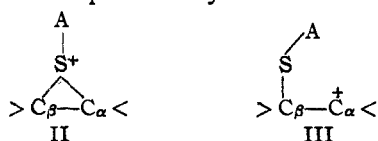


cycle II or the preliminary formation of ion III.



Rates of acetolysis of cyclohexyl *p*-toluenesulfonates give the sequence: unsubstituted, 1.00 > *trans*-2-OAc, 0.30 \gg *cis*-2-OAc, 4.5×10^{-4} . Rates of reaction of the corresponding chlorides with silver acetate are qualitatively similar. Reactivities of 2-butanols and cyclohexanols toward hydrohalogen acids show that a neighboring *trans*-

bromine atom gives a rate comparable to that of the unsubstituted material. A *trans*-iodine atom increases and a *trans*-chlorine atom decreases reactivity by factors of approximately 10^3 and 10^4 , respectively.

These results are taken to indicate that with the *trans*-OAc, Br and I groups, the ionization is directly to II. On the other hand, with *trans*-Cl and *cis*-OAc, ionization is probably to III.

The product of acetolysis of *cis*-2-acetoxycyclohexyl *p*-toluenesulfonate is very predominantly *trans*.

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[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF THE UNIVERSITY OF CALIFORNIA, LOS ANGELES]

The Role of Neighboring Groups in Replacement Reactions. XII. Rates of Acetolysis of 2-Substituted Cyclohexyl Benzenesulfonates¹

BY S. WINSTEIN, ERNEST GRUNWALD AND L. L. INGRAHAM

In the present article are reported further rate measurements which give information on solvolysis rates involving a substantial series of neighboring groups in a cyclohexyl system. The reaction rate measured was that of acetolysis of a series of 2-substituted cyclohexyl *p*-bromobenzenesulfonates or *p*-toluenesulfonates symbolized by formulas VI and VII. These rate measurements serve to establish relative rates in the presence of various neighboring groups in a reaction of one charge-type and lend themselves better to a quantitative discussion than some reported in the previous paper.²

Results

Materials for Acetolysis.—For the most part, the materials for rate measurements (Table I) were prepared by conventional methods from the proper alcohol or glycol IV or V. The assignment of configuration (*trans* or *cis*; IV, VI vs. V, VII) to the various materials has been illustrated sufficiently in previous work³ and is clear from the methods of preparation described in the experimental section.

The *trans*-2-iodocyclohexyl *p*-toluenesulfonate IX is very reactive and unstable and was difficult to obtain. All attempts at preparation by conventional methods from the cyclohexene iodohydrin IV (S-A = I) failed. A successful synthesis was achieved using the reaction of cyclohexene with silver *p*-toluenesulfonate and iodine in absolute ether. Under the special conditions used for

Substituent	M. p., °C.	Analyses, %			
		Carbon		Hydrogen	
		Calcd.	Found	Calcd.	Found
None	48.1–48.6	45.15	45.13	4.73	4.80
<i>trans</i> -OAc	97.4–97.9	44.57	44.69	4.54	4.66
<i>trans</i> -Br	91.9–92.3	36.20	36.16	3.54	3.54
<i>trans</i> -OCH ₃	65.6–66.0	44.71	44.84	4.91	4.92
<i>trans</i> -Cl	77.9–78.3	40.75	40.63	3.99	3.89
<i>cis</i> -OAc	118.4–118.8	44.57	44.44	4.54	4.49
<i>cis</i> -OSO ₂ C ₆ H ₄ Br	128.7–129.2	39.00	38.91	3.27	3.52
<i>trans</i> -OSO ₂ C ₆ H ₄ Br	123.3–123.7	39.00	39.05	3.27	3.32
<i>trans</i> -OH	106.9–108.8	42.99	42.83	4.51	4.56
<i>trans</i> -I ^a	51–52	41.06	40.69	4.51	4.70

^a *p*-Toluenesulfonate.

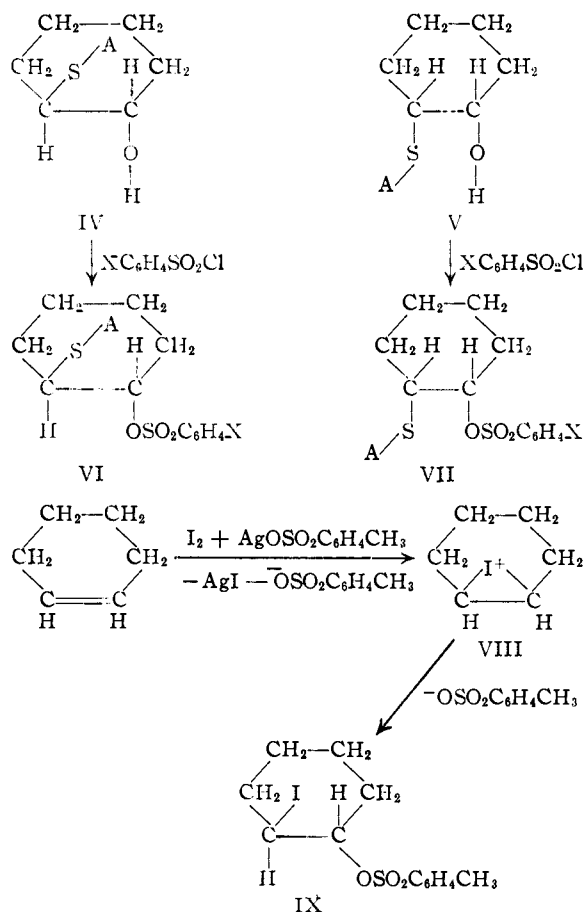
this latter reaction (*e. g.*, absence of pyridine; no reactive solvent necessary in working up the reaction mixture) the product IX survived well enough to be isolated in reasonable yield. The reaction is formulated as proceeding through the iodonium ion VIII which reacts, in the absence of any better nucleophilic agent, with toluenesulfonate ion to yield *trans*-product IX. The material IX, thus prepared, gave a fair carbon-hydrogen analysis (Table I; this was not on the best sample). Also equivalent weight values which averaged within 1.5% of theory were obtained from: (a) titration of the iodine liberated on treatment with potassium iodide; (b) hydrolysis in aqueous acetone to iodohydrin followed by measurement of the quantity of alkali necessary to neutralize the acid and convert the iodohydrin to oxide; (c) the "infinity" titer in the actual acetolysis rate measurements.

Solvolysis Rates.—The solvolysis rates were measured in glacial acetic acid containing a

(1) Most of the material in this paper was presented before the Organic Division at the Atlantic City meeting of the American Chemical Society, April, 1946.

(2) Winstein, Grunwald, Buckles and Hanson, *THIS JOURNAL*, **70**, 816 (1948).

(3) (a) Winstein and Buckles, *ibid.*, **64**, 2780 (1942); (b) Winstein and Buckles, *ibid.*, **64**, 2787 (1942); (c) Winstein, *ibid.*, **64**, 2792 (1942); (d) Winstein, Hess and Buckles, *ibid.*, **64**, 2796 (1942); (e) Winstein and Henderson, *ibid.*, **65**, 2196 (1943).



slight excess of acetic anhydride, and also in some cases in two other stock solvents, one containing 0.025 *M* potassium acetate, and one 0.36 *M* in water. The reactions were followed by titrating at intervals for the arylsulfonic acid liberated during the acetolysis. The observed kinetics were nicely first-order in almost all cases, and the precision of the measurements was usually 2% or better except when the rate constants were below 10^{-7} sec.⁻¹. In the latter case, the reactions were so slow that initial rates were measured (to ca. 15% completion), and the precision attained was about 5%. In the case of the di-*p*-bromobenzenesulfonates, rate constants were evaluated on the assumption that two moles of acid are generated per mole of ester destroyed. With the β -halocyclohexyl esters, no serious difficulty was encountered due to displacement of the halogen atom. Thus, in the case of the iodine compound, the acid titer after 23 half-lives was only 0.7% greater than after 9 half-lives, while with the bromine analog the acid titer after ten half-lives was only 4–8% high. Table II lists the data for a run with *trans*-2-methoxycyclohexyl *p*-bromobenzenesulfonate, while a run with the unreactive di-*p*-bromobenzenesulfonate of *trans*-1,2-cyclohexanediol is illustrated in Table III. It is seen that in the two runs, which are typical

of our measurements, a first-order rate constant $k = (1/t) \ln [a/(a - x)]$, where a is the initial concentration of ester and x is the concentration of sulfonic acid at time t , is satisfactorily constant. The slight upward drift during the runs, which was observed fairly consistently, is probably real and attributable to the salt effect of the liberated acid. In only three cases were the drifts in k outside of experimental error. The acetolysis rate of cyclohexyl *p*-bromobenzenesulfonate in dry acetic acid and in acetic acid 0.36 *M* in water increased during a kinetic run, and a typical set of data is presented in Table IV. A calculated first-order rate constant k decreased during the acetolysis of *trans*-2-acetoxycyclohexyl *p*-bromobenzenesulfonate in dry acetic acid, in qualitative agreement with the behaviour of the *p*-toluenesulfonate described previously,⁴ and a typical set of kinetic data is given in Table V. It is seen that the drifts in either case are small. Initial rate constants were

TABLE II
ACETOLYSIS OF *trans*-2-METHOXYCYCLOHEXYL *p*-BROMOBENZENESULFONATE IN ACETIC ACID (SOLVENT III) AT 74.99°

Time, hours	ROSO ₂ R' 10 ³ <i>M</i>	10 ⁴ <i>k</i> (sec. ⁻¹)
0.000	63.15	..
1.850	59.49	8.99
4.033	55.42	8.99
5.492	52.96	8.90
7.400	49.79	8.92
8.63	47.60	9.10
12.87	41.40	9.12

Mean 9.00 = 0.07

TABLE III
ACETOLYSIS OF DI-*p*-BROMOBENZENESULFONATE OF *trans*-1,2-CYCLOHEXANEDIOL IN AcOH (SOLVENT I) AT 74.95°, $a = 0.05046$ *M*

Time, hours	10 ³ x	100 x/a	10 ⁴ k (sec. ⁻¹)
144.9	0.43	0.43	0.82
318.9	1.02	1.01	.88
476.2	1.47	1.46	.86
644.3	2.07	2.05	.89
954	3.24	3.21	.95
1386	4.51	4.47	.92
1896	6.22	6.16	.93

TABLE IV
ACETOLYSIS OF CYCLOHEXYL *p*-BROMOBENZENESULFONATE IN ACETIC ACID (SOLVENT I) AT 34.95°

Time, hours	ROSO ₂ R' 10 ³ <i>M</i>	10 ⁷ k (sec. ⁻¹)
0.00	57.45	7.52 ^a
19.05	54.54	7.59
41.12	51.28	7.67
67.10	47.69	7.71
91.57	44.30	7.88
136.8	38.80	7.97

^a Extrapolated to $x = 0.00$ mM.

(4) Winstein, Hanson, and Grunwald, *THIS JOURNAL*, **70**, 812 (1948).

TABLE V
ACETOLYSIS OF *trans*-2-ACETOXYCYCLOHEXYL *p*-BROMO-
BENZENESULFONATE IN ACETIC ACID (SOLVENT I) AT
74.91°

Time, hours	$\text{ROSO}_2\text{R}'$ $10^4 M$	$10^4 k$ (sec.^{-1})
...	47.71	2.96 ^a
0.000	45.25	..
1.475	38.95	2.82
2.483	35.17	2.82
3.533	32.01	2.72
4.650	29.07	2.64
6.700	24.24	2.59

^a Extrapolated to $x = 0.00$ mM.

estimated in these cases with satisfactory precision from a plot of k vs. extent of reaction by extrapolation to zero reaction. On the other hand

precise estimate of the initial rate constant could not be obtained. The details of the observed kinetics are described in the experimental part.

Table VI contains a summary of the observed rate-constants and of the quantities of activation derivable from them. ΔH^\ddagger and ΔS^\ddagger symbolize the enthalpy and entropy of activation, and are calculated with the aid of equation 1.⁵

$$k = \frac{k T}{h} e^{-\Delta \tilde{H}^\ddagger / RT} e^{\Delta \tilde{S}^\ddagger / R} \quad (1)$$

We estimate in general probable errors within 0.5 kcal. for $\Delta \tilde{H}^\ddagger$, and within 2 e. u. for $\Delta \tilde{S}^\ddagger$. The specific rates listed in the Table are averages of the observed values, except in the three cases discussed in the preceding paragraph where extrapolated initial rate-constants are given.

TABLE VI
RATE CONSTANTS OF ACETOLYSIS OF 2-SUBSTITUTED CYCLOHEXYL *p*-BROMOBENZENESULFONATES

2-Substituent	Solvent ^a	Temp., °C.	k (sec. ⁻¹)	k/k_H	$\Delta \tilde{H}^\ddagger$ (kcal.)	$\Delta \tilde{S}^\ddagger$ (e. u.)
H	I	34.95	7.52×10^{-7}			
	I	74.90	12.4×10^{-6}	1.00	26.6	-0.3
	II	74.95	15.0×10^{-6}			
	III	34.95	9.68×10^{-7}			
	III	74.90	17.3×10^{-6}		27.0	+1.5
<i>trans</i> -OAc	I	74.95	2.97×10^{-6}	0.240		
	I ^b	74.95	3.99×10^{-6}			
	II	74.95	3.75×10^{-6}			
	III	74.91	4.07×10^{-6}			
	III	99.52	5.23×10^{-4}		26.0	-4.2
<i>trans</i> -Br	I	74.95	1.25×10^{-6}	0.101		
	II	74.95	1.36×10^{-6}			
	III	74.95	1.57×10^{-6}			
	III	99.53	2.53×10^{-4}		28.4	+0.8
<i>trans</i> -OCH ₃	I	74.95	7.04×10^{-6}	0.057		
	II	74.95	7.86×10^{-6}			
	III	74.99	9.04×10^{-6}			
	III	99.53	1.31×10^{-4}		27.3	-3.4
<i>trans</i> -Cl	I	74.95	5.64×10^{-6}	4.6×10^{-4}		
	I	99.72	1.43×10^{-6}		33.0	+2.7
<i>cis</i> -OAc	I	74.95	4.7×10^{-6}	3.8×10^{-4}		
	I	99.60	9.7×10^{-7}		30.9	-3.5
	II	74.95	5.9×10^{-6}			
	III	74.95	$ca. 5.6 \times 10^{-6}$			
<i>cis</i> -OSO ₂ C ₆ H ₄ Br	I	74.95	9.5×10^{-6}	7.7×10^{-5}		
<i>trans</i> -OSO ₂ C ₆ H ₄ Br	I	74.95	8.5×10^{-6}	6.9×10^{-5}		
H ^d	III	34.66	2.61×10^{-7}		27.0	-1.1
	III	75.00	4.9×10^{-6}			
	III ^e	23.60	4.84×10^{-6}	1.00		
<i>trans</i> -I ^d	III	23.60	5.64×10^{-6}	1170 ^f		
	III	34.92	2.26×10^{-4}		21.7	-4.9

^a Solvents: I, acetic acid, 0.0459 *M* in acetic anhydride; II, acetic acid, 0.0088 *M* in acetic anhydride, 0.025 *M* in potassium acetate; III, acetic acid, 0.36 *M* in water, m. p. 15.37°. ^b 0.0247 *M* sodium perchlorate. ^c 0.0351 *M* potassium acetate. ^d *p*-Toluenesulfonate. ^e Calculated from the data at higher temperatures. ^f Previously⁶ estimated at 1800 using k for cyclohexyl *p*-toluenesulfonate at 75° and a previous value of 27.8 kcal. for $\Delta \tilde{H}^\ddagger$.

the acetolysis of *cis*-2-acetoxycyclohexyl *p*-bromobenzenesulfonate in acetic acid 0.36 *M* in water was greatly catalysed by the liberated acid, and a

(5) Glasstone, Laidler and Eyring, "The Theory of Rate Processes," McGraw-Hill Book Co., New York, N. Y., 1941, p. 14.

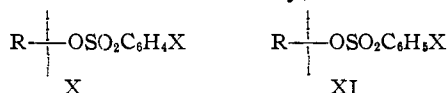
(6) Winstein and Grunwald, *ibid.*, **68**, 336 (1946).

Table VI gives an impression of the effects of solvent changes on the first-order acetolysis rate-constants. The change to the slightly aqueous solvent from the one containing a small amount of acetic anhydride raises the rate, as is to be expected,⁷ by 26–39% in the case of the *trans*-Br, *trans*-OCH₃, *trans*-OAc, and unsubstituted compounds. For these compounds as well as for the *cis*-OAc compound, the change from the solvent containing 0.0459 *M* acetic anhydride to one 0.0088 *M* in acetic anhydride and 0.025 *M* in potassium acetate gives rise to increases in rate-constant of a similar magnitude. A portion of this effect is due to the decrease in acetic anhydride concentration.

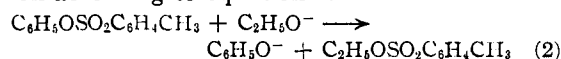
Discussion

Nature of the Acetolysis.—Although the extent of the bimolecular and unimolecular reactions in alcoholysis and hydrolysis of secondary halides is still a matter of doubt,⁸ our measured *k* values must be those for unimolecular ionization of the sulfonate group. Bimolecular reactions of cyclohexyl compounds, at least of halides,⁹ are very slow. Moreover acetic acid is a poor nucleophilic agent and would be expected to cooperate only poorly in bimolecular displacement and elimination reactions which require an attack on carbon or hydrogen coincident with the departure of the sulfonate ion. Addition of acetate ion which would participate more readily in such bimolecular reactions, gives rise to no serious increase in observed rates.

It is assumed that the mode of cleavage of the sulfonate is the usual carbon–oxygen one (X) even in the slowest cases. Actually, there is evidence



of long standing that sulfur–oxygen cleavage (XI) occurs in certain cases. Thus, in the case of phenyl *p*-toluenesulfonate, Lapworth^{10a} reported and discussed the reaction with sodium ethylate, the rate-determining step of which must be a displacement on sulfur of phenolate ion by ethylate ion according to equation 2.



Lapworth's explanation was later supported by Phillips.^{10b} This type of displacement must be responsible for some of the difficult displacements without inversion of a toluenesulfonate group from carbohydrate toluenesulfonates. An example of such a case is the hydrolysis without inversion of 4-*p*-tosyl-trityl-2,3-dimethyl- α -methylglucoside XII to XIII with the aid of sodium methoxide in benzene.¹¹

(7) Hughes, *Trans. Faraday Soc.*, **37**, 603 (1941).

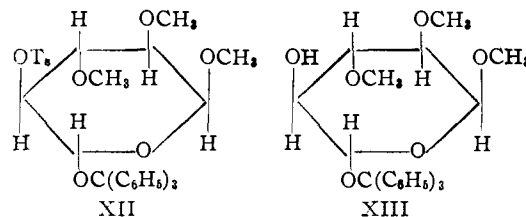
(8) Dostrovsky, Hughes and Ingold, *J. Chem. Soc.*, 173 (1946).

(9) Bartlett and Rosen, *This Journal*, **64**, 543 (1942).

(10) (a) Ferns and Lapworth, *J. Chem. Soc.*, 101, 273 (1912);

(b) Phillips, *ibid.*, **123**, 44 (1923).

(11) Oldham and Robertson, *ibid.*, 685 (1935).



In dry acetic acid as a solvent, the sulfur–oxygen mode of cleavage of the sulfonate ester could depend only on an attack on sulfur by acetic acid to displace alkoxide ion or some type of ionization of the sulfur–oxygen bond, processes which would seem to be at least as favorable with phenyl esters as in our cases. Accordingly, the acetolysis of phenyl *p*-bromobenzenesulfonate was followed, no detectable reaction being observed in glacial acetic acid at 75° in three months. The rate constant was accordingly below 5×10^{-11} sec.⁻¹, the latter value representing an upper figure for the rate that could possibly be assigned to this other mode of cleavage of the sulfonate esters.

***k*/*k*_H Values.**—The relative rates of acetolysis of the cyclohexyl benzenesulfonates are given in Table VI in the column headed *k*/*k*_H, *k*_H signifying the rate of acetolysis of the unsubstituted cyclohexyl ester. The effects of neighboring *trans*-halogen atoms are seen to be very similar in the present reaction to those observed previously² for the reaction of halohydrins with hydrohalogen acids. Again an iodine atom is rate-enhancing by a factor of *ca.* 10³, while a chlorine atom is rate-retarding by *ca.* 10⁴. The rate sequence for the halogens is I ≫ Br ≫ Cl instead of H ≫ I ≈ Br ≈ Cl which would be expected for the carbonium ion mechanism B. Again the qualitative conclusion is that with neighboring iodine and bromine the ionization is very largely by mechanism A.

The contrast in behavior of the *cis*- and *trans*-di-*p*-bromobenzenesulfonates and the *cis*- and *trans*-2-acetoxycyclohexyl esters is striking. The two di-*p*-bromobenzenesulfonates react at nearly equal rates, *k*/*k*_H being less than 10⁻². On the other hand, as observed with the corresponding toluenesulfonates,² the *trans*-2-acetoxycyclohexyl *p*-toluenesulfonate is very much more reactive than the *cis*-isomer, the factor between them being nearly 10³. The data suggest that with the *trans*-2-OAc group, ionization is by step A, while with *cis*-2-OAc group, it is probably by step B. For the di-*p*-bromobenzenesulfonates with the very poorly nucleophilic neighboring *p*-bromobenzenesulfoxy group, a possible explanation of the equality in rates for *cis*- and *trans*-isomers is that ionization is by the carbonium ion mechanism B in both cases. The slow rate is consistent with the powerful electron-removing effect which can be expected from a benzenesulfoxy group. Also, the near equality in rates is not surprising in the mobile cyclohexane system although it would perhaps not be anticipated in a more rigid system.

k_{Δ}/k_c Values.—A more quantitative discussion based on the relative reactivities k/k_H begins with the recognition that the measured rate constants k must represent the sums of k_{Δ} and k_c , where k_{Δ} is the specific rate constant for the ionization **A** to yield the cyclic intermediate II, and k_c is the specific rate constant for ionization **B** to yield the open carbonium ion III. Thus the relative reactivities are given by equation 3. If k_c/k_H can be estimated, it becomes possible to estimate the relative

$$k/k_H = k_c/k_H + k_{\Delta}/k_H \quad (3)$$

values of k_{Δ} and k_c , in other words the relative importance of steps **A** and **B**. The ratio of k_{Δ} to k_c is given by equation 4.

$$k_{\Delta}/k_c = [(k/k_H)/(k_c/k_H)] - 1 \quad (4)$$

Judging by the behavior of the *cis*- and *trans*-*p*-bromobenzenesulfonates, it becomes possible to estimate k_c/k_H for the *trans*-2-acetoxycyclohexyl *p*-bromobenzenesulfonate as the figure observed for k/k_H with the *cis*-isomer. This estimate of k_c/k_H is listed in Table VII, together with the derived value of k_{Δ}/k_c equal to 2.33×10^3 . The values of k/k_H in Table VII have been corrected to the uniform temperature 25° , and the other figures in the table refer to this temperature.

To estimate k_c/k_H for some of the other neighboring groups we have used an approach which has been used before in interpreting the effect of substituents on the strength of carboxylic acids and the rates of saponification of esters. This approach accounts for the effect of the substituent on electrostatic grounds. Kirkwood and Westheimer¹² have made important improvements in the method especially with regard to the calculation of an effective dielectric constant, D_E , and Westheimer and co-workers¹² have made quite successful applications to the interpretation of both equilibria and rates.

The procedure is to calculate the extra work W involved in the generation of the C-O dipole of moment M_1 , due to the partly ionized bromobenzenesulfoxy group in the transition state, against the dipole, moment M_2 , due to the neighboring group. The interaction energy W (in kcal./mole) of two dipoles is given¹³ by equation 5, where r is the length of the vector joining the centers of the dipoles, and ϵ , θ , and θ' are angles between M_1 and M_2 , M_1 and r , and M_2 and r , respectively. The assumed model for the transition state was simplified to involve a coplanar *trans* arrangement of the dipoles M_1 and M_2 and tetrahedral bond angles for carbon. The assumed value of M_1 was $4.6 D$, one half of the moment, $9.2 D$, calculated for complete ionization at the as-

(12) (a) Kirkwood and Westheimer, *J. Chem. Physics*, **6**, 506, 513 (1938); (b) Westheimer, *THIS JOURNAL*, **62**, 1892 (1940); (c) Westheimer and Shookhoff, *ibid.*, **61**, 555 (1939).

(13) Smythe, "Static and Dynamic Electricity." McGraw-Hill Book Co., Inc., New York, N. Y., 1939, p. 7.

sumed¹⁴ transition state distance of 1.93 \AA . All other interatomic distances were derived from the covalent bond radii given by Pauling.¹⁵ The point-dipoles were taken as situated at the midpoints of the respective bonds. The neighboring group dipole moment, M_2 , was taken as $1.87 D$ for C-Cl, $1.78 D$ for C-Br, and $1.59 D$ for C-I.^{12,16} A composite moment of $0.85 D$ was taken for the C-OCH₃ dipole, with the center of the dipole 0.72 \AA . from the β -carbon atom.

For dipole-dipole interaction the effective dielectric constant D_E is close to the internal dielectric constant D_i as Westheimer has pointed out to us in private communications. For D_i Kirkwood and Westheimer have consistently used the value of 2.00. We have treated D_E as a disposable parameter, choosing a value which gives a calculated k_c/k_H equal to k/k_H in the case of chlorine. In the case of neighboring chlorine, the data previously² and now presented, and evidence included and discussed in the following article¹⁷ indicate that the original ionization step is very predominantly by path **B** and thus that $k = k_c$. The relation between W and k_c/k_H is given by equation 6. The value of D_E determined in this way was

$$\ln(k_c/k_H) = W/RT \quad (6)$$

1.23, a value which is quite reasonable, considering that we are requiring this adjusted value for D_E to compensate for the arbitrary choice of the other parameters. Values for D_E as low as 1.00¹⁸ have sometimes been used in situations of this sort. On the whole, it is clear that the calculation along electrostatic lines accounts fairly quantitatively for the magnitude of the reduction in solvolysis rate due to a neighboring *trans*-chlorine atom.

Using the value 1.23 for D_E , equations 5 and 6 have been applied to neighboring Br, I and OCH₃, the values of W and k_c/k_H being summarized in Table VII. The derived values of k_{Δ}/k_c are listed also. Although the treatment is admittedly crude and we comment in the following article¹⁷ on a further complication, the values of k_{Δ}/k_c for neighboring bromine and iodine indicate, just as for *trans*-OAc, the very large predominance of ionization by process **A**, the fraction of this being k_{Δ}/k or $k_{\Delta}/(k_{\Delta} + k_c)$.

On the other hand, the case of *trans*-OCH₃ is in the nature of a borderline one, k_{Δ}/k_c being estimated at 4.3. From the nature of the treatment, when k_{Δ}/k_c is small as it is here, no accuracy can be claimed for the fraction of ionization proceeding by process **A**. For this case k_{Δ} and k_c are more comparable in magnitude and further work¹⁷ will be required to more accurately estimate k_{Δ}/k_c .

(14) The normal C-O distance¹⁴ was increased by 0.50 Ångstrom; see Baughan and Polanyi, *Trans. Faraday Soc.*, **37**, 648 (1941).

(15) Pauling, "Nature of the Chemical Bond," Cornell University Press, Ithaca, N. Y., 1944, p. 164.

(16) Wheland, "The Theory of Resonance," John Wiley and Sons, Inc., New York, N. Y., 1944, p. 123.

(17) Winstein and Grunwald, *THIS JOURNAL*, **70**, 812 (1948).

(18) E. g. Ri and Eyring, *J. Chem. Physics*, **8**, 433 (1940).

TABLE VII
 ACETOLYSIS RATES IN THE PRESENCE OF VARIOUS NEIGHBORING GROUPS

Neighboring group	k/k_H (25°)	W (Eq. 5) kcal./mole	k_p/k_H 25° (Eq. 6)	k_Δ/k_c 25° (Eq. 4)	L kcal./mole 25°
<i>trans</i> -Cl	0.94×10^{-4}	(5.50)	(0.94×10^{-4})
<i>trans</i> -Br	7.18×10^{-2}	5.09	1.87×10^{-4}	383	3.53
<i>trans</i> -I	1120	4.33	6.7×10^{-4}	1.7×10^6	8.49
<i>trans</i> -OCH ₃	5.28×10^{-2}	2.73	1.00×10^{-2}	4.3	0.86
<i>trans</i> -OAc	0.305	..	1.31×10^{-4}	2.33×10^3	4.60

Driving Force Due to Participation.—It is useful to introduce a variable L which will be termed the driving force due to the participation of the neighboring group in the rate-determining process. The variable L is defined by equation 7, and the values for some of the neighboring groups are included in

$$L = RT \ln (k_\Delta/k_c) \quad (7)$$

Table VII. These run from 0.86 kcal./mole in the case of *trans*-OCH₃ to 8.49 kcal./mole for *trans*-I, supplying a quantitative measure for the so-called driving force of neighboring groups.

The driving force L may be discussed in terms of the relative stabilities of the two envisaged cationic intermediates II and III. It is a necessary condition for the existence of a positive driving force due to participation of the neighboring group that the conversion of carbonium ion III to three-membered ring II be attended by a decrease in free energy. The observed driving-force represents that fraction of this decrease in free energy which is already applicable to the transition-states.

It is interesting to consider the relative contributions of enthalpy and entropy terms to the free energy effects associated with the various rate ratios discussed. Inspection of Table VI indicates that variations in k/k_H are due mainly to changes in $\Delta\tilde{H}^\ddagger$. Thus, the relative enthalpies of activation, $\Delta\tilde{H}^\ddagger - \Delta\tilde{H}_H^\ddagger$, vary from -5.3 to $+6.4$ kcal./mole corresponding to a rate-factor of $ca. 10^8$, while the relative entropies of activation, $\Delta\tilde{S}^\ddagger - \Delta\tilde{S}_H^\ddagger$ vary from -5.7 to $+3.0$ e. u., corresponding to a rate-factor of $ca. 10^2$. This indicates the greater importance, in general, of energy over entropy effects in consideration of k_c/k_H and k_Δ/k_c values. Although the differences in the entropies of activation are relatively small, the observed trend in $\Delta\tilde{S}^\ddagger$ for the halogens, with *trans*-I having the lowest value because it is involved in the most constrained transition-state configuration, is consistent with the general interpretations advanced.

Experimental

Carbinols and Glycols.—*trans*-1,2-Cyclohexanediol,³⁰ m. p. 103°, *trans*-2-bromocyclohexanol,³⁰ b. p. 72° (3 mm.), *trans*-2-methoxycyclohexanol,³⁰ b. p. 68.9-70.2° (8 mm.), and *trans*-2-iodocyclohexanol,² m. p. 39-40° were prepared from cyclohexene oxide³⁰ as previously described. *cis*-1,2-Cyclohexanediol, prepared by Criegee's

method,^{3d,19} was converted to the monoacetate, b. p. 112-114° (12 mm.) in the usual manner.²

***trans*-2-Chlorocyclohexanol.**—This material, b. p. 78.7-79.8° (14 mm.), was prepared in 65% yield by reaction of 0.3 mole of cyclohexene oxide with 40 ml. of concentrated hydrochloric acid similarly to the preparation of the analogous bromohydrin.³⁰

Preparation of *p*-Bromobenzenesulfonates (Table I).—The equivalent amount of *p*-bromobenzenesulfonyl chloride was added in one portion to a solution, cooled to 0°, of 0.1 mole of carbinol or glycol in 100 ml. of anhydrous pyridine. The reaction mixture was shaken and left in the cold room, usually overnight. Then it was poured with vigorous stirring into 200 ml. of ice-cold 6 *N* hydrochloric acid. The product, either oily or crystalline, was taken up in carbon tetrachloride. The carbon tetrachloride solution was dried over potassium carbonate and placed in an evaporating dish. After evaporation of the solvent at room temperature, the residue was usually crystalline. In the case of *trans*-2-hydroxycyclohexyl *p*-bromobenzenesulfonate, the product was not soluble in carbon tetrachloride so it was directly filtered and dried. The materials were recrystallized from Skellysolve B (petroleum ether, b. p. 60-70°) or ethyl acetate-Skellysolve B. Methanol was sometimes used with the less reactive materials. Yields of products obtained were in the range of 45-89% except in the case of the di-*p*-bromobenzenesulfonates of *cis*- and *trans*-1,2-cyclohexanediol, where they were much lower.

Phenyl *p*-bromobenzenesulfonate, m. p. 116.6-117.1° (reported²⁰ 115.5°) was prepared by the above general procedure.

The cyclohexyl and *trans*-2-hydroxycyclohexyl *p*-bromobenzenesulfonates were the least stable of the bromobenzenesulfonates prepared and could not be kept long. The latter material showed an equivalent weight of 331.5 (calculated 335.2) on treatment for several minutes with methanolic base and back titration with acid as in the case of *trans*-2-chlorocyclohexanol.²¹

The treatment of *trans*-1,2-cyclohexanediol with 2 equivalents of *p*-bromobenzenesulfonyl chloride gave rise to a product contaminated with monoester which was destroyed with methanolic base before purification of the desired di-ester. In the case of the *cis*-1,2-cyclohexanediol, treatment with one equivalent of acid chloride gave rise to di-*p*-bromobenzenesulfonate as the isolated product just as in the case of the toluenesulfonate.¹⁹

***trans*-2-Acetoxy-cyclohexyl *p*-Bromobenzenesulfonate.**—To a solution of 5 drops of concentrated sulfuric acid in 50 ml. of acetic anhydride cooled in an ice-bath was added 0.1 mole of *trans*-2-hydroxycyclohexyl *p*-bromobenzenesulfonate in approximately 8 portions and with vigorous shaking. There were added 5 drops more of sulfuric acid during the addition and 5 drops at the end. The mixture was shaken for one hour at room temperature, then treated with 300 ml. of water. The crude product obtained in nearly quantitative yield gave material, m. p. 97.4-97.9°, in 70-80% yield on recrystallization from ethyl acetate-Skellysolve B.

***trans*-2-Iodocyclohexyl *p*-Toluenesulfonate.**—A mixture of 5 ml. of cyclohexene, 20 ml. of absolute ether, 5.8 g.

(19) Criegee and Staeger, *Ber.*, **69B**, 2753 (1936).

(20) Sekera, *THIS JOURNAL*, **55**, 421 (1933).

(21) Bartlett, *ibid.*, **57**, 224 (1935).

(0.021 mole) of silver toluenesulfonate²² and 5.08 g. (0.020 mole) of resublimed iodine was shaken in a glass-stoppered flask for thirty minutes with occasional cooling in tap water. The silver iodide was removed on a filter and washed with two 10-ml. portions of a wash liquid containing 2 parts of absolute ether to 1 part of dry Skellysolve B. To the filtrate and washings was added dry Skellysolve B until no more precipitation of toluenesulfonic acid occurred. The mixture was filtered rapidly and the filtrate was cooled to Dry Ice temperature. An oil was obtained which crystallized as the mixture warmed up with shaking. Renewed cooling to Dry Ice temperature produced a crop of white crystals. Rapid filtration and washing with dry Skellysolve B with precautions against access of moisture gave rise to material, m. p. 51–52°, in yields of 20–50%. The material was quite unstable and a batch was prepared and used immediately for equivalent weight determinations and rate-runs.

A mixture of 2.0 g. of potassium iodide, 20 ml. of absolute acetone and 0.1376 g. of the iodocyclohexyl *p*-toluenesulfonate was left for two hours at room temperature. After acidification, 14.12 ml. of 0.0499 *N* thiosulfate was required for titration: equivalent weight 195.3, calcd. 190.1. A sample of the iodohydrin *p*-toluenesulfonate weighing 0.3570 g. was held in 100 ml. of 80% aqueous acetone at 35° for twenty-two hours. There was then added 39.15 ml. of 0.05063 *N* sodium hydroxide and the solution was left ten minutes. Back titration to the brom thymol blue end-point required 1.39 ml. of 0.0962 *N* acid. From these data the equivalent weight is 193.1, calcd. 190.1. From the rate runs, the iodocyclohexyl *p*-toluenesulfonate appeared to contain 1–2% by weight of toluenesulfonic acid.

The attempted preparation of the toluenesulfonate and also the bromobenzenesulfonate from cyclohexene iodohydrin by the ordinary method gave rise to an oil, from which was recovered a small amount of crude cyclohexene iodohydrin, m. p. 37°. An attempted preparation of the bromobenzenesulfonate in absolute ether using 1.2 molecular proportions of pyridine was unsuccessful with cyclohexene iodohydrin as well as with cyclohexanol. Reaction times of three to eighteen hours at 0° were employed, good recoveries of bromobenzenesulfonyl chloride being obtained.

Titration.—Analyses were performed with approximately 0.05 *N* standard perchloric acid and/or sodium acetate in glacial acetic acid. The standard perchloric acid in acetic acid was prepared from 70% aqueous acid which was compared with Bureau of Standards potassium acid phthalate. The sodium acetate reagent was obtained by dissolving reagent grade sodium carbonate in glacial acetic acid and making the solution up to volume. Titrations were carried out with 5 ml. micro-burets.

The indicator which we empirically found to be advantageous was brom phenol blue (supplied by Paragon Testing Laboratories, Orange, New Jersey), used in the form of a saturated acetic acid solution (ca. 0.1%). The indicator is colorless in acidic acetic acid solution, dim yellow in neutral solution and brilliant yellow in basic solution, the strongest color change occurring at an acetate ion concentration approximately 10⁻⁶ to 10⁻⁵ *M*. It is most convenient to approach the end-point from the acid side, the accuracy being good with either perchloric, bromobenzenesulfonic or toluenesulfonic acid. Several checks on the titration procedure were carried out.

The standard sodium acetate and perchloric acid were many times compared. A complete summary of data obtained in a six months working period showed that the normality of perchloric acid based on the sodium acetate normality and the acid-base ratio agreed with the normality based on the weight of the standard perchloric acid within 0.0 = 0.15%.

A slightly impure sample of cyclohexyl *p*-bromobenzenesulfonate was solvolyzed in methanol-water and also in acetic acid. The aqueous solution was titrated with base to the methyl orange end-point, the acetic acid solution

with sodium acetate to the brom phenol blue end-point. The equivalent weight of the bromobenzenesulfonate was 324.0 in acetic acid, 324.4 in water-methanol.

A sample of *p*-toluenesulfonic acid monohydrate was titrated in aqueous solution to the phenolphthalein end-point, the equivalent weight being 192.4 ± 0.4. In acetic acid solution, the equivalent weight proved to be 191.7 ± 0.5.

For the titration of 5 ml. quantities of both toluenesulfonic and perchloric acids, variation in the concentration of acid from 0.05 *N* to 0.001 *N* gave rise to no systematic error in the volume of sodium acetate solution required. The precision of titration remained within the larger of the two errors, ±0.5% or ±0.004 ml.

Solvents. (Table VI).—The stock solvents were prepared from J. T. Baker reagent glacial acetic acid, pure acetic anhydride, and dried reagent grade potassium acetate. Concentrations of acetic anhydride were determined by Kilpi's anthranilic acid method.²³

Rate Measurements.—Solutions, 0.03 to 0.05 *M*, of the compounds to be solvolyzed were made up at room temperature in a volumetric flask from a weighed portion of the material. In case of insufficient solubility at room temperature, solutions were made up gravimetrically. About 6-ml. portions of the solutions were sealed in ampoules and immersed in a suitable thermostat. At suitable times reaction was interrupted by removing an ampoule and immersing it in ice. The ampoule was then brought to room temperature and opened, a 5-ml. aliquot being removed for analysis. The time of the first analysis was called "zero time."

On complete acetolysis, the equivalent weight of cyclohexyl *p*-bromobenzenesulfonate was 320.8 (calcd. 319.2), of *trans*-2-acetoxycyclohexyl *p*-bromobenzenesulfonate 378.5 (calcd. 377.3), and of *trans*-2-iodocyclohexyl *p*-toluenesulfonate 380.1 ± 4.0 (calcd. 380.2).

With the *cis*-2-acetoxycyclohexyl *p*-bromobenzenesulfonate, the rate constant in solvent III at 75° climbed rapidly an effect which disappeared on addition of potassium acetate to the solvent. A plot of *x* against *t* gave, with the aid of a tangent meter, a rough estimate of the initial rate constant and a more accurate estimate of the instantaneous rate constant $k' = [(dx/dt)/(a-x)]$.

The variation of k' with *x* is given quite accurately by equation 8

$$10^3 k' = 27.76 x^{1/2} - 0.23 \quad (8)$$

obtained from the data by the method of least squares. This equation is based on the assumption of some preliminary rate-determining reaction of the acetoxybromobenzenesulfonate which is hydrogen ion-catalyzed, toluenesulfonic acid being treated simply as a weak acid. The experimental data as well as the values of k' calculated from equation 8 are summarized below.

$10^3 x$	obsd.	$10^3 k'$	calcd.
1.12	0.73		0.70
2.18	1.05		1.07
3.61	1.42		1.44
5.39	1.74		1.81
7.56	2.25		2.18
9.62	2.56		2.49
11.70	2.71		2.77

Summary

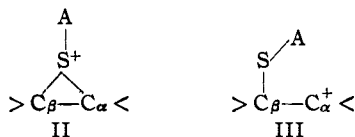
A series of 2-substituted cyclohexyl *p*-bromobenzenesulfonates and a toluenesulfonate have been prepared. A study of the acetolysis of these esters has given the relative rates of ionization of the alkyl-oxygen bond. These relative rates of solvolysis, k/k_H at 25° are in the sequence: *trans*-

(23) Kilpi, *Suomen Kemistilehti*, **13B**, 19 (1940); *C. A.*, **35**, 2445 (1941).

(22) Claesson and Wallin, *Ber.*, **12**, 1851 (1879).

I, 1120; *trans*-OAc, 0.305; *trans*-Br, 7.18×10^{-2} ; *trans*-OCH₃, 5.28×10^{-2} ; *cis*-OAc, 1.31×10^{-4} ; *trans*-Cl, 0.94×10^{-4} ; *cis*-OSO₂C₆H₄Br, 1.6×10^{-5} ; *trans*-OSO₂C₆H₄Br, 1.4×10^{-5} . Variations in rate are largely due to variations in ΔH^\ddagger .

The rate-determining ionization step appears to be largely a direct formation of the cycle II (rate constant k_Δ) in the case of neighboring *trans*-I, Br, and OAc and predominantly the formation of carbonium ion III (rate constant k_c) with neigh-



boring *trans*-Cl and OSO₂C₆H₄Br and *cis*-OAc and OSO₂C₆H₄Br.

Using k/k_H for neighboring Cl to determine an effective dielectric constant, the interaction energy between the C_β-SA and C_α-O dipoles in the transition state for formation of III has been calculated for neighboring I, Br and OCH₃. Thus estimates of k_c/k_H have been obtained and corresponding values of k_Δ/k_c have been calculated from the relation $k_\Delta/k_c = [(k/k_H)/(k_c/k_H)] - 1$.

The driving force L due to the *trans*-neighboring groups, defined as $RT \ln (k_\Delta/k_c)$, has the following values in kcal./mole at 25°: I, 8.49; OAc, 4.60; Br, 3.53; OCH₃, 0.86.

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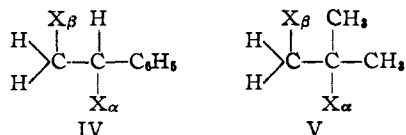
[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF THE UNIVERSITY OF CALIFORNIA, LOS ANGELES]

The Role of Neighboring Groups in Replacement Reactions. XIII.¹ General Theory of Neighboring Groups and Reactivity

BY S. WINSTEIN AND ERNEST GRUNWALD

In the previous^{2,3} rate work involving effects of neighboring groups, C_α and C_β were both secondary in the molecules (I)² whose ionization rates were measured. In considering further structural variations, it must be expected that the relative energies of the closed and open forms of the ionic intermediate,² II and III, respectively, will change with *alpha* and *beta* substitution. Thus there will be a change in L , the driving force,³ which reflects that portion of the free energy difference between II and III which already appears in the transition states for ionization of I. In this paper, with the aid of relative reactivities here reported and others from the literature, we attempt to generalize the theory to cover the whole range of possible structures for the *alpha* and *beta* carbon atoms. Also, the discussion will logically lead to a consideration of the nucleophilic closure of small rings of the classical sort, most attention being given the ethylene oxide ring.

Rate Comparisons.—A group of the rate constants to be considered deals with solvolysis in alcohol or aqueous alcohol of some of the styrene dihalides IV and isobutylene dihalides V.



Although there were some difficulties in the determination of the desired solvolysis rates, it was

(1) Much of the material in this paper was presented before the Organic Division at the Atlantic City meeting of the American Chemical Society, April, 1946.

(2) Winstein, Grunwald, Buckles and Hanson, *THIS JOURNAL*, **70**, 816 (1948).

(3) Winstein, Grunwald and Ingraham, *ibid.*, **70**, 821 (1948).

possible to obtain rate constants reliably enough for the purpose. The rates were in some cases so slow that the measurements were complicated by reaction of hydrogen bromide, produced by solvolysis of a dibromide, with the ethanol solvent. This difficulty was met by determination of the initial rate of solvolysis. With olefin iodochlorides, the solvolysis was accompanied by a slight amount of iodine production but analyses for iodine showed this was not extensive enough to be very serious.

The first-order rate constants determined as described in a later section are summarized in Table I. It seems clear from our procedure in obtaining initial rate constants and from the chemistry of the materials IV and V and analogous ones that the rate constants relate to the solvolysis of the first and most reactive halogen atom, labelled *alpha* in IV and V. Thus styrene iodochloride is reported⁴ to react with water to give iodohydrin and with silver nitrate to yield first its chlorine atom and next its iodine atom. Similarly, isobutylene iodochloride gives the *beta*-iodo-*t*-butyl methyl ether⁵ on refluxing with methanol. Analogous to the styrene derivatives are such materials as indene dibromide^{6a} VI and 1-phenyl-1,2-dibromopropane^{6b} VII.

The rate constants for solvolysis are interpreted as rates of unimolecular⁷ solvolysis.⁸ In

(4) Ingle, *J. Soc. Chem. Ind.*, **21**, 587 (1902).

(5) Istomin, *J. Russ. Phys.-Chem. Ges.*, **36**, 1199 (1904); *Chem. Centr.*, **76**, I, 429 (1905).

(6) (a) Porter and Suter, *THIS JOURNAL*, **57**, 2022 (1935); (b) Spaeth and Koller, *Ber.*, **58**, 1269 (1925).

(7) (a) Bateman, Church, Hughes, Ingold and Taher, *J. Chem. Soc.*, 979 (1940); (b) Hughes, *Trans. Faraday Soc.*, **37**, 603 (1941).

(8) Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, Chapters V and VI.