Reduction of D-Galacturonate Ion to L-Galactono-γ-lactone.—The hexahydrated sodium calcium mixed salt of D-galacturonic acid[21] was reduced with sodium borohydride by the procedure described above for sodium D-glucuronate. A solution of sodium borohydride (1.0 g.) in 40 ml. of water was added to a suspension of sodium calcium D-galacturonate hexahydrate (5.0 g.) in 50 ml. of water at room temperature under slightly basic conditions. At the end of the reaction the solution became almost clear and was then acidified with dilute HCl. Lactonization was achieved as described above for L-gulono-γ-lactone and the lactone was extracted with hot absolute ethanol. The sirup obtained from the ethanolic solution was dissolved in water and passed through the ion exchange columns. The sirup from the effluent was dissolved in a small amount of absolute ethanol and was crystallized by seeding with L-galactono-γ-lactone; yield 0.85 g. (24%), m.p. 132–133°, $[\alpha]^{26}D$ +73.4° (*c* 3, water, initial). Recrystallization from absolute ethanol gave pure material; m.p. 134–135° with sintering at 128°, $[\alpha]^{22}D$ +77° (*c* 4, water, initial) in agreement with recorded[22] values.

Reduction of Methyl (Methyl α-D-Galactopyranosid)-uronate Monohydrate (I) to Methyl α-D-Galactopyranoside Monohydrate (II).—A solution of methyl (methyl α-D-galactopyranosid)-uronate monohydrate[23–25] (0.50 g.) in 5 ml. of water was added dropwise to a stirred solution of sodium borohydride (0.20 g.) in 3 ml. of water at room temperature (25–35°) during a period of 5 min. After stirring for an additional 10 min., the reaction mixture was acidified with dilute acetic acid, diluted with 2 volumes of water and passed through columns of Amberlite IR-100-H[15] and IR-4-B.[15] The effluent was concentrated under reduced pressure to a sirup. The sirup (0.4 g.) was dissolved in 10 ml. of water and 20 ml. of 0.2 *N* $Ba(OH)_2$ was added. After standing at room temperature (28–30°) for 4 hr., the alkaline solution was deionized by passage through columns of Amberlite IR-100-H and IR-4-B. The effluent was concentrated under reduced pressure to a sirup which was crystallized from absolute ethanol and ether; yield 0.27 g. (61%), m.p. 104–106°, $[\alpha]^{27}D$ +170° (*c* 0.5, water). Pure methyl α-D-galactopyranoside monohydrate was obtained on recrystallization from the same solvent; m.p. 108–109°, $[\alpha]^{25}D$ +177° (*c* 3, water) in agreement with recorded[26–28] values. The X-ray powder diffraction diagram of this substance was exactly identical with that of an authentic specimen. The principal lines are 7.08[29]–15,[30] 6.10–20, 5.27–100, 4.57–80, 4.35–30, 3.97–50, 3.53–25, 3.20–30, 2.32–30.

This reaction was repeated except that the addition of the reducing agent was made at 5–10° during 20 min. and the reaction was maintained at this temperature for 20 min. before acidification; yield 45 or 70% on correction for a 36% recovery of starting material (recrystallized from 95% ethanol) obtained from the ion exchange effluent material before saponification.

Reduction of Methyl (Methyl β-D-Galactopyranosid)-uronate to Methyl β-D-Galactopyranoside.—Methyl (methyl β-D-galactopyranosid)-uronate, first described by Ehrlich and Guttmann,[23] was obtained on concentrating the mother liquor from the preparation of the α-D-anomer according to the method of Jones and Stacey.[25] This substance (0.50 g.) was reduced with sodium borohydride (0.20 g.) in the same manner as described above, in the first instance, for the anomer and the product was isolated in the same manner; yield 0.28 g. (64%), m.p. 175–176°, $[\alpha]^{24}D$ −0.8° (*c* 3, water). One recrystallization from absolute ethanol gave pure methyl β-D-galactopyranoside; m.p. 177–178°, $[\alpha]^{27}D$ −0.6° (*c* 2.5, water) in agreement with recorded[27,31] values.

Reduction of Methyl (Methyl D-Glucopyranosid)-uronate to Methyl α-D-Glucopyranoside.—A crude sirupy preparation[32] of methyl (methyl D-glucopyranosid)-uronate (0.50 g.) in 5 ml. of water was reduced with sodium borohydride (0.20 g.) in 3 ml. of water as described above for the corresponding derivatives of D-galacturonic acid with omission of the hydrolysis with alkali. Crystals were obtained from absolute ethanol; yield 0.16 g. (37%), m.p. 164–165°, $[\alpha]^{30}D$ +151° (*c* 1, water). Further recrystallization from absolute ethanol gave pure material; m.p. 164.5–165.5°, $[\alpha]^{30}D$ +155° (*c* 0.9, water) in agreement with recorded[33] values for methyl α-D-glucopyranoside.

(21) P. P. Regna and B. P. Caldwell, THIS JOURNAL, **66**, 244 (1944); H. S. Isbell, *J. Research Natl. Bur. Standards*, **33**, 45 (1944).

(22) N. K. Richtmyer, R. M. Hann and C. S. Hudson, THIS JOURNAL, **61**, 340 (1939).

(23) F. Ehrlich and R. Guttmann, *Ber.*, **66**, 220 (1933).

(24) S. Morell and K. P. Link, *J. Biol. Chem.*, **100**, 385 (1933).

(25) J. K. N. Jones and M. Stacey, *J. Chem. Soc.*, 1340 (1947).

(26) E. Fischer and L. Beensch, *Ber.*, **27**, 2478 (1894).

(27) E. Fischer, *ibid.*, **28**, 1145 (1895).

(28) J. K. Dale and C. S. Hudson, THIS JOURNAL, **52**, 2534 (1930).

(29) Interplanar spacing, Å., $CuK\alpha$ radiation.

(30) Relative intensity as percentage strongest line; estimated visually.

(31) E. Bourquelot, *Ann. chim.*, [9] **7**, 153 (1917).

(32) L. N. Owen, S. Peat and W. J. G. Jones, *J. Chem. Soc.*, 339 (1941).

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COLUMBUS 10, OHIO

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

Role of Neighboring Groups in Replacement Reactions. XIX. Polarimetric Acetolysis Rate of *trans*-2-Acetoxycyclohexyl *p*-Toluenesulfonate

BY S. WINSTEIN AND RICHARD HECK

RECEIVED MAY 23, 1952

The polarimetric and titrimetric rates of acetolysis of *trans*-2-acetoxycyclohexyl *p*-toluenesulfonate have been shown to be equal. This shows that internal rearrangement does not accompany solvolysis as in other cases of neighboring group participation. The absence of the internal phenomenon in the present case, ascribed to the special nature of the neighboring acetoxy group, supports the "internal return" interpretation for the observed internal rearrangements.

So-called internal rearrangements accompany solvolysis in cases of allylic, homoallylic and Wagner–Meerwein rearrangements. These have been observed, for example, in acetolysis of α,α-dimethylallyl chloride,[1] *exo*-norbornyl *p*-bromobenzenesulfonate,[2] 3-phenyl-2-butyl *p*-toluenesulfonate,[3a,b] 2-phenyl-1-propyl *p*-bromobenzenesulfonate,[4] dehydronorbornyl *p*-bromobenzenesulfonate[5] and *i*-cholesteryl derivatives.[6] The preferred interpretation[3a] of these internal rearrangements involves formation of an ion-pair (*e.g.*, II) which gives solvolysis products or returns to the covalent condition (internal return) giving either racemized ester (I and III) or rearranged material (III). In the case of norbornyl[2] and 3-phenyl-2-butyl[3a] esters, the internal phenomenon results in a

(1) W. G. Young, S. Winstein and H. L. Goering, THIS JOURNAL, **73**, 1958 (1951).

(2) S. Winstein and D. Trifan, *ibid.*, **74**, 1154 (1952).

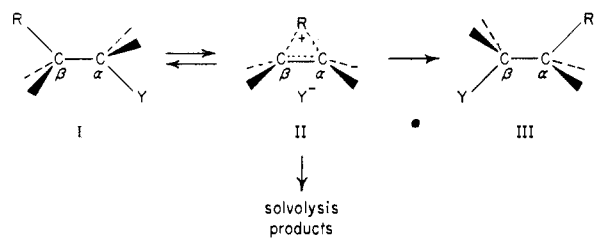
(3) (a) S. Winstein and K. C. Schreiber, *ibid.*, **74**, 2165 (1952); (b) D. J. Cram, *ibid.*, **74**, 2129 (1952).

(4) S. Winstein and K. C. Schreiber, *ibid.*, **74**, 2171 (1952).

(5) S. Winstein and H. J. Schmid, unpublished work.

(6) S. Winstein and E. Kosower, unpublished work.

larger polarimetric solvolysis rate than the titrimetric one. In the case of 2-phenyl-1-propyl[4] or dehydronorbornyl[5] esters, the internal rearrangement gives rise to a new structure.



The complication of a competing internal phenomenon should accompany functional neighboring group participation as well as participation by neighboring carbon. Indeed, with neighboring bromine, internal rearrangement has already been demonstrated to be important in the mutarotation of the 5,6-dibromocholestanes.[7] The present article is concerned with the neighboring acetoxy group.

The case which has been scrutinized is that of acetolysis of *trans*-2-acetoxycyclohexyl *p*-toluenesulfonate (VIII). This material acetolyzes in glacial acetic acid by way of an intermediate mesomeric ion[8] to an optically inactive[8] *trans*-1,2-diacetoxycyclohexane when the acetic acid solution is free of water and contains acetate ion. In this case, internal return of ion-pair X to racemic acetoxycyclohexyl *p*-toluenesulfonate (VIII) and XI would cause the polarimetric acetolysis rate to exceed the titrimetric one. These two rates have been compared in the present investigation.

As in the previous work[8] the *trans*-1,2-cyclohexanediol (VI) was resolved by way of the mono-*l*-menthoxyacetate (V). While this method of resolution is not economical in materials it is convenient. In the present work we used the device of preparing the *l*-menthoxyacetate (V) of the *trans*-1,2-cyclohexanediol by opening cyclohexene oxide IV with *l*-menthoxyacetic acid using a trace of sulfuric acid as a catalyst. The high melting diastereomer, m.p. 126–127°, was obtained by crystallization from benzene and the dextrorotatory *trans*-1,2-cyclohexanediol VI was obtained by saponification of this material and sublimation of the glycol. In the present work the mono-*p*-toluenesulfonate VII of the dextrorotatory glycol and the *trans*-2-acetoxycyclohexyl *p*-toluenesulfonate VIII derived by acetylation of the latter material, were obtained in crystalline form. The latter is a low melting material, m.p. 47–48°.

As summarized in Table I the titrimetric and polarimetric acetolysis rates of the dextrorotatory *trans* - 2 - acetoxycyclohexyl *p* - toluenesulfonate (VIII) were measured in anhydrous acetic acid solution at a concentration of approximately 0.06 *M* with potassium acetate at 0.0740 *M* at 75.07°. The titrimetric rate constant agreed well with the value previously reported[9] at 75° for the racemic material at slightly different conditions of solvent.

(7) C. A. Grob and S. Winstein, *Helv. Chim. Acta*, **35**, 782 (1952).

(8) S. Winstein, H. V. Hess and R. E. Buckles, THIS JOURNAL, **64**, 2796 (1942).

(9) S. Winstein, C. Hanson and E. Grunwald, *ibid.*, **70**, 812 (1948).

TABLE I

TITRIMETRIC AND POLARIMETRIC ACETOLYSIS RATES OF ACTIVE *trans*-2-ACETOXYCYCLOHEXYL *p*-TOLUENESULFONATE
Temp. = 75.07°, concn. = 0.06312 *M*; (KOAc) = 0.07396 *M*.

Procedure	Rotation Initial	Rotation Final	$10^5\ k$(sec.$^{-1}$)
Titrimetric			1.37 ± 0.09
Polarimetric	+0.604	+0.010	1.34 ± 0.11
Polarimetric (graphical)[a]			1.30

[a] Rate constant obtained from straight line drawn in Fig. 1 by inspection.

The polarimetric decrease in rotation followed good first-order kinetics illustrated graphically in Fig. 1, where log $[(\alpha_0 - \alpha_\infty)/(\alpha - \alpha_\infty)]$ is plotted against time. Considering that the initial observed rotation was of the order of 0.6° (Table I), the kinetics were very satisfactory. As is clear from Table I, the polarimetric rate of acetolysis agrees with the titrimetric one within experimental error; thus, in the case of participation by the neighboring acetoxy group in *trans*-2-acetoxycyclohexyl *p*-toluenesulfonate, internal return is not a competing phenomenon.

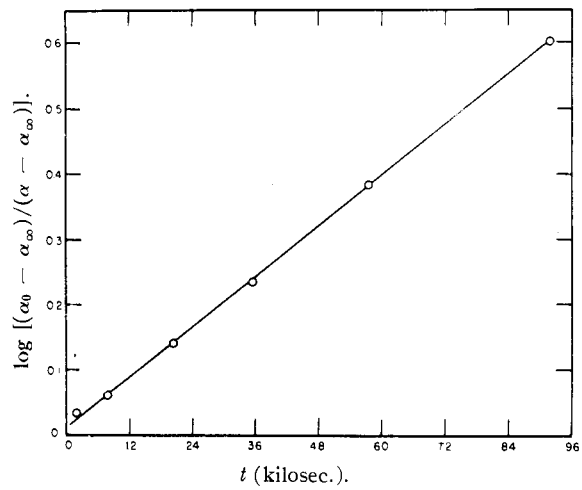


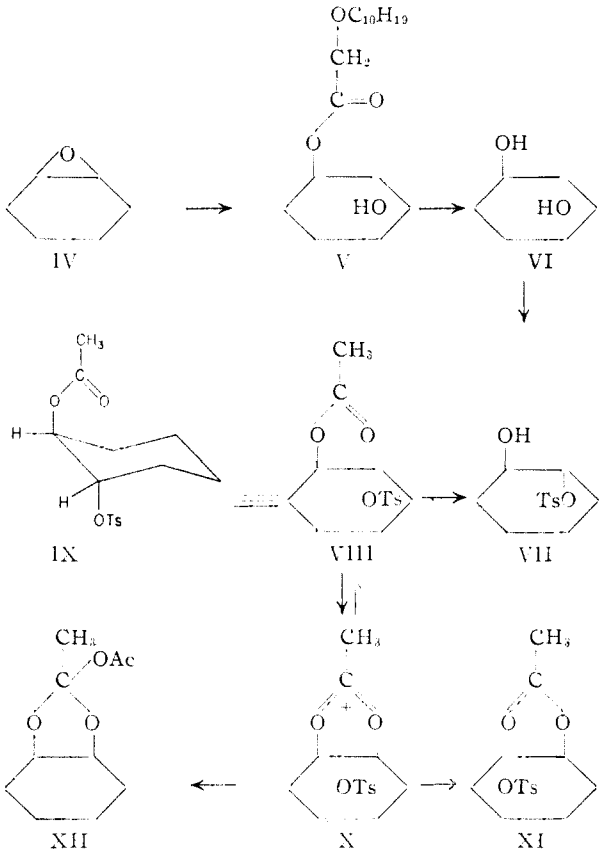
Fig. 1.—Polarimetric rate of acetolysis of *trans*-2-acetoxycyclohexyl *p*-toluenesulfonate at 75.07°.

The failure of internal return to be a competing factor in the present case is interesting in two ways. First, there is the question why this phenomenon fails to appear with the neighboring acetoxy group in acetic acid as a solvent whereas it does appear in cases of neighboring carbon.[2–4] While it is not yet clear what the general scope of the internal phenomenon will be in cases of functional neighboring group participation it appears likely that the failure is due to the special nature of the acetoxy group. The intermediate cyclic ion from acetoxy participation can react at the acyl carbon atom to give an orthodiacetate[10,11] XII and this provides a competing mode of escape for the cation which is not available in cases of other participations. This reaction of the ion-pair X apparently competes very successfully with internal return.

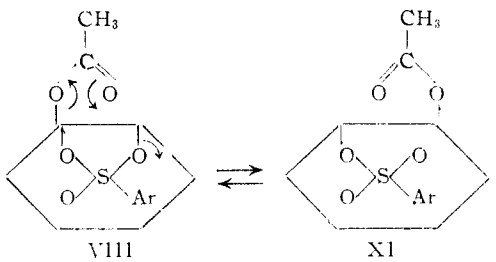
The other reason that the present failure of internal return to appear in the case of the neighbor-

(10) S. Winstein, *Bull. soc. chim.*, **18**, C55 (1951).

(11) S. Winstein, R. M. Roberts, J. Corse and R. Boschan, unpublished work.



ing acetoxy group is interesting, is that this sheds some light on the nature of the internal rearrangements observed in other cases. As explained previously[3a] an alternative explanation of the discrepancy between polarimetric and titrimetric rates in cases such as the norbornyl one involves an internal cyclic rearrangement mechanism independent of solvolysis. If a cyclic rearrangement mechanism were the general route for the internal rearrangements observed, then internal rearrangement (VIII ⇄ XI) would be expected to be favored in the present case for the neighboring acetoxy group and the migrating *p*-toluenesulfonate group are both well disposed for a cyclic rearrangement mechanism (VIII, IX).



The absence of internal rearrangement in the present case lends support to the interpretation involving internal return.[3a]

Experimental

Resolution of Cyclohexanediol.—To a solution of 155 g. of *l*-menthoxyacetic acid and 73 g. of redistilled cyclohexene oxide in *ca.* 1 liter of redistilled Skellysolve B was added a solution of 1 ml. of concd. sulfuric acid in 2 ml. of ether, and the mixture was refluxed for two days on a steam-bath. After the flask was cooled in the refrigerator overnight, the deposited solid (130 g., 57%) was filtered off and air-dried. Concentration of the mother liquors yielded a further 21 g. for a total yield of 151 g. (66%).

Resolution was carried out with the first 130 g. of crystals, which were dissolved in 300 ml. of hot benzene. The solution was shaken with anhydrous potassium carbonate, filtered, and allowed to crystallize in the refrigerator overnight. After four recrystallizations from benzene, there was obtained material, m.p. 126–127°. One more recrystallization from ligroin yielded 9.3 g. of long transparent needles, m.p. 126–127°.

The ester was hydrolyzed in a refluxing solution of 2.1 g. of potassium hydroxide in 72 ml. of methanol for two hours. The solution was cooled, treated with Dry Ice and evaporated to dryness in vacuum. Sublimation of the active diol at 100°, under *ca.* 0.5 mm. pressure, yielded 1.85 g. (52.9%) of (+)-cyclohexanediol, m.p. 108–109°.

(+)-*trans*-1,2-Cyclohexanediol Mono-*p*-toluenesulfonate.—The diol (1.80 g.) was tosylated overnight in *ca.* 5 ml. of dry pyridine with 3 g. of purified tosyl chloride. When ice and cold dilute sulfuric acid were added to the pyridine solution an oil separated which soon solidified. The solid was filtered off, washed with water, and dried in a vacuum desiccator. Recrystallization yielded 0.95 g. of material, m.p. 85–87°, $[\alpha]^{26}D$ 14.81° (*c* 5.1 in chloroform), $\alpha^{26}D$ 0.76° (1 dcm.).

Anal. Calcd. for $C_{13}H_{18}O_4S$: C, 57.76; H, 6.71. Found: C, 57.57; H, 6.76.

(+)-*trans*-2-Acetoxycyclohexyl *p*-Toluenesulfonate.—Acetylation of the (+)-mono-*p*-toluenesulfonate in pyridine with redistilled acetic anhydride produced an oil on working up the reaction mixture. The product was taken up in ether and the ether extract was washed and dried over anhydrous magnesium sulfate. The ether solution was concentrated, and the colorless oil which remained was crystallized from pentane at −80°. Further purification was effected by chromatography. The compound was dissolved in a minimum of redistilled pentane and then poured onto a column of activated alumina. After *ca.* 1 liter of redistilled pentane was put through, the compound was eluted with 50% ether–pentane. Evaporation of the ether–pentane solution yielded a colorless oil which was crystallized twice from pentane at −80°. The product was obtained in the form of colorless needles, m.p. 47–48°. The rotation of a sample, m.p. 46.0–47.5°, was $[\alpha]^{23}D$ 24.4° (*c* 2 in chloroform), $\alpha^{23}D$ 1.04° (2 dcm.).

Anal. Calcd. for $C_{15}H_{20}O_5S$: C, 57.67; H, 6.45. Found: C, 57.71; H, 6.46.

Kinetic Measurements.—The titrimetric and polarimetric rate measurements in anhydrous acetic acid were carried out as in previous work.[3,12,13]

Acknowledgment.—This work was subsidized out of a grant from the Eli Lilly Co.

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(13) S. Winstein and D. Trifan, *ibid.*, **74**, 1147 (1952).