periodic acid,[32] and this yield was used with relative g.c. responses to estimate the yield of 1,4-diol. The product composition data are summarized in Tables I and II. The average of the total yields of identified products in each solvolysis is 89%, the median being 91%. The lowest total yield (79%) was from chlorohydrin without silver nitrate, and the highest (96%) was from chlorohydrin with silver nitrate.

When 2- and 3-cyclooctenol were subjected separately to the aqueous solvolysis conditions (75 ml. of THF–HOH solvent, 10 mmoles of cyclooctenol, 2 mmoles of $AgNO_3$, 10 mmoles of AgCl, and 10 mmoles of HNO_3; reflux for 4 hr.), each was recovered unchanged in about 95% yield. Other solvolysis products were not detected by g.c.

Kinetic Data. The rates of solvolysis of bromocyclooctane and *trans*-2-bromocyclooctanol in refluxing aqueous THF (2 THF–1 HOH, v./v.) were followed titrimetrically. Dilute solutions (approximately 0.01 *M*) were prepared by adding the required amount of bromide to refluxing solvent. Aliquots (5 ml.) were withdrawn periodically (1–2-hr. intervals) through a septum seal with a hypodermic syringe, and the product acid was titrated with 0.0025 *M* sodium hydroxide. Treated in a pseudo-first-order fashion (ln concentration *vs.* time), the data gave good linear plots from which rate constants were calculated. For bromocyclooctane, $k = 0.0570 \pm 0.0002$ hr.$^{-1}$ and for *trans*-2-bromocyclooctanol, $k = 0.0466 \pm 0.0016$ hr.$^{-1}$.

Rearrangements of cis-Cyclooctene Oxide. Solutions of *cis*-cyclooctene oxide in mixed aqueous and in 97–100% formic acid solvents were heated until the epoxide was all rearranged, and a solution in trifluoroacetic acid was stirred at 0° for 3 hr. Periodic g.c. analysis was used to follow disappearance of epoxide. One solution (50% acetic acid) contained silver nitrate and another sodium nitrate to permit evaluation of the effect of salts on epoxide solvolysis. The solutions were extracted with ethyl ether after appropriate dilution with water or saponification. Each extract was dried, the solvent was removed by rotary evaporation, and the product mixture was analyzed as were the mixtures from halohydrin solvolyses. *cis*-1,4-Diol, identified by melting point (84–84.5°, lit.[6a] m.p. 85–86.5°) and derivatives (bis-*p*-nitrobenzoate, m.p. 156.5–157.5°, lit.[6a] m.p. 161.5–162.7°, and bisphenylurethan, m.p. 182–183°, lit.[6a] m.p. 186.0–186.7°), was isolated directly from some of the mixtures; no evidence for *trans*-1,4-diol was obtained. Total yields of identified products averaged about 85%. Product distribution data are summarized in Table III.

Acknowledgment. We gratefully acknowledge helpful suggestions received from correspondence with Professor Paul E. Peterson, St. Louis University, and a lengthy discussion with Professor Saul Winstein, University of California at Los Angeles, about the results reported here.

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[32] S. Siggia, "Quantitative Organic Analysis *via* Functional Groups," 3rd Ed., John Wiley and Sons, Inc., New York, N. Y., 1963, p. 39.

Rates of Reaction of 4-Substituted Bicyclo[2.2.2]octylmethyl Tosylates with Sodium Thiophenolate. The Role of Polar Effects in the Displacement Reaction[1]

Hans D. Holtz[2] and Leon M. Stock

Contribution from the George Herbert Jones Laboratory of the University of Chicago, Chicago 37, Illinois. Received January 30, 1965

The reaction of sodium thiophenolate with 4-substituted 1-bicyclo[2.2.2]octylmethyl tosylates is second order and yields unrearranged phenyl thioethers. Relative rate data for the reaction in ethanol at 75° indicate that electron-withdrawing substituents accelerate this reaction. The influence of saturated dipolar substituents on the energy requirements for SN2 *reactions is discussed.*

Introduction

The influence of structure on the rate of SN2 reactions has received considerable attention and excellent discussions of the work in this area are available.[3–8] However, the role of saturated, dipolar substituents in these reactions remains uncertain. The interpretation of the available data is difficult because conflicting steric and resonance effects introduce serious ambiguities. Thus, saturated β-substituents slow the displacement reactions of aliphatic molecules. The major importance of steric effects is recognized, but opinions differ concerning the polar effect.[3–9] Steric effects are

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[1] Chemistry of the bicyclo[2.2.2]octanes, part IV. This research was supported by Grants G14211 and G25190 from the National Science Foundation.

[2] Esso Educational Foundation Fellow, 1961–1962; Union Carbide Corporation Fellow, 1962–1963.

[3] C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, pp. 316–338.

[4] A. Streitwieser, "Solvolytic Displacement Reactions," McGraw-Hill Book Co., Inc., New York, N. Y., 1962.

[5] J. Hine, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, pp. 169–178.

[6] C. A. Bunton, "Nucleophilic Substitution at Saturated Carbon," Elsevier Publishing Co., New York, N. Y., 1963, Chapter 2.

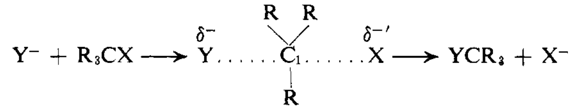
[7] F. G. Bordwell and W. T. Brannen, *J. Am. Chem. Soc.*, **86**, 4645 (1964).

[8] E. R. Thornton, "Solvolysis Mechanism," The Ronald Press, New York, N. Y., 1964.

[9] (a) C. K. Ingold, *Quart. Rev.* (London), **11**, 1 (1957); (b) J. Hine and W. H. Brader, *J. Am. Chem. Soc.*, **75**, 3964 (1953); (c) J. Hine and R. G. Ghirardelli, *J. Org. Chem.*, **23**, 1550 (1958); (d) E. T. McBee, R. D. Battershell, and H. F. Braendlin, *J. Am. Chem. Soc.*, **84**, 3157 (1962).

avoidable with *meta-* and *para*-substituted benzylic compounds.[10–13] However, substituents influence the S_N2 reactions of such substrates in a very complex manner.[12c] Hammett correlations fail. Often both the *p*-methyl and *p*-nitro derivatives react more rapidly than the unsubstituted compound.[10] Resonance interactions and the position of the reaction site adjacent to a π-system[14] complicate the interpretation in this case. These factors are unimportant with nuclear substituted β-phenylethyl substrates.[15–17] The rate data for the reaction of benzylamine at the benzylic and β-phenylethyl positions of styrene oxide offer a striking example of the distinct character of substituent effects at these two positions. The customary complex pattern is observed for reaction at the benzylic position. At the β-phenylethyl site, on the other hand, substituent effects are regular and electron-withdrawing groups accelerate the reaction as in other β-phenylethyl derivatives.[15,16]

The diverse experimental results have led to a diversity of emphasis in explanation. One proposal suggests that electron donor groups decrease the rate constants for S_N2 reactions.[3,9] This viewpoint stresses the importance of the developing negative charge in the transition state. Another suggestion is that the central carbon atom actually develops a positive charge in the reaction $(\delta^- + \delta^{-\prime} > 1.0)$ with the inverse polar effect.[4] A third idea is that the polar effect of the



$$Y^- + R_3CX \longrightarrow \overset{\delta^-}{Y}\cdots\cdots\overset{R\ \ R}{\underset{R}{C_1}}\cdots\cdots\overset{\delta^{-\prime}}{X} \longrightarrow YCR_3 + X^-$$

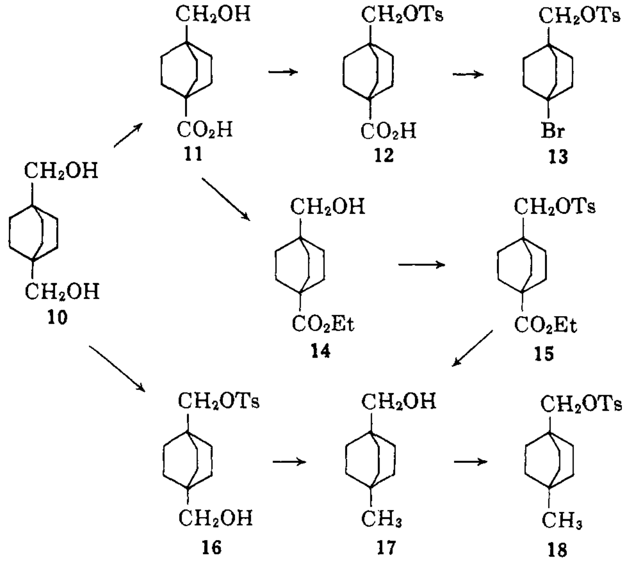
substituent is ambiguous because substituents alter the degree of bond making and bond breaking at the transition state.[8,10]

Study of a new aliphatic substrate in which the substituent could be isolated from the reaction site appeared necessary to define the role of polar effects in the S_N2 reaction with more confidence. The interposition of the rigid bicyclo[2.2.2]octane nucleus between the substituent and the reaction site was attractive for this purpose. The polar group is only 4 Å. from the reaction site in this compact structure. Accordingly, we prepared a series of 1-(4-substituted) bicyclo[2.2.2]octylmethyl tosylates and studied their reactivity.

Results

Preparation of Tosylates. 1-Carboethoxybicyclo-[2.2.2]oct-2-ene (**1**) was converted to 1-tosyloxymethylbicyclo[2.2.2]octane (**6**) by the known procedure.[18] The lithium aluminum hydride reduction of the ester **1** yielded the unsaturated alcohol **2** which was converted to 1-tosyloxymethylbicyclo[2.2.2]oct-2-ene (**3**). The same route was used for the synthesis of 1-chloro-4-tosyloxymethylbicyclo[2.2.2]octane (**9**) from 1-chloro-4-carboxybicyclo[2.2.2]octane (**7**).[19] Four tosylates were prepared from 1,4-di(hydroxymethyl)bicyclo[2.2.2]octane[19] (**10**) as outlined in Chart I.

Chart I



The brominative decarboxylation of **12** was accomplished by the method developed for the preparation of 1-bromobicyclo[2.2.2]octane from the corresponding acid.[20,21] The lithium aluminum hydride reduction of tosylates **15** and **16** to **17** proceeded smoothly even though the reaction requires the displacement of the tosylate group from a neopentyl center. Well known methods were employed for the other conversions.

Kinetic Results. Bordwell and his students report that neopentyl tosylate reacts with good nucleophiles (iodide, thiophenolate, thiourea, etc.) to provide unrearranged products by an S_N2 reaction.[22] The neopentyl character of the bicyclic tosylates dictated the selection of a nucleophile from this group and sodium thiophenolate was chosen. The reactions were carried out in an inert atmosphere or *in vacuo* to avoid the oxidation of thiophenolate.[23] We first examined the reaction of sodium thiophenolate with 4-methyl-(**18**) and 1-tosyloxymethylbicyclo[2.2.2]octane (**6**) and neopentyl tosylate in diethylene glycol. The kinetic observations are summarized in Table I.

These experiments establish that the reaction is second order. Unfortunately, the precision of the rate data was adversely affected by the slow, but competitive reactions of the nucleophile with the solvent and with adventitious impurities. Moreover, the

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Many of the pertinent results are discussed by Bordwell and Brannen, ref. 7.

(10) C. G. Swain and W. P. Langsdorf, *J. Am. Chem. Soc.*, **73**, 2813 (1951).

(11) Reference 4, Table 8 presents a summary of the data.

(12) (a) R. Fuchs, *J. Am. Chem. Soc.*, **79**, 6531 (1957); (b) R. Fuchs and A. Nisbet, *ibid.*, **81**, 2371 (1959); (c) R. Fuchs and D. M. Carlton, *ibid.*, **85**, 104 (1963).

(13) R. F. Hudson and G. Klopman, *J. Chem. Soc.*, 1062 (1958).

(14) The enhancement of S_N2 reactions of *p*-cyano and *p*-nitrobenzyl derivatives may reflect a contribution of the π-electrons in a manner analogous to that in α-halo ketones (ref. 4).

(15) G. Baddeley and G. M. Bennett, *J. Chem. Soc.*, 261 (1933); 1819 (1935).

(16) The results are summarized in Table 6 of ref. 4.

(17) R. M. Laird and R. E. Parker, *J. Am. Chem. Soc.*, **83**, 4277 (1961).

(18) C. A. Grob, M. Ohta, E. Renk, and A. Weiss, *Helv. Chim. Acta*, **41**, 1191 (1958).

(19) H. D. Holtz and L. M. Stock, *J. Am. Chem. Soc.*, **86**, 5183 (1964).

(20) S. J. Cristol and W. C. Firth, *J. Org. Chem.*, **26**, 280 (1961).

(21) F. W. Baker, H. D. Holtz, and L. M. Stock, *ibid.*, **28**, 514 (1963). The brominative decarboxylation of **12** in carbon tetrachloride yielded a mixture of 40% **13** and 60% 4-chloro-1-tosyloxymethylbicyclo[2.2.2]-octane (**9**), presumably by the path suggested for the same reaction of 1-carboxybicyclo[2.2.2]octane.

(22) F. G. Bordwell, B. M. Pitt, and M. Knell, *J. Am. Chem. Soc.*, **73**, 5004 (1951).

(23) T. J. Wallace and A. Schriesheim, *J. Org. Chem.*, **27**, 1514 (1962).

Table I. Second-Order Rate Constants for the Reactions of Sodium Thiophenolate with Neopentyl and Bicyclic Tosylates in Diethylene Glycol

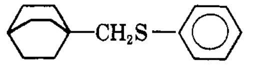
Tosylate	Temp., °C.	—Concn., 10^2 *M*— [ROTs]	[Na$^+$, PhS$^-$]	10^5k_2, M^{-1} sec.$^{-1}$
Neopentyl	100.5	8.60	8.60	73.3 ± 0.6
		14.05	11.79	70.6 ± 0.1
		14.05	4.74	76.7 ± 2.5
	79.6	14.25	4.23	10.9 ± 0.1
		14.25	8.75	10.7 ± 0.3
	60.0	8.73	5.76	1.6 ± 0.05
Bicyclo[2.2.2]-octylmethyl (**6**)	80.5	2.35	2.35	35.4 ± 0.8
		5.55	5.55	35.2 ± 1.7
	60.0	7.21	5.80	4.6 ± 0.5
		5.34	5.34	4.4 ± 0.1
4-Methylbicyclo-[2.2.2]octyl-methyl (**18**)	80.5	1.77	1.77	39.3 ± 2.0
		2.18	2.18	33.3 ± 2.2
		2.21	2.21	36.5 ± 0.5

viscosity of diethylene glycol hindered the quantitative transfer of the reagents. These problems were circumvented by the adoption of anhydrous ethanol as the solvent. Precise and easily reproducible rate data were obtained when precautions were taken to remove oxygen.[23] The results are summarized in Table II.

Table II. Second-Order Rate Constants for the Reaction of Sodium Thiophenolate with Neopentyl and Bicyclic Tosylates in Ethanol at 75.3°

Tosylate	Substituent	—— Concn., 10^2 *M* —— [ROTs]	[Na$^+$, PhS$^-$]	10^5k_2, M^{-1} sec.$^{-1}$	Relative rate
Neopentyl		8.40	2.55	7.1 ± 0.2	0.32
Bicyclo[2.2.2]octylmethyl					
6	H	2.12	2.43	22.0 ± 0.8	1.00
18	Me	2.00	2.42	23.6 ± 0.3	1.07
16	CH_2OH	1.97	2.43	25.7 ± 0.4	1.17
15	CO_2Et	1.94	2.43	33.4 ± 0.8	1.52
9	Cl	1.95	2.37	40.8 ± 0.7	1.84
13	Br	1.78	2.42	44.2 ± 1.6	2.01
Bicyclo[2.2.2]oct-2-enylmethyl					
3		2.05	2.42	45.1 ± 1.0	2.05

The products of the least (**6**) and most reactive (**3**) tosylates were examined to establish that nucleophilic attack occurred on carbon (rather than on sulfur) and that rearrangement to a bicyclo[3.2.2]nonane derivative did not take place. The reaction was carried out in ethanol at 75°. The only product isolated from the reaction of the saturated tosylate **6** analyzed for $C_{15}H_{20}S$. Structure **19** is assigned on the basis of the n.m.r. spectrum. Resonance is observed at δ 1.5 (6.9 H, singlet, 3 c.p.s. broad at half-height),[24] 2.7 (1.0 H, singlet), and 7.2 (2.6 H, multiplet). The three signals may be confidently identified with the bicyclooctyl, methylene,[25] and aryl protons of **19**. The unsaturated tosylate **3** also yields a single product, $C_{15}H_{18}S$. Structure **20** is assigned on the basis of the n.m.r. spectrum. Resonance is observed at δ 1.4 (9.0 H, multiplet split over 35 c.p.s., 2.5 (1.0 H, unresolved, 12 c.p.s. broad), 3.1 (2.0 H, singlet, 2 c.p.s. broad at half-height), 6.2 (2.0 H, ABX multiplet), and 7.2 (5.2 H, multiplet). The signals may be identified with the ethano, bridgehead,[24] methylene,[25] vinyl, and aryl protons of **20**. The retention of the methylene resonance in each case secures the unrearranged nature of the products.



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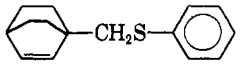

20

The n.m.r. spectra of concentrated solutions of the reaction products were examined prior to purification. These spectra were identical in all respects with those eventually recorded for analytically pure **19** and **20**. No other signals were detected nor were the lines broadened or otherwise altered from those of the pure compounds. Thus, other substances, *e.g.*, 1-bicyclo[3.2.2]nonyl phenyl thioethers, are not formed.

Discussion

Four experimental criteria permit the confident description of the reaction as an SN2 process. First, the kinetic observations for individual experiments and with variable concentrations of the reagents obey a second-order rate law. Second, the SN1 reactions of 1-tosyloxymethylbicyclo[2.2.2]octane (**6**) and neopentyl tosylate are much slower under these conditions.[26] Third, the activation parameters for the reaction of thiophenolate ion with neopentyl tosylate in diethylene glycol (ΔH^* 22.9 kcal. mole^{-1}, ΔS^* −12.2 cal. deg.$^{-1}$ mole^{-1}) and **6** (ΔH^* 23.0 kcal. mole^{-1}, ΔS^* −10 cal. deg.$^{-1}$ mole^{-1}) are very similar to the parameters for the reaction of potassium iodide with neopentyl bromide (ΔH^* 24.0 kcal. mole^{-1}, ΔS^* −13.9 cal. deg.$^{-1}$ mole^{-1}) in acetone.[27] Fourth, the products are unrearranged thioethers in contrast to the SN1 reaction of **6** which yields only rearranged bicyclo[3.2.2]nonanol-1.[26]

The rate data for the SN2 process are related to the

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[24] The bridgehead protons in 1-substituted bicyclo[2.2.2]octanes and in the octane itself experience the same chemical shift as the protons of the ethano bridge. The bridgehead proton in the 1-substituted bicyclo[2.2.2]oct-2-enes is shifted to δ 2.5, appearing as a broad multiplet.

[25] The methylene resonance occurs at δ 2.6 in neopentyl phenyl thioether. For comparison, the CH_2O resonance in **3** is at δ 3.9 and in **6** at 3.5.

[26] The rate constants for **6** and neopentyl tosylate are 4.4 × 10^{-5} and 2.1 × 10^{-5} sec.$^{-1}$, respectively, in 80% ethanol at 116°: C. A. Grob, R. M. Hoegerle, and M. Ohta, *Helv. Chim. Acta*, **45**, 1823 (1962).

[27] L. Fowden, E. D. Hughes, and C. K. Ingold, *J. Chem. Soc.*, 3187 (1955).

thermodynamic dissociation constants of the corresponding 4-substituted bicyclo[2.2.2]octane-1-carboxylic acids[28] (Figure 1).

The reasonable linear relationship defines ρ_I for the displacement reaction as 0.65.[29] Variable steric requirements are apparently responsible for the more rapid rate of 1-tosyloxymethylbicyclo[2.2.2]oct-2-ene (**3**) than predicted by the dissociation constant of 1-carboxybicyclo[2.2.2]oct-2-ene, $K_A = 3.8 \times 10^{-7}$.[30] Indeed, the rate constants for neopentyl, the saturated bicyclic (**6**), and the unsaturated bicyclic (**3**) tosylate are in the order 1:3:6. Presumably, the rate sequence reflects, in part, the accelerating influence of the double bond in **3** and, in part, the decreasing steric requirements in the three tosylates.

Substituent Effects on the SN2 *Reaction.* The methyl group has a very minor influence on this displacement reaction. The ratio, $k_{4\text{-Me}}/k_H$, is 1.07 ± 0.05 and 1.03 ± 0.09 for ethanol and diethylene glycol, respectively. Recent work in this laboratory[28,30,31] and elsewhere[32,33] has revealed that the polar influence of the methyl group is slight when bonded to sp^3 carbon and that the methyl group does not always act as an electron donor. The pK_A data[28,30] for 4-methylbicyclo[2.2.2]octane-1- and 4-methylbicyclo[2.2.2]oct-2-ene-1-carboxylic acids define apparent σ_I^{Me} constants of -0.008 ± 0.018 and $+0.013 \pm 0.016$, respectively. It is evident that the methyl group bonded to sp^3 carbon is a poor probe for the definition of the influence of electron-donor substituents on reactivity. Accordingly, we hesitate to assign the small rate difference for the methyl derivative in the SN2 reaction to a polar effect.

The methyl group is clearly an electron donor when bonded to sp^2 carbon. It is perhaps pertinent that the *p*-methyl substituent has a small retarding influence on the reaction of 2-chloroethyl phenyl thioether with potassium iodide[15] and that the 3,4-dimethyl-, *m*-, and *p*-methyl derivatives of styrene oxide react more slowly with benzylamine (at the β-carbon atom) than does styrene oxide.[34]

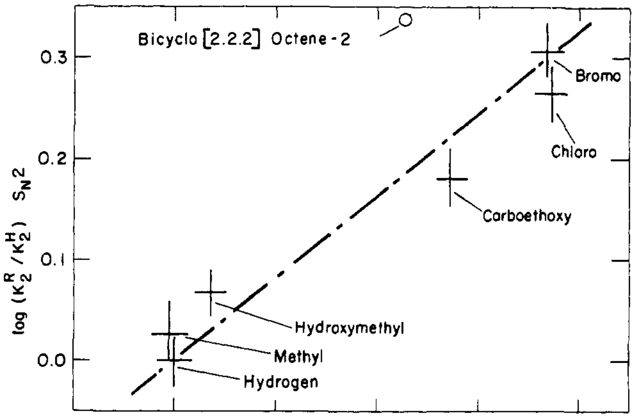
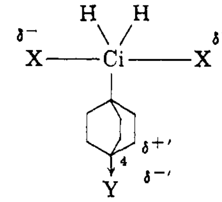


Figure 1. Relationship between log (k/k_H) for the reaction of the tosylates with sodium thiophenolate and log (K/K_H) for 4-substituted bicyclo[2.2.2]octane-1-carboxylic acids.

The significant finding of this study is that the electron-withdrawing groups accelerate the reaction. The reliability of the experimental methods and the reasonable linear relationship between the rate data and the equilibrium constants for the corresponding acids (Figure 1) establish this point with some confidence. Further, the SN2 reactions of β-phenylethyl chloride, phenyl 2-chloroethyl thioether, the corresponding sulfone, and the β-position of styrene oxide are each accelerated by these same groups.[15-17,34] These observations which have been regarded as somewhat anomalous are in accord with the results for the bicyclic compounds with regard to the direction and magnitude (ρ is 0.6–0.8 in each case) of the substituent effect. Further, there is no apparent dependence on the character of the leaving group or the nucleophile in these reactions.

If the reaction is viewed as a quasi-thermodynamic process, the lessened energy requirements for the achievement of the transition state are reasonably ascribed to the decreased work necessary to locate the partial negative charges in the field of the substituent dipole. In principle, electrostatic considerations allow the calculation of log ($k_{4\text{-Y}}/k_H$). In practice, the uncertainties associated with the charge distribution, *i.e.*, the dispersal of the charge on X to solvent molecules, and the structure of the transition state make any calculation approximate. We estimate that log ($k_{4\text{-Br}}/k_H$) is $2.5/D_E$ at 350°K. for the bromide exchange reaction of 4-bromobicyclo[2.2.2]octylmethyl bromide.[35] The effective dielectric constant, D_E, is about 5 for the bicyclo[2.2.2]octane-1-carboxylic acids in 50% ethanol[28] and is presumably similar for the SN2 transition state. It is evident that the simple electrostatic model does predict a rate ratio compatible with the experimental result.



There is an important distinction between our interpretation based on a field effect model and other viewpoints. For example, the polar effects on the SN2 reaction of these bicyclic compounds might be ascribed to the importance of bond formation at the transition state such that C_i becomes electron rich. This description emphasizes the changing charge density at C_i and depends on the concept of inductive transmission of

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[28] H. D. Holtz and L. M. Stock, *J. Am. Chem. Soc.*, **86**, 5188 (1964).

[29] The reaction constant for the dissociation of the carboxylic acids is 1.65 in 50% by weight ethanol-water at 25° based on σ_I: R. W. Taft, E. Price, I. R. Fox, I. C. Lewis, K. K. Anderson, and G. T. Davis, *ibid.*, **85**, 709 (1963).

[30] F. W. Baker and L. M. Stock, unpublished results.

[31] R. C. Parish and L. M. Stock, unpublished results.

[32] H. Kwart and L. J. Miller, *J. Am. Chem. Soc.*, **83**, 4552 (1961); H. Kwart and T. Takeshita, *ibid.*, **86**, 1161 (1964).

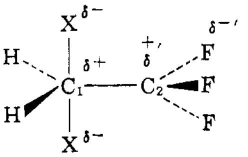
[33] R. C. Fort and P. von R. Schleyer, *ibid.*, **86**, 4194 (1964).

[34] Substituent effects on this reaction may not be representative of a typical SN2 reaction because, as Laird and Parker[17] point out, the development of charge on the leaving oxide is influenced by the substituents, *i.e.*, the polar effects may simply reflect the changing character of the leaving group.

[35] The value of log ($K_{4\text{-Br}}/k_H$) represents the work necessary ($\Delta W = \Delta\Delta F^*$) to locate two δ$^-$ charges in the presence and absence of the dipole on the basis of simple electrostatic interactions. The result is based on the distances C_iBr, 2.3 Å. (ref. 9a); C_iC_4, 4 Å.; C_4Br, 2 Å.; and the charge on X, δ$^-$, -2.4×10^{-10} e.s.u. and the bond moment of 2 D.

polar effects. In contrast, the field effect model emphasizes the interaction of the dipolar substituent with the large negative charges present in the transition state.

It is well known that halo substituents on the β-carbon atom of ethyl bromide, iodide, or tosylate slow the SN2 reaction relative to alkyl derivatives.[7,9b-d] Bordwell and Brannen suggest that the large decrease in the rate of the trifluoroethyl derivatives ($k_{CF_3CH_2OTs}/k_{n\text{-}C_3H_7OTs}$ is about 10^{-4} with potassium iodide in acetone) results from increasing steric requirements and an unfavorable electrostatic repulsion between the negative charge on the fluorine atoms ($\delta^{-\prime}$) and the nucleophile, (δ^-).[7] Hine and others propose that the slower rate is largely the consequence of a polar effect originating in the development of a positive charge at C_1 (δ^+) near the partial charge at C_2 ($\delta^{+\prime}$). Kreevoy has advanced the view that substituent effects in SN2 reactions may not reflect conventional polar influences because the C_1–C_2 bond is altered in the course of reaction.[36]



The interpretation of the results for the β-halogen derivatives is difficult because many potentially significant factors change simultaneously. The magnitude of the steric effect is a major uncertainty. van der Waals' radii indicate that the fluorine and bromine atoms are in contact in all conformations in the bromide ion exchange reaction (X = Br, C_1Br 2.3 Å.). Presumably, the association of polar solvent molecules with the C–F bond[37] would augment the steric requirements for the SN2 reaction. The model proposed by Bordwell and Brannen[7] infers that the positive charge at C-2 has a negligible influence on the reaction. However, electrostatic considerations suggest that the charge at C_2 must facilitate the reaction in the absence of charge at C_1. Indeed, the energy requirements for the formation of the transition state for bromide exchange are increased (relative to a hypothetical derivative with no dipolar group) only when the charge on each fluorine atom (δ^-) exceeds the partial charge on C_2 (δ^+) by about 30%. Hine's proposal emphasizing the importance of a short range inductive effect requires the development of positive charge at C_2. This suggestion is compatible with the available experimental results. However the importance of the steric effect is, as noted, in doubt. This factor may determine the energy requirements for these SN2 reactions. Additional experimental work is desirable to settle this intriguing problem.

Experimental[38]

1-Hydroxymethylbicyclo[*2.2.2*]*oct-2-ene* (**2**). Ester **1**[18,19] (8 g., 0.044 mole) was reduced with lithium aluminum hydride (1.7 g., 0.045 mole) in the usual way. The product (5.4 g., 89%, n^{25}D 1.5070) was purified by fractionation, b.p. 95–96° (11 mm.).

Anal. Calcd. for $C_9H_{14}O$: C, 78.20; H, 10.22. Found: C, 78.00; H, 10.38.

1-Tosyloxymethylbicyclo[*2.2.2*]*oct-2-ene* (**3**). Alcohol **2** (2.35 g., 0.017 mole) and p-toluenesulfonyl chloride (3.27 g., 0.017 mole) were reacted in pyridine (15 ml.) at 0° for 4 hr. and at room temperature for 31 hr. Product **3** was precipitated by the addition of water (10 ml.) and was recrystallized from cyclohexane (4.1 g., 79%, m.p. 96.5–97.5°).

Anal. Calcd. for $C_{16}H_{20}O_3S$: C, 65.70; H, 6.89. Found: C, 65.86; H, 7.06.

1-Hydroxymethylbicyclo[*2.2.2*]*octane* (**5**). Compound **5**, b.p. 98–99° (10 mm.), was prepared from 1-carboethoxybicyclo[2.2.2]octane (**4**)[18,19] by the method of Grob, *et al.*,[18] in 98% yield.

1-Tosyloxymethylbicyclo[*2.2.2*]*octane* (**6**). Tosylate **6** (m.p. 72–73° and 79–80°) was prepared from **5** by the method of Grob, *et al.*,[18] in 81% yield.

1-Chloro-4-toxyloxymethylbicyclo[*2.2.2*]*octane* (**9**). 1-Chloro-4-carboxybicyclo[2.2.2]octane[19] (**7**) (1.8 g., 0.017 mole) was reduced with lithium aluminum hydride (3.0 g., 0.08 mole) in the usual way. The product was not purified. The crude material was treated with p-toluenesulfonyl chloride as for **3**. Chromatography on alumina (ether–benzene eluent) yielded **9** (2.5 g., 79% based on **7**) which was recrystallized from cyclohexane–acetone, m.p. 140–141°. The infrared spectrum was identical with that of **13**.

Anal. Calcd. for $C_{16}H_{21}ClO_3S$: C, 58.40; H, 6.44; Cl, 10.77. Found: C, 58.32; H, 6.85; Cl, 10.75.

1-Tosyloxymethylbicyclo[*2.2.2*]*octane-4-carboxylic Acid* (**12**). Hydroxy acid **11** was converted to **12** under the conditions described for **3**. This tosylate was recrystallized four times from benzene to yield **12** (58%, m.p. 203.5–204.5°).

Anal. Calcd. for $C_{17}H_{22}O_5S$: C, 60.32; H, 6.55. Found: C, 60.40; H, 6.65.

1-Tosyloxymethyl-4-bromobicyclo[*2.2.2*]*octane* (**13**). Compound **13** was prepared by the brominative decarboxylation of **12**.[20,21] Acid **12** (0.9 g., 0.0027 mole), mercuric oxide (0.5 g., 0.0023 mole), and bromine (0.5 g., 0.0031 mole) yielded **13** (0.5 g., 55%, m.p. 133–134°).

Anal. Calcd. for $C_{16}H_{21}BrO_3S$: C, 51.47; H, 5.67; Br, 21.40. Found: C, 51.38; H, 5.59; Br, 21.59.

1-Carboethoxy-4-hydroxymethylbicyclo[*2.2.2*]*octane* (**14**). Ester **14** was obtained by the partial oxidation of diol **10**[19] and esterification of the resulting mixture of acids. The acid-catalyzed esterification of a mixture (21.3 g.) of **11** and the 1,4-diacid yielded a mixture of esters (22 g.). Compound **14**, 7 g., b.p. 144–146° (3 mm.), n^{25}D 1.4840, was isolated by chromatography on acid-washed alumina. The structure was proved by hydrolysis to **11**.[19]

Anal. Calcd. for $C_{12}H_{20}O_3$: C, 67.90; H, 9.48. Found: C, 67.91; H, 9.30.

1-Carboethoxy-4-tosyloxymethylbicyclo[*2.2.2*]*octane* (**15**). Ester **14** was converted to **15** under the condi-

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(36) M. Kreevoy, "Symposium on Linear Free Energy Relationships," Army Research Office (Durham), 1964, p. 39.

(37) R. W. Taft, G. B. Klingensmith, E. Price, and I. R. Fox, ref. 36, p. 265.

(38) All melting points are uncorrected. Infrared spectra were recorded on Perkin-Elmer Model 21 or Beckman IR-7 spectrometers. N.m.r. spectra were recorded on Varian A60 equipment. Microanalyses were performed by Mr. William Saschek. The n.m.r. spectrometer was purchased through an equipment grant (G827) from the National Science Foundation.

tions described for **3**. After drying, the product was chromatographed on alumina (eluent, benzene) to yield **15** (87%, m.p. 91–92°).

Anal. Calcd. for $C_{19}H_{26}O_5S$: C, 62.20; H, 7.15. Found: C, 62.36; H, 7.08.

1-Methyl-4-toxyloxymethylbicyclo[2.2.2]octane (**18**). The conversions of **10** to **16** and **16** to **17** were described previously.[19] Compound **17** could also be obtained from **15** by lithium aluminum hydride reduction. Tosylate **18** was obtained as described for **3**. Chromatography (eluent 10:2 ether–benzene) on alumina and recrystallization from cyclohexane yielded pure **18** (52% from **16**, m.p. 127.5–129°). The n.m.r. spectrum consisted of a quartet at 7.5 (Ar*H*) and singlets at 3.55 (CH_2O), 2.45 ($ArCH_3$), 1.35 (bicyclic CH_2), and 0.8 (CH_3) p.p.m. from TMS. The integrated areas of $ArCH_3$ and CH_3 were the same.

Anal. Calcd. for $C_{17}H_{24}O_3S$: C, 66.20; H, 7.84. Found: C, 66.30; H, 7.95.

Kinetic Measurements. Solvents were purified by rectification. Only center fractions were retained for kinetic experiments. The ethanol analyzed for 0.01% water (Karl Fischer method). Sodium thiophenolate was prepared by the addition of thiophenol to a solution of sodium ethanolate in ethanol (or sodium diethylene glycolate in diethylene glycol) such that 1% excess ethanolate remained. The reaction solutions were saturated with and stored under dry, oxygen-free nitrogen. Transfers were made in a nitrogen atmosphere. These precautions appreciably reduced the oxidation of thiophenolate but did not eliminate the problem.

Kinetic samples were prepared by the addition of the tosylate to a solution of sodium thiophenolate. Aliquots of the homogeneous solution were transferred to ampoules and flushed with nitrogen. In the experiments with ethanol, the ampoules were cooled to −78°, evacuated to 1 mm., and then sealed. The samples were equilibrated for 45 min. at the appropriate reaction temperature before the $t = 0$ sample was withdrawn. Blanks containing only sodium thiophenolate were used in each run. At appropriate times the samples were quenched (by cooling) and subsequently analyzed by titration with iodine.

Corrections were made for the thermal expansion of the solvent. For ethanol these were based on the known density.[39] For ethylene glycol the volume expansion factors of 1.026, 1.03, and 1.04 were determined at 60, 79.6, and 100° relative to 25°.

Thiophenolate slowly reacts with diethylene glycol even under conditions rigorously excluding oxygen. The loss of thiophenolate approached 5% of the available quantity in the time necessary for the completion of the SN2 reaction in the glycol solvent at 100°. This loss was less important at the lower temperatures. With ethanol the loss of thiophenolate was much less important and never exceeded 2%. Typical kinetic data are summarized in Table III.

Table III. Kinetic Observations for the Reaction of Sodium Thiophenolate with 4-Bromo-1-tosyloxymethylbicyclo[2.2.2]-octane in Ethanol at 75.3°

Time, min.	Titer,[a] ml.	Concn.,[b] M		10^4k_2, M^{-1} sec.$^{-1}$
		[Na^+-$C_6H_5S^-$]	[ROTs]	
0	8.98	0.021	0.015	
686	7.11	0.0174	0.0113	4.20
1401	5.93	0.0145	0.0085	4.11
2156	5.01	0.0122	0.0062	4.58
2590	4.67	0.0114	0.0054	4.58
3550	4.15	0.0101	0.0041	4.52
4109[c]	3.60	0.0088	0.0028	4.51
Average value				4.42 ± 0.17

[a] Ml. of 0.01293 N I_2 required for a 5-ml. aliquot at 25°. [b] At 75.3°. The correction factor is 1.06. The original concentrations were [$Na^+C_6H_5S^-$] 0.02285 M and [ROTs] 0.01683 M. [c] Blank samples, $t = 0$, titer 9.35 ml.; $t = 5515$ min., titer 9.27 and 9.25 ml.

Product Study. Tosylate **6** (0.434 g., 0.00147 mole) and sodium thiophenolate (0.7 g., 0.00584 mole) were dissolved in ethanol (10 ml.). The ampoule was sealed and thermostated at 75.3° for 5 hr. After cooling, the contents was poured into aqueous potassium hydroxide. The organic materials were extracted into ether. The extract was washed with aqueous base and water and dried. The ether was removed (rotary evaporator), the residue dissolved in a minimum of carbon tetrachloride, and the n.m.r. spectrum was obtained. The carbon tetrachloride solution was then chromatographed on alumina (eluent benzene). After recrystallization from benzene analytically pure 1-bicyclo[2.2.2]octylmethyl phenyl thioether (**19**) (0.2 g., m.p. 55–56°) was obtained.

Anal. Calcd. for $C_{15}H_{20}S$: C, 77.45; H, 8.67. Found: C, 77.30; H, 8.77.

Tosylate **3** (0.4227 g., 0.00145 mole) and sodium thiophenolate (0.7 g., 0.0058 mole) were reacted under the conditions described for **6**. The product isolation differed only in that 1-bicyclo[2.2.2]oct-2-enylmethyl phenyl thioether (**20**) was sublimed after recrystallization to yield the analytical sample (0.2 g., m.p. 33–35°).

Anal. Calcd. for $C_{15}H_{18}S$: C, 78.13; H, 7.87. Found: C, 78.09; H, 7.99.

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(39) H. W. Wooley, R. B. Scott, and F. G. Brickwedde, *J. Res. Natl. Bur. Std.*, **44**, 379 (1948).