement steps are much faster than the reaction of the carbonium ion with solvent.
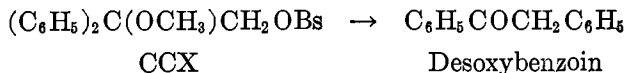
iv. Other systems

The acetolysis of 2-phenyl-2-methyl-1-propyl tosylate is 460 times faster at 50°C. than that of neopentyl tosylate (685). The relatively high reactivity is probably due to anchimeric assistance.

Because of the relatively high stabilities of ordinary tertiary carbonium ions, phenyl participation in solvolyses of tertiary systems is not expected to possess an appreciable driving force. Acetolysis and formolysis of the optically active diastereoisomers of 4-phenyl-3,4-dimethyl-3-hexyl p-bromobenzoate (CCIX) produced a mixture of partially racemic or racemic olefins (182). The product mixture was complex but corresponded to relatively limited phenyl rearrangement which was only partially stereospecific.
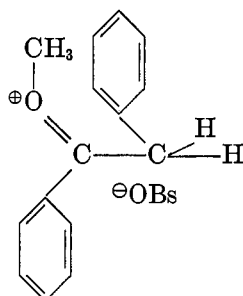
$$p\text{-BrC}_6\text{H}_4\text{COO}$$
$$\mathrm{CH_3\,CH_2(CH_3)\,C\!\!-\!\!C(CH_3)\,CH_2\,CH_3}$$
$$\mathrm{C_6H_5}$$
$$\text{CCIX}$$
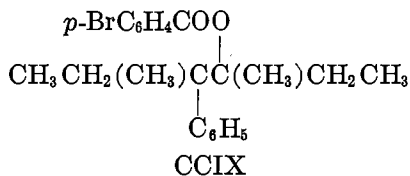
Solvolysis of 2-methoxy-2,2-diphenylethyl brosylate (CCX) in aqueous dioxane yields desoxybenzoin (679). The acetolysis of CCX is 160 times faster

$$(\mathrm{C_6H_5})_2\mathrm{C(OCH_3)\,CH_2\,OBs} \quad \rightarrow \quad \mathrm{C_6H_5\,COCH_2\,C_6H_5}$$
$$\text{CCX} \qquad\qquad\qquad \text{Desoxybenzoin}$$

than that of neopentyl brosylate at 75°C. despite the inductive electron attraction of two phenyl groups and an oxygen in CCX (679). The presence of the β-oxygen function provides substantial driving force for phenyl participation,

undoubtedly because of the contribution of structures such as CCXI in the first transition state.

$$
\begin{array}{c}
\text{CH}_3 \\
| \\
\overset{\oplus}{\text{O}} \\
\diagdown \\
\text{C}\text{---}\text{C}\overset{\text{H}}{\diagup}\text{---}\text{H} \\
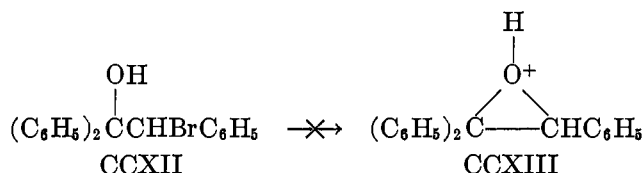\diagup \quad \ominus\text{OBs}
\end{array}
$$

CCXI

The acetolysis of 2-methoxy-2-phenylethyl brosylate is 3.5 times as fast as that of neopentyl brosylate (679). Since the unassisted rate would undoubtedly be much lower because of inductive effects, the observed rate corresponds to a significant driving force for participation. A number of solvolyses of 2-methoxy-2-phenylethyl iodide yield phenylacetaldehyde derivatives, the products of phenyl group rearrangement (677).

The silver-ion- or mercuric-ion-catalyzed solvolysis of 1,1,2-triphenyl-2-bromoethanol (CCXII) in aqueous dioxane yields phenyl benzhydryl ketone. In the absence of the Lewis acid catalysts, mixtures of the ketone with 1,1,2-triphenylethylene glycol result (407). In the ordinary aqueous solvolysis of CCXII, unassisted solvolysis and phenyl-assisted solvolysis are apparently competitive. Under more limiting conditions (the reactions catalyzed by Lewis acids) the product of phenyl participation predominates, completely in accord with theoretical expectations.

From the results of a kinetic and product study of the solvolyses of CCXII, Lane and Walters (408) concluded that the glycol product resulted from a normal, unassisted solvolysis and not by way of the hydroxyl-bridged intermediate (CCXIII). Since hydroxyl groups show little driving force for participation (page 684), the fact that CCXIII does not form in this system is not surprising.

$$
\begin{array}{ccc}
\text{OH} & & \overset{\text{H}}{\underset{|}{\text{O}^+}} \\
| & & \diagup \diagdown \\
(\text{C}_6\text{H}_5)_2\text{CCHBrC}_6\text{H}_5 & \rightarrow\!\!\!\times\!\!\!\leftarrow & (\text{C}_6\text{H}_5)_2\text{C}\text{---}\text{CHC}_6\text{H}_5 \\
\text{CCXII} & & \text{CCXIII}
\end{array}
$$

(b) Neighboring double bond

The solvolysis of allylcarbinyl chloride in 50 per cent aqueous ethanol at 100°C. is about one-fourth as rapid as that of n-propyl chloride (535, 636). The ethanolysis of allylcarbinyl benzenesulfonate at 55°C. is one-half as rapid as that of n-butyl benzenesulfonate (83, 410). Participation by the neighboring

β-vinyl group in these systems apparently does not occur. On the other hand, the treatment of 5-chloro-2-methyl-2-pentene with water yields dimethyl-cyclopropylcarbinol (129a, 250a). A structure such as CCXIV, which has tertiary carbonium ion character in part, is probably involved in the reaction.
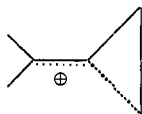
CCXIV

Simonetta and Winstein (574a) have indicated, on the basis of molecular orbital calculations, that orbital interaction between the double bond and the developing p orbital of the reacting center as in figure 28 can provide significant stabilization of the positive center.
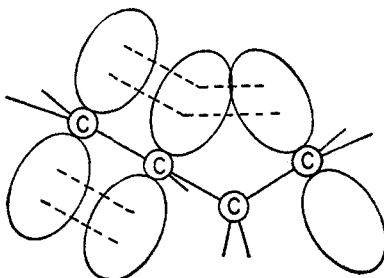
FIG. 28. Orbital representation of homoallylic resonance

i. Cholesteryl systems

Although solvolytic reactions of cholestanyl chloride (CCXV) are accompanied by a normal predominance of configurational inversion, the corresponding reactions of cholesteryl chloride (CCXVI) proceed with complete retention; Shoppee (566) suggested that participation by the double bond is important in the latter case.
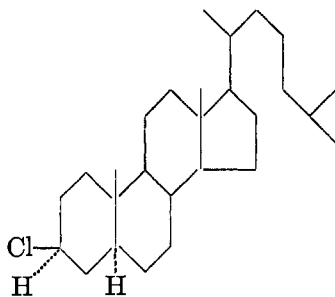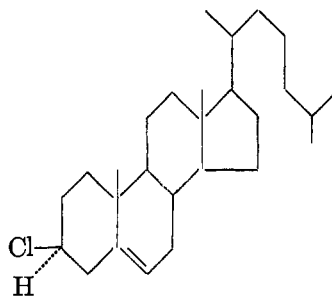
CCXV   CCXVI

Consistent with the postulate of anchimeric assistance by the double bond are the rate enhancements observed. Cholesteryl bromide is 79 times as reactive as

isopropyl bromide in acetic acid at 100°C. (149, 190); cholesteryl tosylate is 119 times as reactive as cyclohexyl tosylate in acetic acid at 50°C. (658).

The product of the solvolysis of cholesteryl tosylate in methanol containing potassium acetate is the *i*-ether, CCXVII (R = OCH₃) (see reference 658 for earlier references). Winstein and Adams (658) have pointed out that this result is not due to an unusual nucleophilic attack in the rate-determining step because
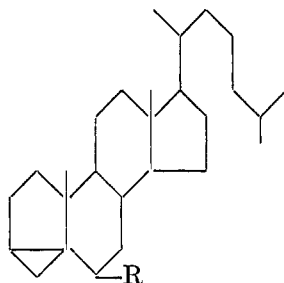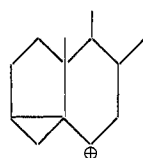

CCXVII

the solvolysis rates of cholesteryl tosylate in ethanol and in acetic acid are about equal. Furthermore, the solvolysis rate of cholesteryl tosylate in methanol is not appreciably affected by the presence of methoxide ion (567).
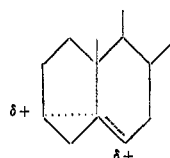
The observed rate enhancement indicates that something more is involved than a simple ionization to CCXVIII. The direct formation of the cation (CCXIX) is probably not involved, for the positive center is conjugated with a three-membered ring (page 710). The most satisfactory hypothesis is that a
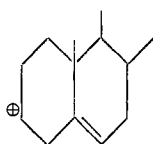

CCXVIII   CCXIX   CCXX

hybrid ion (CCXX) is formed directly. CCXX is completely analogous to structure CLXXIIIb, which was used to explain the high reactivities of cyclopropylcarbinyl systems. The *i*-chloride, CCXVII (R = Cl), is about 10^8 times more reactive than cholesteryl chloride (CCXVI) in aqueous dioxane (401a).

The bond conformations in the cholesteryl system are such that the formation of CCXX probably involves relatively little strain or realignment of atoms. The system of cholesteryl tosylate in acetic acid is one for which the unusual salt effects have been observed (664), indicative of relatively stable carbonium intermediates and of "internal" and "external" "ion-pairs."

The methanolysis of cholesteryl tosylate at 35°C. is seven times faster than that of its epimer, epicholesteryl tosylate (CCXXI) (393a). A comparable rate ratio is observed in acetic acid (568). The rates of CCXXI correspond to an appreciable rate enhancement; however, the geometry of the system does not permit neighboring double bond participation. Furthermore, the solvolysis

products of the two epimers differ completely; CCXXI does not yield any
i-cholesteryl derivatives such as CCXVII, but instead gives large amounts of
3,5-cholestadiene (CCXXII) (393a, 568). The rate enhancement of CCXXI
and the formation of CCXXII rather than the ion (CCXX) strongly suggest
participation by the 4-H. This explanation is made plausible by the axial hydro-
gen migrations observed with other axial leaving groups in cyclohexyl systems
(page 715) and by the fact that a presumably activated allylic hydrogen is
involved in CCXXI. However, there is apparently some question about the
structure of CCXXl (401a).
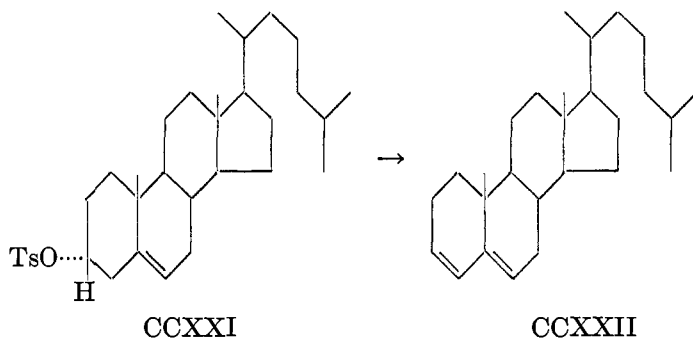
CCXXI   CCXXII

ii. Bicyclo[2.2.1]heptyl systems

The acetolysis of *exo*-norbornenyl brosylate (CCXXIII) at 25°C. is reported
to be 7000 times faster than that of the *endo* isomer (CCXXIV) (694). The
reactivities of the corresponding chlorides in 80 per cent ethanol at 85°C. are
>150 (529, 530). Neighboring double bond participation at the backside is
geometrically favored in CCXXIII but not in CCXXIV.
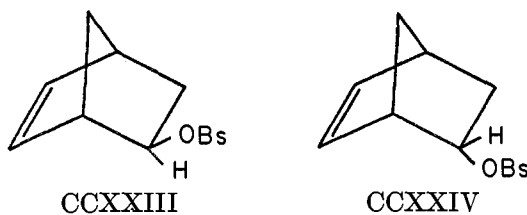
CCXXIII   CCXXIV

The acetolysis products of both CCXXIII and CCXXIV are predominantly
3-acetoxynortricyclene (CCXXV) with lesser amounts of *exo*-norbornenyl ace-
tate. Experiments with C^{14}-labeled CCXXIII and CCXXIV demonstrated
partial but not complete rearrangement in acetic acid consistent with the postu-
lated formation of the intermediate cation (CCXXVIa) and a subsequent re-
arrangement to CCXXVIb, similar to the corresponding rearrangement in the
norbornyl series (page 704) (534), but different in that the amount of rearrange-
ment is less than 50 per cent; hence, this case serves as an example of a neces-
sarily unsymmetrical ion which could have become symmetrical with only a

slight rearrangement of atoms. In formic acid the rearrangement is substantially complete.

CCXXV   CCXXVIa   CCXXVIb
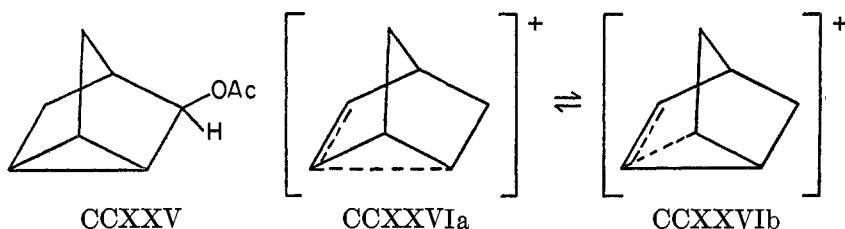
Anchimeric assistance by a neighboring double bond with an amazing amount of rate acceleration was recently described in the case of *anti*-7-norbornenyl tosylate (CCXXVII). The acetolysis of CCXXVII is faster than that of 7-norbornyl tosylate (CCXXVIII) by a factor of 10^{11} (690a, 690b). CCXXVII reacts

CCXXVII   CCXXVIII
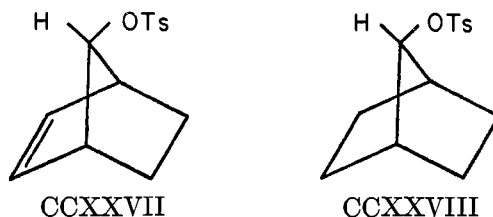
with complete retention of configuration with the formation of *anti*-7-norbornenyl derivatives. The geometry of the system is apparently ideal for overlap of the π-electrons of the double bond with the developing p orbital of the reacting carbon.

Both 7-chloronorbornane and *syn*-7-chloronorbornene have been previously described as "exceptionally unreactive" in 80 per cent aqueous ethanol (532a). Hence the high reactivity of CCXXVII must be due to the *trans*-orientation of the double bond.

VI. Related Reactions

In addition to the set of reactions included in this review are a number of closely related reactions. Many of the concepts developed in the study of solvolytic displacement reactions apply to these related reactions and, in fact, find support in some observations which pertain to the related reactions. A few of the pertinent developments in some of these related reactions will be discussed in this section insofar as they relate to solvolytic concepts.

A. ALKYLATION OF AROMATIC SYSTEMS

The Lewis-acid-catalyzed alkylation of aromatic systems with alkyl halides may be regarded as a type of solvolysis reaction. A characteristic feature of most alkylation reactions is the relatively low nucleophilicity of the leaving group and of the aromatic attacking group. Consequently, other modes of reaction of the intermediates involved, such as hydrogen or alkyl group rearrangements, cleav-

age or polymerization reactions, and eliminations, are frequently faster than the reaction of the electron-deficient intermediates with the aromatic ring. The relative rates of such side reactions compared to the alkylation reaction itself may be expected to vary in a predictable way and to depend on the catalytic power of the Lewis acid, the nucleophilicity of the aromatic system, and the ability of the central carbon system to distribute positive charge.
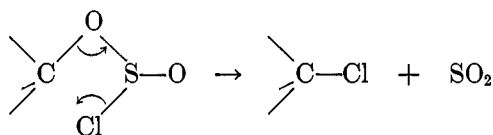
The reaction of 3,4-dichlorobenzyl chloride with benzene and aluminum chloride in nitrobenzene solution has been found to follow third-order kinetics, first order in each of the reactants (121). Brown and Grayson (121) have suggested nucleophilic attack by benzene on the alkyl halide–aluminum chloride complex. The system seems rather analogous to Swain's methanolysis of triphenylmethyl chloride in benzene (page 634 and 649) (597).

Early objections (500) to the use of carbonium-ion intermediates in alkylation reactions on the grounds that the solvents of low dielectric constant generally used for such reactions could not sustain, electrostatically, the generation of ions clearly do not apply to ion-pair intermediates.

An important bridge between ordinary solvolytic reactions and Friedel–Crafts alkylations is the uncatalyzed alkylation of phenols shown by a number of alkyl halides. The reaction of phenol with triphenylmethyl chloride in an inert solvent yields the p-alkylated phenol and can be catalyzed by hydrogen chloride (309). Alkylation of phenols by α-phenylethyl chloride may be similarly accomplished to give ortho or para substitution or a mixture depending on the structure of the phenol used. Substitution in the para position occurs with a small amount of net inversion of configuration, a result which is normally obtained in solvolytic reactions. Ortho substitution, however, is accompanied by a small amount of net *retention* of configuration. This result has been interpreted as an $S_N i$ reaction (311), but like most reactions in solution which have been called $S_N i$, this example could also be explained as a consequence of internal return. The explanation is plausible for a system which contains only poorly nucleophilic species.

B. CHLOROSULFITES AND CHLOROCARBONATES

Alkyl chlorosulfites, which are formed by the reaction of alcohols with thionyl chloride, readily lose sulfur dioxide to form the corresponding alkyl chlorides. In the presence of chloride ion or tertiary amines which can react with the chlorosulfite to liberate chloride ion, a direct displacement by the chloride ion can occur to yield inverted product (97, 168). In an inert solvent, systems which contain an α-phenyl group readily produce the alkyl chloride with a *retention* of configuration. This result has been interpreted by an "$S_N i$" mechanism (168):

$$\underset{Cl}{\overset{O}{\underset{\diagdown}{\overset{\diagup}{C}}}}\ \diagdown C \diagdown \overset{O}{\underset{\diagdown}{S}}{-}O \ \rightarrow \ \diagdown C{-}Cl \ + \ SO_2$$

The authors of this mechanism have never made clear whether the central

carbon atom is expected to be planar, as in a carbonium ion, or non-planar; e.g., with a transition state such as CCXXIX.
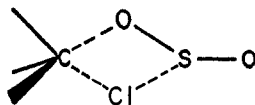

CCXXIX

If CCXXIX were involved in the reaction, it is difficult to see why the tendency to give chloride of retained configuration as the structure is varied should parallel the ability of the system to form carbonium ions.

In solvolytic reactions, the OSOCl group behaves like a normal, if somewhat reactive, leaving group. Acetolysis of optically active 2-octyl chlorosulfite, for example, produces 2-octyl acetate with a predominant inversion of configuration (594). Boozer and Lewis (97, 422) have shown that the stereochemistry of the decomposition of secondary carbinyl chlorosulfites to form chlorides is strongly solvent-dependent. They found that a predominant retention of configuration occurred in relatively basic but inert solvents of low dielectric constant (e.g., dioxane). Many other solvents caused a predominant inversion of configuration. They showed further that the reaction rates in *both* types of solvents showed the same type of isotope effect as solvolytic reactions (page 670) when β-hydrogens were substituted by deuterium. The stereochemical and isotope results were interpreted in terms of an ionization to an ion-pair in the manner of typical solvolytic reactions. The anionic part of the ion pair, $^-$OSOCl, plausibly decomposes to sulfur dioxide and chloride ion. Many of the results can then be explained on the basis of an "internal return" of the chloride ion to give the alkyl halide with retention of configuration (97). Consistent with this interpretation, retention of configuration is less important in the primary case (594).

Cram (177) has also postulated that the intermediates involved are of the carbonium ion–ion-pair type. He found that *threo*-2-phenyl-3-butanol reacts with thionyl chloride to produce racemic alkyl chloride, although no racemization occurs with the *erythro* isomer. In these cases, bridged-ion pairs (CCXXX) are presumably involved.
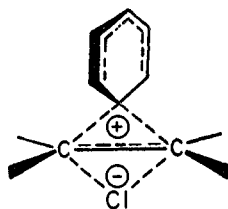
CCXXX

The decomposition of chloroformate esters, ROOCCl, occurs in a manner similar to that of the chlorosulfite esters, with formation of alkyl chloride and

carbon dioxide. More vigorous conditions are generally required than for the corresponding chlorosulfite decompositions. The thermal decomposition of 2-octyl chlorocarbonate (345) or α-phenylethyl chlorocarbonate (653), either alone or in an inert solvent, produces the corresponding chloride with retention of configuration. In the latter case, electron-releasing substituents on the benzene ring strongly accelerate the reaction rate. Production of intermediates of the carbonium-ion type is indicated (653). With a large excess of tertiary amine, inversion of configuration occurs (346), presumably the result of displacement by chloride ion generated by the reaction:

$$ROCOCl + R_3'N \rightarrow ROCO\overset{+}{N}R_3' + Cl^-$$
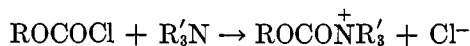
### C. REACTIONS OF CARBINOLS WITH ACIDS

Many of the acid-catalyzed reactions of alcohols and ethers may be regarded as solvolytic displacements in which the leaving group is water or an alcohol, respectively. Recent kinetic experiments on the acid-catalyzed elimination of water from *tert*-butyl alcohol and the oxygen exchange with O^{18}-labeled water are consistent with a common carbonium-ion intermediate (223). The rate of racemization of 2-butanol is twice the rate of O^{18} exchange in the reaction with heavy water containing perchloric acid (132). The result implies that each substitution is accompanied by inversion of configuration:

$$H_2O^{18} + (+)-CH_3CH_2CHOHCH_3 \rightarrow (-)-CH_3CH_2CHO^{18}HCH_3 + H_2O$$
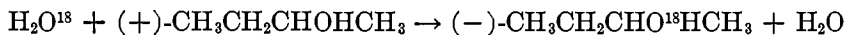
Over a limited range of acidity, the rate is found to be linear in the acidity function, H_0. In common with many reactions which follow H_0 rather than the acid concentration, the result has been taken to mean that water is not involved in a rearward attack at the transition state (132); however, it is not at all certain that the usual interpretation of H_0 extends to systems in which the bond strength of the carbon–solvent bond is as low as it presumably is at the transition state in this system.

p-Anisylcamphenilol (CCXXXI) on solution in either formic acid or concentrated hydrochloric acid yields the intensely colored intermediate carbonium ion, presumably CCXXXII, and eventually the formate or hydrochloride of 1-anisylapoisoborneol (CCXXXIII). The build-up of the colored intermediate and its subsequent reaction to form the product are amenable to precise kinetic treatment (42a).


CCXXXI   CCXXXII

OCH₃

CCXXXIII
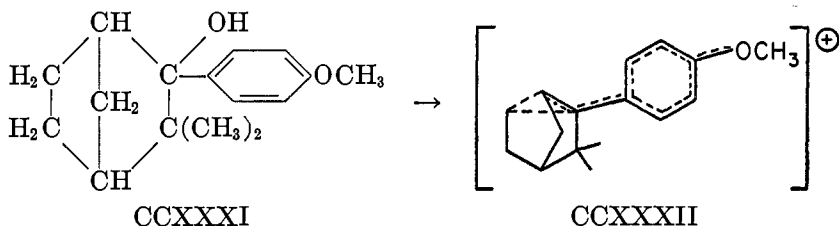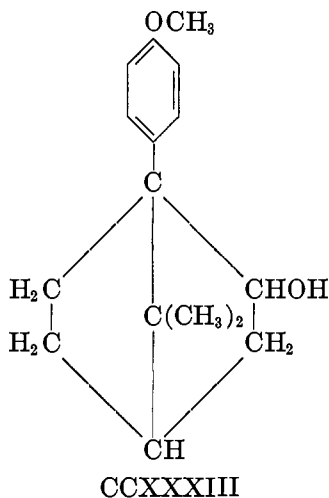
Acid-catalyzed isomerizations of allylic alcohols have been recognized in which a partial net retention of configuration occurs. Examples are the isomerizations of 2-hexen-4-ol to 3-hexen-2-ol (3) and of 1-phenyl-2-buten-1-ol to 1-phenyl-1-buten-3-ol (388). The results may be explained by an isomerization of the oxonium salt to a structure similar to the "ion-pairs" suggested in solvolytic reactions of allylic systems (page 659). Internal return with rearrangement will accommodate the stereochemical results. In these cases the intermediates are not ion-pairs, for no charge separation is involved.

D. SIMULTANEOUS DOUBLE REARRANGEMENTS

The rearrangement of *trans*-9-decalyl perbenzoate (CCXXXIV) to a mixture of products which includes benzoic acid, the benzoate ester (CCXXXV), and the bicyclic oxo-compound (CCXXXVI) is unimolecular and intramolecular (45a, 278a).

OCOC₆H₅   O—COC₆H₅

→   + , etc.

CCXXXIV   CCXXXV   CCXXXVI
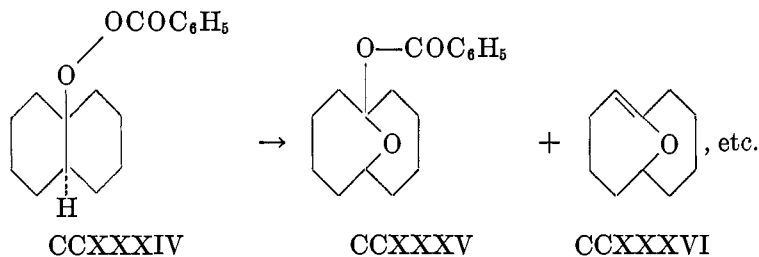
Electron-attracting substituents in the benzene ring (45a) and solvents of higher ionizing power (278a) promote the rate of the reaction. The ion-pair CCXXXVII has been suggested as an intermediate (278a; see also 45a). Denney (200a) followed the reaction with the carbonyl group of CCXXXIV labeled with O^{18}. All of the labeled oxygen remained in the carbonyl group of the product (CXXXV). Hence, neither structure CCXXXVII nor any structure in which

the carbonyl oxygen and another oxygen become equivalent can be involved. A consistent interpretation involves structure CCXXXVIII as a transition state or intermediate (200a).

CCXXXVII   CCXXXVIII
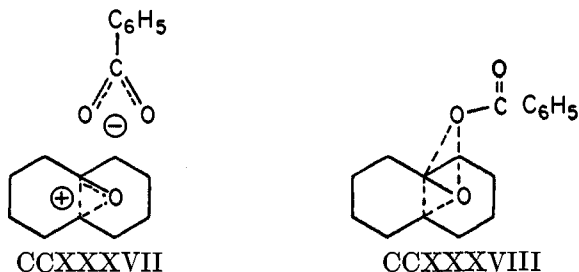
A similar type of structure is apparently involved in the intramolecular isomerization of $5\alpha,5\beta$-dibromocholestane (CCXXXIX) to the stable $5\beta,6\alpha$-isomer (CCXL) (293). The relatively rapid rate of the isomerization in heptane solution and the low dependency of the rate on the dielectric constant or ionizing power of the solvent indicate that the transition state possesses only slight charge separation (293).

CCXXXIX

CCXL
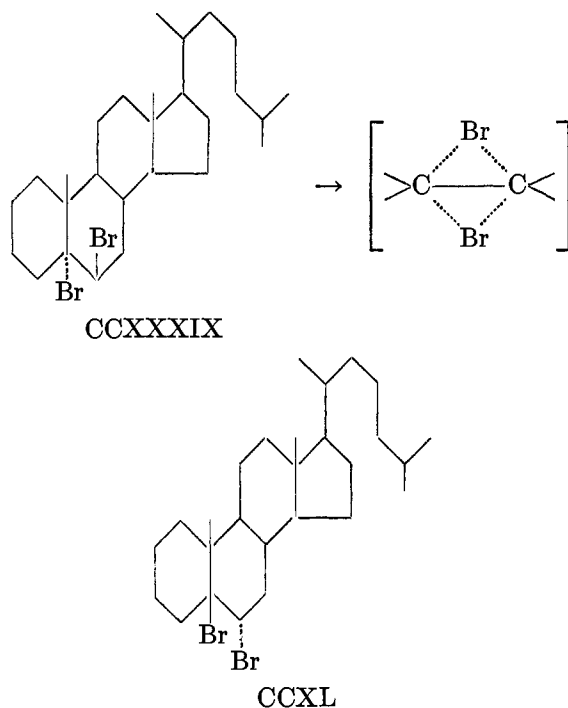
Noyce and Weingarten (479) have recently found that one of the chief products resulting from the treatment of cis-3-methoxycyclohexanecarboxylic acid with acetic anhydride and sulfuric acid is methyl trans-4-acetoxycyclohexanecar-

boxylate. The rearrangement was shown to be intramolecular and is formulated as proceeding through structure CCXLI as a transition state or intermediate.

CCXLI
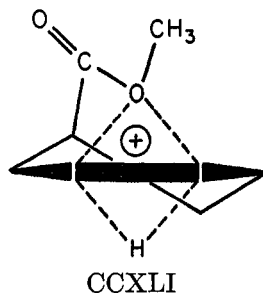
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