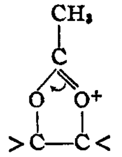
rate-determining step in the solvolysis is the formation of the ion II.



II

Water and acetate ion, which control the nature of the product and the steric result, do not exercise this control in the rate-determining step.

Similarly, for alcoholysis of *trans*-2-acetoxycyclohexyl *p*-toluenesulfonate, II appears to be the intermediate, orthoester formation being accomplished at a later step than the rate-determining one.

The rate constants for acetolysis of the toluenesulfonate in acetic acid not containing water or acetate ion decrease seriously as acid develops and then increase again. The best interpretation of the downward drift is that *trans*-2-acetoxycyclohexyl *p*-toluenesulfonate is regenerated by the action of acid and toluenesulfonate ion on an intermediate such as orthodiacetate.

LOS ANGELES, CALIFORNIA RECEIVED APRIL 3, 1947

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

# The Role of Neighboring Groups in Replacement Reactions. XI. Some Reactivities Involving Neighboring Groups[1]

BY S. WINSTEIN, E. GRUNWALD, R. E. BUCKLES AND C. HANSON

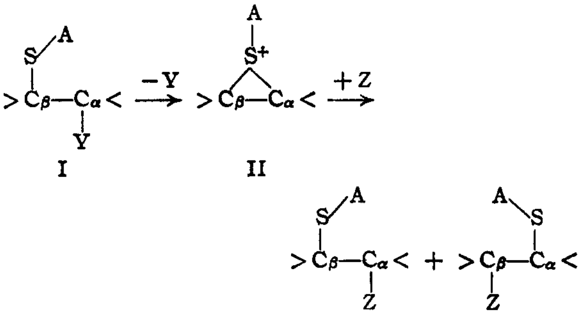
Participation of neighboring groups in displacement reactions has long been known with such groups as $O^-$ (from OH) and $NH_2$, prior ring closure[2] to isolatable oxide or imine occurring on attempted displacement of halide in a halohydrin or aminohalide. In these cases the groups are those which also take part in known bimolecular displacements[3] symbolized in equations 1 and 2.

$$RO^- + R'X \longrightarrow ROR' + X^- \qquad (1)$$

$$RNH_2 + R'X \longrightarrow (RNH_2R')^+ + X^- \qquad (2)$$

While the so-called classical groups, $O^-$, $NR_2$ and SR have been mentioned in preceding articles of this series,[4] the main stress[5] has been on participation in nucleophilic displacement reactions by such neighboring groups as OAc, Br and $OCH_3$, which are not known to participate in external displacements. Actually there is no sharp division between the latter groups and the more classical ones.

Participation by a neighboring group S-A is symbolized[4a] below, Y and Z indicating the leaving and entering groups, respectively.



We have previously indicated there are questions of intimate mechanism with respect to both the closing and opening of the ring in II.[4a] Rate measurements are helpful in this connection, and in the present article and subsequent ones are reported reactivity measurements in some unimolecular-type[6] nucleophilic displacement reactions.

As is brought out in this paper and articles XII and XIII in the series, the rate measurements yield important formation concerning the nature of the rate-determining ionization step. Using a common set of symbols for all three papers, the ionization step may be[4a] either A, a one-stage ring closure to the cyclic intermediate II with Walden inversion (W.I.) at $C_\alpha$ or B, an ionization to the substituted carbonium ion III.[3,4a,7]

Two different criteria for distinguishing between the two rate-determining steps A and B have been employed in the work described in this paper. First, the effect on the rate of the disposition of the neighboring group *cis* or *trans* to the departing

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(1) Most of the material contained in this paper was reported before the Organic Division of the American Chemical Society at the Cleveland and Atlantic City meetings, April, 1944, and April, 1946.

(2) (a) Smith and Nilsson, *J. prakt. Chem.*, **162**, 63 (1943); (b) Braun and Weissbach, *Ber.*, **63**, 3052 (1930); (c) Freundlich and Salomon, *Z. physik. Chem.*, **A166**, 161 (1933).

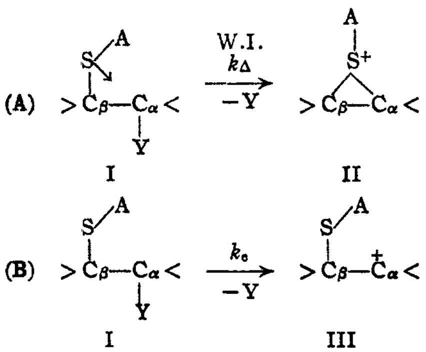
(3) Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, Chapters V and VI.

(4) (a) Winstein and Buckles, THIS JOURNAL, **64**, 2780 (1942); (b) Winstein and Buckles, *ibid.*, **64**, 2787 (1942); (c) Winstein, *ibid.*, **64**, 2791 (1942); (d) Winstein, *ibid.*, **64**, 2792 (1942); (e) Winstein, Hess and Buckles, *ibid.*, **64**, 2796 (1942); (f) Winstein and Buckles, *ibid.*, **65**, 613 (1943); (g) Winstein and Henderson, *ibid.*, **65**, 2196 (1943); (h) Winstein and Seymour, *ibid.*, **68**, 119 (1946); (i) Winstein, Hanson and Grunwald, *ibid.*, **70**, 812 (1948).

(5) Very recently a number of cases of participation by $NR_2$ and SR have been noted, *e. g.*: (a) Schultz, Robb and Sprague, THIS JOURNAL, **69**, 188 (1947); (b) Gilman and Philips, *Science*, **103**, 409 (1946); (c) Golumbic, Stahmann and Bergmann, *J. Org. Chem.* **11**, 550 (1946); (d) Fuson, Price and Burness, *ibid.*, **11**, 475 (1946).

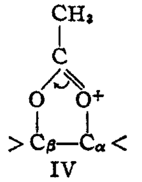
(6) This term is used to indicate nucleophilic displacement reactions which do not involve in the rate-determining step a nucleophilic attack on carbon by an external reagent. The term *SN1* type was used previously[4] but this expression is best reserved for step B.

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



group has been investigated. Second, rates of substitution involving various neighboring halogens are reported, and the influence of a change in the halogen atom on the reactivity is observed.

In order to appraise the influence of the geometric position of the neighboring group on the substitution rate, the reactivities of cyclohexyl chloride and the *cis*- and *trans*-2-acetoxycyclohexyl chlorides toward silver acetate in glacial acetic acid have been compared. After a reaction period of thirty-two hours in acetic acid at 100–110°, cyclohexyl chloride was converted partly to cyclohexyl acetate and largely to cyclohexene. Under the same conditions, *trans*-2-acetoxycyclohexyl chloride reacted only incompletely in dry and slightly aqueous acetic acid to give 40–50% yields of materials of steric configurations identical with those reported before[4a,b] for the acetoxybromide and interpreted on the basis of the cyclic intermediate IV.



IV

Under the same conditions, *cis*-2-acetoxycyclohexyl chloride proved so unreactive that only unreacted starting material was recovered. Similarly only unreacted starting material was recovered when a reaction temperature some 20° higher was employed.

A more quantitative evaluation of the effect of a *cis*- and *trans*-acetoxy group is derived from the rates of first-order acetolysis of the cyclohexyl *p*-toluenesulfonates. The rate of acetolysis of trans-2-acetoxycyclohexyl *p*-toluenesulfonate is reported in a preceding paper,[4i] and we now add for comparison the rates for the cyclohexyl and *cis*-2-acetoxycyclohexyl esters.

In Tables I and II are given typical data obtained in the determination of the first-order rate constants *k* of acetolysis of the cyclohexyl and the *cis*-2-acetoxycyclohexyl esters. In Table III are collected first-order rate constants for the three compounds in anhydrous acetic acid with and without added 0.1 *M* diphenylguanidinium acetate. It is evident from the data in Table III that the specific rates remain quite unchanged, allowing for salt effects, upon the addition of 0.1 *M* acetate salt, indicating that the reactions are of the unimolecular type. On the basis of these data, the relative reactivities in anhydrous acetic acid at 99.7° are in the following sequence: unsubstituted, 1.00 > *trans*-2-OAc, 0.30 ≫ *cis*-2-OAc, $4.5 \times 10^{-4}$.

TABLE I

ACETOLYSIS OF CYCLOHEXYL *p*-TOLUENESULFONATE (ROTs) IN ACETIC ACID AT 74.9°

| Time, min. | ROTs, *M* | $10^5 k$, sec.$^{-1}$ |
|---|---|---|
| 0 | 0.0896 | .. |
| 11 | .0876 | .. |
| 31 | .0834 | 4.13 |
| 71 | .0755 | 4.16 |
| 171 | .0586 | 4.18 |
| 371 | .0336 | 4.44 |
| 581 | .0192 | 4.44 |
| | | Mean 4.27 ± 0.14 |

TABLE II

ACETOLYSIS OF *cis*-2-ACETOXYCYCLOHEXYL *p*-TOLUENESULFONATE (ROTs) IN ACETIC ACID AT 99.7°

| Time, min. | ROTs, *M* | $10^7 k$, sec.$^{-1}$ |
|---|---|---|
| 0 | 0.09689 | .. |
| 50 | .09665 | .. |
| 630 | .09563 | 3.05 |
| 1620 | .09412 | 2.82 |
| 2565 | .09252 | 2.89 |
| | | Mean 2.92 ± 0.09 |

TABLE III

RATE CONSTANTS OF ACETOLYSIS OF *p*-TOLUENESULFONATES IN ACETIC ACID

| *p*-Toluenesulfonate | Other solute | Temp., °C. | *k* (sec.$^{-1}$) |
|---|---|---|---|
| Cyclohexyl | ............ | 74.9 | $(4.27 \pm 0.14) \times 10^{-5}$ |
| | 0.095 *M* DPG[a] | 74.9 | $(6.13 \pm 0.06) \times 10^{-5}$ |
| | ............ | 99.7 | $(6.42 \pm 0.13) \times 10^{-4}$ |
| | 0.100 *M* DPG[a] | 99.7 | $(8.7 \pm 0.2) \times 10^{-4}$ |
| *trans*-2-Acetoxycyclohexyl[4i] | ............ | 99.7 | $1.9 \times 10^{-4}$ |
| | 0.100 *M* DPG[a] | 99.7 | $2.1 \times 10^{-4}$ |
| *cis*-2-Acetoxycyclohexyl | ............ | 99.7 | $(2.92 \pm 0.09) \times 10^{-7}$ |
| | 0.108 *M* DPG[a] | 99.7 | $(5.3 \pm 0.7) \times 10^{-7}$ |
| | ............ | 131 | $(8.0 \pm 0.3) \times 10^{-6}$ |

[a] Diphenylguanidinium acetate.

The relatively high reactivity of the *trans*-isomer, and the striking difference in reactivity between the *cis*- and *trans*-isomers are not readily explained on the basis of the carbonium ion mechanism B alone. It is clear from the available data on inductive effects, such as Branch and Calvin's inductive constants,[8] that the acetoxy group is strongly electron-removing. As a result, the reaction by way of a carbonium ion intermediate is expected to be considerably slower in the presence of a neighboring acetoxy group as is actually the case only with the *cis*-material. In order to correlate the observed reactivities, it is suggested

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[8] Branch and Calvin, "The Theory of Organic Chemistry," Prentice-Hall, Inc., New York, N. Y., 1941, Chapter VI.

that the reaction of the *trans*-2-acetoxycyclohexyl ester proceeds by way of the one-stage ring-closure mechanism **A** which apparently involves a more favorable free-energy of activation than the carbonium ion mechanism **B**. On the other hand, the acetolysis of the *cis*-ester proceeds very probably by way of a carbonium ion mechanism because in the *cis*-position the neighboring acetoxy group cannot form a cyclic intermediate with inversion of configuration at $C_\alpha$ without essentially prohibitive strain.

Whereas the *cis*-2-acetoxycyclohexyl chloride was too inert to the action of silver acetate to allow isolation of the product, the acetolysis of *cis*-2-acetoxycyclohexyl *p*-toluenesulfonate proceeded rapidly enough so the stereochemistry of the displacement could be examined. The *cis*-toluenesulfonate yielded after a twenty-four hour reflux period in a potassium acetate solution in anhydrous acetic acid a diacetate which, on direct saponification and subsequent sublimation, gave rise to quite pure *trans*-glycol. Thus the steric result with the *cis*-compound is very predominant inversion of configuration in contrast to the very predominant retention of configuration in contrast to the very predominant retention of configuration observed[4e] under the same conditions with the *trans*-compound. Thus we have here another example of the tendency for production of *trans*-product from *cis*- and *trans*-2-substituted materials.[4a] The analogous action of an acetoxy group in the reactions of acetohalogen sugars with silver acetate has already been discussed.[4a]

The comparison of the effects of the various neighboring halogen atoms was based on semiquantitative measurements of the rate of reaction of some alcohols with hydrobromic or hydrochloric acid. The reactions were followed by observing the rate of growth of the halide layer from a solution of the proper alcohol in the hydrobromic or hydrochloric acid and estimating the time for half-reaction. One set of reactivities deals with 2-butanol and the related bromohydrin and chlorohydrin, while another set is available for cyclohexanol and the related halohydrins. The pertinent data are summarized in Table IV. The rates of the unsubstituted and $\beta$-bromo and $\beta$-chloro-substituted alcohols were conveniently compared in fuming hydrobromic acid. The reactivity in the presence of neighboring iodine was so high that the less active concentrated hydrochloric and 48% hydrobromic acids were employed as reagents. Even though the half-life of cyclohexanol in 48% hydrobromic acid was 500 times that in the fuming acid, *trans*-2-iodocyclohexanol reacted so fast in the former solvent that the solution was cloudy before solution of the solid iodohydrin was complete. It is evident from the data in Table IV that a neighboring *trans*-iodine atom raises the reactivity of cyclohexanol almost to that of *t*-butyl alcohol.

TABLE IV

REACTIVITY OF VARIOUS ALCOHOLS TOWARD HALOGEN ACIDS

| Compound | Solvent | Half-life *ca.* 20° | Rel. rate |
|---|---|---|---|
| Cyclohexanol | Fuming HBr | 20 min. | 1.0 |
| Cyclohexanol | 48% HBr | 7 days | 1.0 |
| Cyclohexanol | Concd. HCl | 12 days | 1.0 |
| *trans*-2-Chlorocyclohexanol | Fuming HBr | 85 days | $1.6 \times 10^{-4}$ |
| *trans*-2-Bromocyclohexanol | Fuming HBr | 4 hr. | 0.08 |
| *trans*-2-Iodocyclohexanol | 48% HBr | *ca.* 15 min. | 700 |
| *trans*-2-Iodocyclohexanol | Concd. HCl | *ca.* 15 min. | 1200 |
| 2-Butanol | Fuming HBr | 75 min. | 1.0 |
| 2-Butanol | 48% HBr | 76 hr. | ... |
| *threo*-3-Bromo-2-butanol | Fuming HBr | 3 hr. | 0.4 |
| Mixed 3-chloro-2-butanols | Fuming HBr | No halide layer in 25 days | $3 \times 10^{-4}$[a] |
| *t*-Butyl alcohol | Concd. HCl | 45 sec. | ... |

[a] Conservative estimate.

Again, the reactivities in Table IV are not compatible with the carbonium ion mechanism **B** alone. In the case of a rate-determining formation of a carbonium ion, the rates in the presence of a $\beta$-halogen atom are expected to be considerably slower than those of the unsubstituted alcohol due to the strong electron-removal by halogen which clearly opposes the formation of a positive charge on carbon. Moreover, from such physical evidence as ionization constants of aliphatic acids[8] and dipole moments of alkyl halides,[9] it would be reasonable to expect the retardation of the unimolecular rate to be not very far from equal for the various halogen atoms. The predicted rate sequence is therefore: unsubstituted $\gg$ I $\approx$ Br $\approx$ Cl. It is clear that the observed rates are not even in qualitative accord with this sequence, a neighboring iodine atom increasing reactivity by three powers of ten and a neighboring chlorine atom decreasing it by four powers of ten. In order to correlate the high reactivities in the presence of neighboring bromine and iodine, we suggest that we are here dealing with the one-stage mechanism of ring-formation, **A**. The sequence I $\gg$ Br is reasonable because iodine is generally a better nucleophilic agent than bromine. The data do not permit a definite decision regarding the substitution mechanism in the presence of neighboring chlorine although the sluggishness of the substitution suggests a carbonium ion intermediate, III. More evidence on this point is presented in succeeding papers.

It has been assumed in the preceding discussion that the reactions of the cyclohexanols and 2-butanols with halogen acids proceed by way of a unimolecular-type mechanism. This assumption is reasonable for the cyclohexanols since the alternate substitution process, bimolecular attack on carbon, has been shown to proceed only very slowly in the cyclohexyl system.[10] Moreover, the

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[9] Wheland, "The Theory of Resonance," John Wiley and Sons, Inc., New York, N. Y., 1944, p. 123.

[10] *E. g.*, Bartlett and Rosen, THIS JOURNAL, **64**, 543 (1942).

stereochemistry of the replacement process in the presence of neighboring bromine[4d] rules out the possibility of considerable bimolecular reaction with inversion of configuration in the reaction of the bromohydrins. On the other hand, the reaction of 2-butanol may well proceed to a considerable extent by way of the bimolecular process C.

$$\text{(C)}\quad \mathrm{Br^- + ROH_2^+ \longrightarrow Br - R + OH_2}$$

This fact is indicated by the rather high survival of optical activity together with the change in sign of rotation in the transformation.[11] In the analogous case of 2-octanol, we can estimate from the observed optical rotation data and data in the literature[11] a 57% survival of activity with predominant inversion in the reaction with fuming hydrobromic acid. As is clear from experiments described in the experimental section, racemization is of some importance during these transformations, so inversion would be even more prominent after proper correction.

Another indication that the reaction of 2-butanol may be largely bimolecular in type is the contrast in the reaction rates of cyclohexanol and 2-butanol in various halogen acids. While the reactivity of cyclohexanol is reduced to 1/500 by a change in reagent from fuming hydrobromic to 48% hydrobromic acid, the reactivity of 2-butanol is lowered only by a factor of 50. Moreover, while the rates of cyclohexanol in 48% hydrobromic and concentrated hydrochloric acid are quite comparable, solution of optically active 2-butanol in concentrated hydrochloric acid gives rise to no appreciable reaction and no change in optical activity after elapsed times comparable to the half-life in 48% hydrobromic acid. On the basis of these data it is probable that the relative rate of *threo*-3-bromo-2-butanol in a unimolecular-type displacement may well be above the figure 0.4 listed in Table IV.

## Experimental

***cis*-2-Chlorocyclohexanol.**—This material was prepared by the method of Bartlett.[12] Careful distillation of the material after destruction of the *trans*-isomer with base yielded a solid product, b. p. 92.5–93.0° (27 mm.), m. p. 31.5°.

***cis*-1-Acetoxy-2-chlorocyclohexane.**—Acetylation of 20 g. of *cis*-chlorohydrin by the procedure used with the *trans*-bromohydrin[4a] gave rise to an 87% yield of acetate, b. p. 98.3–99.0° (12 mm.) $n^{25}\mathrm{D}$ 1.4654.

*Anal.*[13,14] Calcd. for $\mathrm{C_8H_{13}O_2Cl}$: C, 54.39; H, 7.42; Cl, 20.07. Found: C, 53.83; H, 7.41; Cl, 19.64.

***trans*-1-Acetoxy-2-chlorocyclohexane.**—*trans*-Chlorohydrin, prepared by the method of Coleman and Johnstone,[15] was acetylated by the procedure used with the *trans*-bromohydrin[4a] to yield material, b. p. 98.0–98.5° (12 mm.), $n^{25}\mathrm{D}$ 1.4630.

**Treatment of Cyclohexyl Halides with Silver Acetate.**—Cyclohexyl chloride and the *cis*- and *trans*-2-acetoxycyclohexyl chlorides were treated with silver acetate in glacial acetic acid in the manner used previously with the analogous bromides.[4a,b] A bath temperature of 100–110° and a reaction time of thirty-two hours were employed.

From 17.7 grams (0.10 mole) of the *trans*-2-acetoxycyclohexyl chloride, using anhydrous acetic acid, was obtained on distillation at 12 mm.: 5.5 g., b. p. 98.5–100.0°, $n^{25}\mathrm{D}$ 1.4609; 4.0 g., b. p. 100.0–117.4°; and 4.0 g., b. p. 117.4–118.8°, $n^{25}\mathrm{D}$ 1.4482; the residue being 0.5 g. The saponification analysis procedure[4a] with the diacetate fraction (high-boiling) gave rise to a glycol, m. p. up to 95° (98–102° on mixing with *trans*-glycol), 103–103.5° after recrystallization from carbon tetrachloride.

Similarly from the treatment in acetic acid with an equivalent amount of water was obtained at 12 mm.: 5.5 g., b. p. 97.5–100.0°, $n^{25}\mathrm{D}$ 1.4600; 4.0 g., b. p. 100.0–112.5°; 4.0 g., b. p. 112.5–115.0°, $n^{25}\mathrm{D}$ 1.4568; residue 0.5 g. The high boiling fraction yielded largely *cis* glycol, m. p. up to 85° (m. p. lowered on mixing with *trans*-glycol), 97.0–97.5° after recrystallization from carbon tetrachloride.

Analogous treatment under anhydrous conditions of 17.7 g. (0.10 mole) of the *cis*-2-acetoxycyclohexyl chloride gave rise at 12 mm. to a 1.5 g. forerun up to 98.5°, 11.5 g., b. p. 98.5–100.0°, $n^{25}\mathrm{D}$ 1.4651, and a 2 g. tarry residue from which diacetate could not be distilled. A similar run with a stoichiometric amount of water yielded at 12 mm. 2 g. of forerun, 11.5 g., b. p. 98.5–100.0°, $n^{25}\mathrm{D}$ 1.4654, and a 0.5 g. residue. A run with xylene, b. p. 136–141°, as a solvent at the reflux temperature gave at 12 mm. 15 g., b. p. 97.5–100.5°, $n^{25}\mathrm{D}$ 1.4674, and a 0.5 g. residue.

Treatment of 11.9 g. (0.10 mole) of cyclohexyl chloride, filtration, dilution with water and extraction with ether gave an ether extract of the product. This was washed with carbonate solution and dried over anhydrous potassium carbonate. Distillation gave rise to 2.5 g. (30%) of cyclohexene, b. p. 82°, and 2.1 g. (15%) of cyclohexyl acetate, b. p. 95–99° (67 mm.).

***cis*-2-Acetoxycyclohexanol.**—To a mixture of 59 g. (0.51 mole) of *cis*-1,2-cyclohexanediol (m. p. 98°), 51 g. (0.50 mole) of acetic anhydride and 10 ml. of ether was added 10 drops of concentrated sulfuric acid. Ten more drops of acid were added after a time. After the mixture had returned to room temperature it was shaken with calcium carbonate to neutralize the acid. Then it was filtered and distilled. From the distillate, 4 g. of solid glycol were filtered out. The remaining 62 g. of product, b. p. 114–115° (12 mm.) $n^{25}\mathrm{D}$ 1.4618, saponification equivalent weight 149, 92 mole per cent. monoacetate, 8 mole per cent. diacetate, represented an 84% yield allowing for recovered glycol.

***cis*-2-Acetoxycyclohexyl *p*-Toluenesulfonate.**—This material was prepared analogously to the *trans*-isomer[4e,16] by treatment of the *cis*-1,2-cyclohexanediol monoacetate–diacetate mixture with *p*-toluenesulfonyl chloride in pyridine. Stirring the reaction mixture with water which was later acidified with sulfuric acid gave rise to an oil which was taken up in ligroin. Drying of the ligroin solution over anhydrous potassium carbonate and storage in the refrigerator gave rise to a 67% yield (on a 40 g. batch) of crude crystalline product, m. p. 76–77° after one recrystallization from aqueous methanol and 77–78° after another recrystallization.

*Anal.* Calcd. for $\mathrm{C_{15}H_{20}O_5S}$: C, 57.67; H, 6.45. Found: C, 57.65; H, 6.53.

**Cyclohexyl *p*-Toluenesulfonate.**—This material was prepared in 46% yield by the general method of Gough, Hunter and Kenyon.[17] After recrystallization from petroleum ether the m. p. was 43.5–44.0° (reported[18] 44–45°).

**Rate Measurements.**—The procedure for the acetolysis measurements in anhydrous acetic acid was the same as

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[11] (a) Pickard and Kenyon, *J. Chem. Soc.*, 45 (1911); (b) Hughes, Ingold and Masterman, *ibid.*, 1196 (1937); (c) Cowdrey, Hughes, Ingold, Masterman and Scott, *ibid.*, 1252 (1937).

[12] Bartlett, THIS JOURNAL, **57**, 224 (1935).

[13] C, H analyses by Mr. Fukushima.

[14] Chlorine analysis by courtesy of Dr. Haagen-Smit of the California Institute of Technology.

[15] Coleman and Johnstone, "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, New York, N. Y., 1932, p. 151.

[16] Criegee and Stanger, *Ber.*, **69B**, 2753 (1936).

[17] Gough, Hunter and Kenyon, *J. Chem. Soc.*, 2052 (1926).

[18] Hückel, Neunhoeffer, Gercke and Frank, *Ann.*, **477**, 99 (1929).

described previously.[4i] Refluxing chlorobenzene was used as a thermostat liquid at 131°. The *cis*-2-acetoxycyclohexyl *p*-toluenesulfonate reacted very slowly and was followed to 5–6% reaction at 99.7 ± 0.10° and to 20% reaction at 131°. In the case of cyclohexyl *p*-toluenesulfonate the reaction was followed to 70–80% reaction.

**Acetolysis of *cis*-2-Acetoxycyclohexyl *p*-Toluenesulfonate.**—A 1.5 g. portion of *cis*-2-acetoxycyclohexyl *p*-toluenesulfonate was held under reflux twenty-four hours in 6 ml. of acetic acid containing a trace of acetic anhydride and a slight excess of potassium acetate. The neutralization of the reaction mixture, extraction of the ester product with ether, drying of the ether solution and evaporation of the ether yielded the ester product. Saponification of the ester, treatment of the reaction mixture with carbon dioxide, evaporation and then sublimation gave rise to 0.11 g. (20%) of glycol, m. p. 90–92°, 101–102.5° after recrystallization from carbon tetrachloride (103–104° on mixing with authentic *trans*-glycol). A blank saponification of *cis*-2-acetoxycyclohexyl *p*-toluenesulfonate followed by sublimation did not give glycol.

The yield of glycol (20%) was quite normal if one allows for the fact that, interpolating with the aid of the available rate constants in Table III, it is estimated that the extent of acetolysis of *cis*-2-acetoxycyclohexyl *p*-toluenesulfonate in twenty-four hours at *ca.* 120° is 35%.

***trans*-2-Iodocyclohexanol.**—To 100 ml. of 46% reagent-grade hydriodic acid (density 1.50) cooled in a salt–ice-bath was slowly added with effective stirring 49.2 g. (0.50 mole) of cyclohexene oxide. After approximately three fourths of the oxide had been added, solid precipitated. Stirring was continued for fifteen minutes after the addition of oxide was complete. Then the iodohydrin was filtered off and air-dried. The crude product obtained in nearly quantitative yield was dissolved in ether. The iodine color was discharged by the addition with vigorous shaking of small portions of solid sodium bisulfite. The ether solution was decanted and dried over anhydrous potassium carbonate. The ether was then removed at room temperature with the aid of the water pump, and 100 ml. of petroleum ether was added. Cooling gave crystalline product which was recrystallized from petroleum ether to yield 75 g. (66%) of air-dried material, m. p. 39–40°. Another recrystallization gave material, m. p. 39.9–40.4° (reported[19] m. p. 41.5–42.0°), which was slower to develop color on standing. The equivalent weight of the iodohydrin on treatment with base[12] was 226.3 (calculated 226.1).

**Treatment of Alcohols and Halohydrins with Fuming Hydrobromic Acid.**—This was usually carried out as previously described,[20] the reaction mixture being sealed at 0° and allowed to warm up to and remain at room temperature. The preparation of the samples of *threo*-3-bromo-2-butanol,[20] *trans*-2-bromocyclohexanol,[4a,d] and the mixed 3-chloro-2-butanols[21] needs no further description.

From the treatment of cyclohexanol, isolation of the product after 2 days gave rise to a 75% yield of cyclohexyl bromide, b. p. 69.5–69.8° (31 mm.), $n^{25}\mathrm{D}$ 1.4932.

From the treatment of a 17.5 ml. volume of partially resolved 2-butanol, b. p. 98.5–99.0° (745 mm.), $\alpha^{22.5}\mathrm{D}$ (1 dcm.) 1.20° was obtained after two days 24 g. of crude, 19.0 g. of distilled bromide, b. p. 89–91°, $n^{21.5}\mathrm{D}$ 1.4365, $\alpha^{23}\mathrm{D}$ (1 dcm.) −2.32°.

The bromide layer from the treatment of a 22.13 g. quantity of 2-butanol, prepared by mixing 11.15 g. of active 2-butanol, b. p. 99.0–99.3° (754 mm.), $\alpha^{24}\mathrm{D}$ (1 dcm.) 4.93°, with 10.98 g. *dl*-2-butanol, b. p. 98.8–99.0° (745 mm.), was removed three times so that three nearly equal portions of halide were obtained. The fractions, 12.4 g. 12.9 g. and 12.5 g., totaled 37.8 g. (92%) before distillation. Distillation of the portions gave materials boiling at 90.2–90.3° (750 mm.), $\alpha^{20}\mathrm{D}$ (1 dcm.) for the fractions, −5.33°, −5.12°, −4.45°, average −4.97°.

Partially active 2-bromobutane, $\alpha^{24}\mathrm{D}$ (1 dcm.), −5.03°, b. p. 90.3° (746 mm.), was sealed with fuming aqueous hydrobromic acid saturated at 0°. The mixture was kept on a shaker for seven hours and then left overnight. Isolation yielded bromide, b. p. 90.3° (746 mm.), $\alpha^{25}\mathrm{D}$ (1 dcm.) −4.26°.

Octanol-2 (14.5 g.), $\alpha^{22.5}\mathrm{D}$ (1 dcm.) −6.20°, was treated with fuming hydrobromic acid prepared from 100 g. of the 48% material. The octanol did not dissolve but with occasional shaking the reaction proceeded with shrinkage of the upper layer. This shrinkage appeared complete in about four hours. After two days the bromide was isolated to yield 19.5 g. crude, 15.5 g. of pure material, b. p. 77.8–78.5° (17 mm.), $n^{22}\mathrm{D}$ 1.4508, $\alpha^{23}\mathrm{D}$ (1 dcm.) 16.31°.

A solution of 7.75 g. of *trans*-2-chlorocyclohexanol in 54 g. of 48% hydrobromic acid was saturated with hydrogen bromide at 0°, sealed, shaken and observed at room temperature. The estimated weights of separated dihalide after 12, 17, 26, 40 and 102 days were 0.08, 0.3, 1.0, 1.6 and 5.8 g., respectively. After 139 days, the oil layer was removed with the aid of 15 ml. of petroleum ether, the extract was washed with carbonate solution and dried over magnesium sulfate. Distillation through a small Vigreux column yielded 4.0 g. of a colorless material, b. p. 66–69° (3.5–4.5 mm.), $n^{22.6}\mathrm{D}$ 1.5321, $d_4^{23}$ 1.602. The equivalent weight on halogen analysis[22] of this material was 108.8. Analysis for chlorohydrin by treatment of a methanol solution with excess standard base and back-titration to the brom thymol blue end-point after four minutes showed only 0.3% chlorohydrin. The equivalent weight indicates the material was a 50–50 by weight mixture of cyclohexene bromochloride and dibromide, some exchange of bromide for chloride taking place in the reagent or product during the lengthy reaction period.

**Treatment of Alcohols and Halohydrins with Concentrated Hydrochloric Acid or 48% Hydrobromic Acid.**—The concentration of the cyclohexanols in each of the reagents was approximately 1 *M*.

Upon mixing 0.01 mole of *trans*-2-iodocyclohexanol with 10 ml. of concentrated hydrochloric acid or 48% hydrobromic acid at 0° the iodohydrin partly or largely dissolves and rapidly forms the insoluble liquid dihalide which wets and dissolves the remainder of the solid iodohydrin. The volume of the oily layer amounts to about 70% of the final volume after a period of about ten minutes with either halogen acid. The oily layer proved to be a mixture of dihalide and iodohydrin.

A 0.100 mole quantity of iodohydrin was shaken twenty-five minutes with 100 ml. of ice-cold concentrated hydrochloric acid. Then 25 ml. of carbon tetrachloride was added and the organic layer was separated, washed, dried and distilled at reduced pressure. There was obtained 20.5 g. (*ca.* 85%) of an iodochloride fraction b. p. 73–74° 2 mm.), $n^{24}\mathrm{D}$ 1.5674. Stephanov analysis[22] for halogen gave an equivalent weight of 154.3, corresponding to 55% by weight iodochloride.

A 10 ml. volume of *dl*-2-butanol was dissolved in 50 ml. of 48% hydrobromic acid at room temperature. The approximate volume of oil layer was 1.5 ml. after twenty-one hours, 6.0 ml. after six days and 7.5 ml. after twelve days.

Approximately 2 ml. of active 2-butanol, $\alpha^{24}\mathrm{D}$ (1 dcm.) 4.93°, was dissolved in approximately an equal volume of concentrated hydrochloric acid. The $\alpha_\mathrm{D}$ (1 dcm.) remained at 2.21 ± 0.01° for twenty-three hours at the end of which time the solution was very slightly turbid. The reading after seventy-one hours was 2.17°.

## Summary

In connection with participation of neighboring groups in nucleophilic displacements of the unimolecular type, rate measurements lead to an understanding of the rate-determining ionization step. This may be either a direct formation of the

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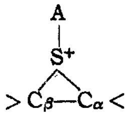
[19] Brunel, *Ann. chem.*, [8] **6**, 221 (1905).

[20] Winstein and Lucas, THIS JOURNAL, **61**, 1576, 1581 (1939).

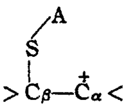
[21] Wilson and Lucas, *ibid.*, **58**, 2396 (1936).

[22] Kamm, "Qualitative Organic Analysis," John Wiley and Sons, New York, N. Y., 1942, p. 200.

cycle II or the preliminary formation of ion III.



II



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 $\times 10^{-4}$. 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*.

LOS ANGELES 24, CALIF. RECEIVED APRIL 3, 1947

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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 Benzenesulfonates[1]

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 work[3] 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 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.

TABLE I

2-SUBSTITUTED CYCLOHEXYL *p*-BROMOBENZENESULFONATES

| Substituent | M. p., °C. | Analyses, % Carbon Calcd. | Carbon Found | Hydrogen Calcd. | Hydrogen Found |
|---|---|---|---|---|---|
| None | 48.1–48.6 | 45.15 | 45.13 | 4.73 | 4.80 |
| *trans*-OAc | 97.4–97.9 | 44.57 | 44.69 | 4.54 | 4.66 |
| *trans*-Br | 91.9–92.3 | 36.20 | 36.16 | 3.54 | 3.54 |
| *trans*-$OCH_3$ | 65.6–66.0 | 44.71 | 44.84 | 4.91 | 4.92 |
| *trans*-Cl | 77.9–78.3 | 40.75 | 40.63 | 3.99 | 3.89 |
| *cis*-OAc | 118.4–118.8 | 44.57 | 44.44 | 4.54 | 4.49 |
| *cis*-$OSO_2C_6H_4Br$ | 128.7–129.2 | 39.00 | 38.91 | 3.27 | 3.52 |
| *trans*-$OSO_2C_6H_4Br$ | 123.3–123.7 | 39.00 | 39.05 | 3.27 | 3.32 |
| *trans*-OH | 106.9–108.8 | 42.99 | 42.83 | 4.51 | 4.56 |
| *trans*-I[a] | 51–52 | 41.06 | 40.69 | 4.51 | 4.70 |

[a] *p*-Toluenesulfonate.

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

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[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).