yield benzoic and acetic acid, respectively. No difference in chemical behavior was found between sulfuric acid solutions of these acyl sulfates and the free acids. In one case evidence for alkyl oxygen fission was obtained. When *t*-butyl benzoate which is a liquid is added carefully to 100% sulfuric acid a white solid is formed which will quickly dissolve if the mixture is agitated. This solid was isolated and found to be benzoic acid indicating that this ester is first converted to benzoic acid rather than to the benzoyl ion which is in agreement with the proposed mechanism. More convincing evidence might be obtained by using esters with labelled oxygen and determining whether this oxygen is retained or lost by the benzoic acid which is recovered in the hydrolysis experiments.

Experimental

Preparation of Esters.—The methyl and ethyl esters were obtained from commercial sources and were carefully fractionated before use. The isopropyl and *t*-butyl esters were prepared by the method used by Cohen and Schneider.[10] The only new ester is isopropyl anisate, b. p. 112–113 (2 mm.), $n^{25}\text{D}$ 1.5107, d^{25}_4 1.060. *Anal.* Calcd.: C, 68.0; H, 7.22. Found: C, 67.62; H, 7.18.

The freezing point depression measurements were made according to the method of Newman, *et al.*,[6b] except that a Beckmann thermometer was used instead of a resistance thermometer. Table II contains the results of the freezing point depression measurements for those compounds which have not been previously measured. In the first column is the weight of the sample, the second column gives the molality of the solution, the third column shows the observed freezing points as measured with a Beckmann thermometer, the fourth column gives the freezing point depression and the last column gives the "*i*" value calculated from the equation

$$``i" = \Delta T/\Delta m \times 6.154\ (1 - 0.0047t)$$

where *t* is the difference between the freezing point of 100% sulfuric acid and the observed freezing point.

TABLE II

Wt., g.	Δm	F. p., °C.		ΔT	"*i*"
		Isorpropyl Alcohol			
0.1184	0.0267	3.757	3.140	0.507	3.11
		3.250		.617	3.78
		t-Butyl Alcohol			
.2305	.0417	4.394	3.374	.813	3.19
		3.581		.874	3.42
		3.520		1.020	3.97
		Isopropyl Acetate			
.0988	.0132	4.440	4.155	0.252	3.11
		4.188		.285	3.52
		t-Butyl Acetate			
.1795	.0211	4.530	4.015	.452	3.48
		4.078		.515	3.95
		Isopropyl Benzoate			
.1402	.0122	3.734	3.480	.235	3.14
		3.499		.204	3.40
		t-Butyl Benzoate			
.1972	.0150	3.786	3.460	.316	3.44
		3.470		.326	3.55
		Isopropyl Anisate			
.2299	.0159	4.100	3.680	.410	4.21
		3.690		.420	4.32

The hydrolysis experiments were carried out as previously described.[7]

Summary

In a series of compounds of the general formula RCOOR′, the tendency to cleave and the magnitude of the "*i*" values in sulfuric acid depends upon R′ in the manner H > methyl > ethyl < isopropyl < *t*-butyl. It is suggested that isopropyl and *t*-butyl esters ionize by a mechanism which differs from that of the other members of the series and that this mechanism which has not been observed before in sulfuric acid involves alkyl oxygen fission. The "*i*" values and the yield of ionization products for a number of esters in sulfuric acid are given.

ABERDEEN PROVING GROUND
MARYLAND RECEIVED MAY 27, 1948

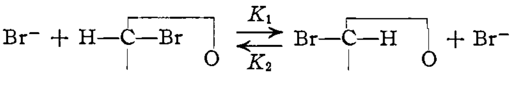
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF STANFORD UNIVERSITY]

The Action of Some Lithium Salts on Acetobromoglucose

BY WILLIAM A. BONNER

Recently it was observed[1] that a solution of lithium bromide and acetobromoglucose in acetic acid underwent a marked mutarotation which was unaffected by the presence of diphenyl disulfide. This note describes several additional observations of this and related phenomena.

Since the heterogeneous reaction of silver chloride with polyacetyl-α-D-glycosyl halides is known[2] to yield the anomeric polyacetyl-β-D-glycosyl chlorides, it seemed reasonable that the following inversion might explain the present reaction



$$\text{Br}^- + \text{H—C—Br} \underset{K_2}{\overset{K_1}{\rightleftarrows}} \text{Br—C—H} + \text{Br}^- \quad (1)$$

An attempt was made to establish this mechanism kinetically by observing the effect of lithium bromide concentration on the mutarotation.

The rate expression for (1) is given by

$$dx/dt = K_1a(c - x) - K_2ax \quad (2)$$

where *c* is the initial concentration of α-acetobro-

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(1) Bonner, THIS JOURNAL, **70**, 3496 (1948).

(2) Schlubach, *Ber.*, **59**, 840 (1926); Schlubach, Stadler and Wolf, *ibid.*, **61**, 287 (1928); Haworth, Hirst and Steacy, *J. Chem. Soc.*, 2864 (1931).

moglucose, a is the concentration of bromide, independent of time, and x is the concentration of β-acetobromoglucose at time t. Equation (2) readily develops to

$$K_1 + K_2 = \frac{2.3}{at}\log\frac{r_0 - r_e}{r_t - r_e} \qquad (3)$$

which is analogous to that developed by Hudson[3] for polarimetric rate studies of simpler reversible processes of the type A $\rightleftarrows$ B.

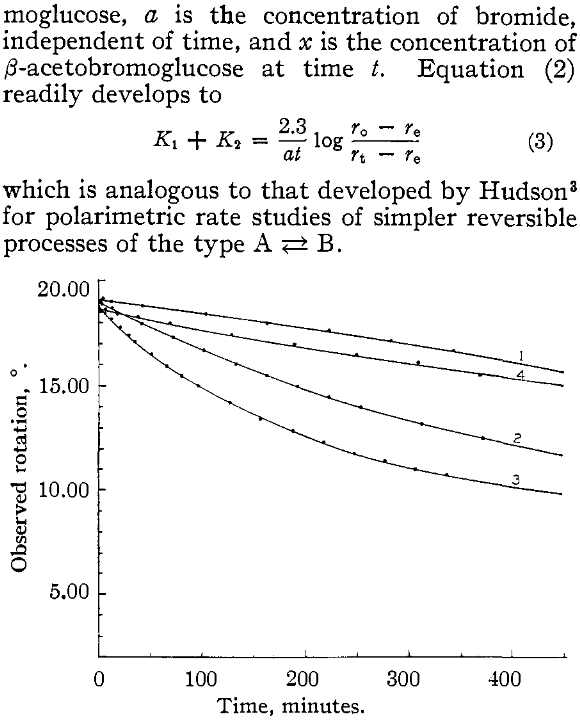

Fig. 1.—Mutarotation of acetobromoglucose in acetic acid in the presence of lithium bromide:

Curve	LiBr, equiv.	$(K_1 + K_2) \times 10^3$
1	1.0	3.19 ± 0.39
2	3.0	3.17 ± .09
3	5.0	3.61 ± .16
4	5.0[a]	1.49 ± .15

[a] In HOAc containing 20% Ac_2O.

Equation (3) was used to calculate rate constant sums given in Fig. 1. The essential agreement of these sums indicates that the action of bromide ion on acetobromoglucose is indeed a second order process in the concentration ranges studied. That this second order process did not correspond to the simple equation (1), however, was shown by several further observations. First, the yield of crude sirup isolated from such mutarotations was only 20 to 27% the weight of the starting material. In contrast, acetobromoglucose in acetic acid alone showed no mutarotation and was recoverable in 88% yield. Second, the mutarotation mixtures darkened considerably and evolved hydrogen bromide, phenomena not observed in the absence of lithium bromide. Third, sirups from the mutarotations analyzed for about 4.5% bromine in contrast to 19.4% required for the equilibrated mixture from (1). Fourth, the aqueous layers obtained on processing the mutarotation mixtures were optically active, indicating that traces of moisture in the glacial acetic acid solvent promoted partial deacetylation. When acetic anhydride was included in the reaction mixture the mutarotation rate was repressed, coloration eliminated, and a crude product containing 5% bromine was isolable in 79% yield. A small amount of α-D-glucose pentaacetate was recovered from the crude sirup in this case, indicating that acetate ion is probably involved in a competing displacement like (1).

The complex interaction of acetobromoglucose, lithium bromide and acetic acid is obscure at present, but it appears that the lithium ion itself influences the reaction in some specific capacity. Thus hydrogen bromide in acetic acid is almost without action on acetobromoglucose, in contrast to lithium bromide. Similarly, lithium perchlorate caused a rapid mutarotation of acetobromoglucose in acetic acid, while that caused by perchloric acid was much slower. As seen in Figs. 2 and 3 lithium salts also enhance the rate of mutarotation of acetobromoglucose in dilute aqueous solutions of acetic acid.

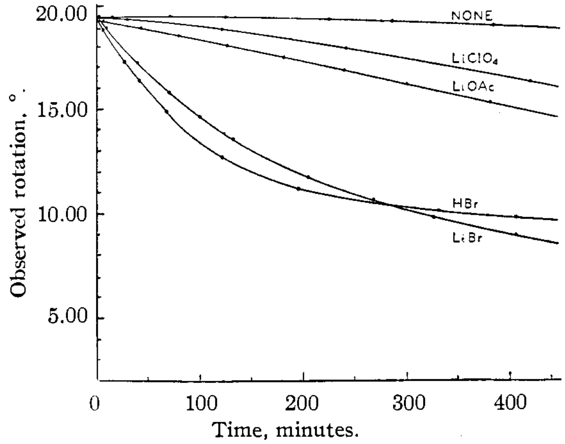

Fig. 2.—Mutarotation of acetobromoglucose in acetic acid–5% water in the presence of several added substances.

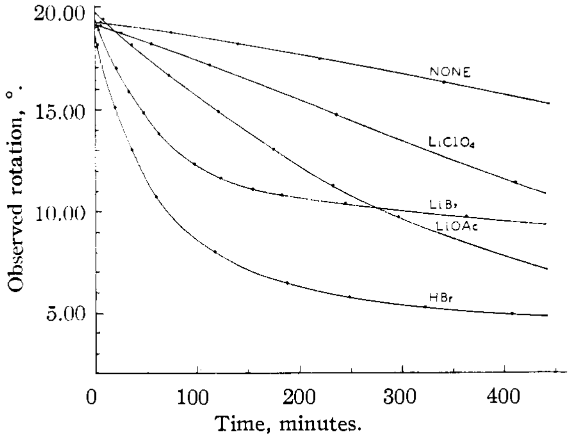

Fig. 3.—Mutarotation of acetobromoglucose in acetic acid–15% water in the presence of several added substances.

Experimental

Mutarotations of Acetobromoglucose and Lithium Bromide.—In the experiments of Fig. 1 acetobromoglucose

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[3] Hudson, *Z. physik. Chem.*, **44**, 487 (1903).

(1.000 g., 0.00243 mole) was dissolved in acetic acid containing the requisite quantity of lithium bromide. The mixture was diluted to 10.0 ml. with acetic acid, thermostated at 25° in a one-decimeter, jacketed tube, and the mutarotation followed. The mixture for the first two experiments darkened so much that the equilibrium value (7.85°) of the third experiment was used in the first two calculations. The equilibrium rotation of the fourth experiment was 10.11°.

The products from each experiment were isolated as follows. The equilibrium mixture was poured into water (40 ml.), the solution saturated with sodium chloride, and extracted twice with 40-ml. portions of ether. The extract was washed thrice with water (20-ml. portions), then with saturated bicarbonate solution (20 ml.), and finally with water (20 ml.). After drying, decolorizing and removing the solvent, sirups were obtained weighing, respectively, 0.27, 0.22, 0.20, 0.79 g. in each experiment. The specific rotation of the crude products in each case were 104.8, 97.7, 88.8, 94.5° in chloroform. On standing the last sirup partially crystallized. It was recrystallized thrice from 2-propanol to give a small quantity of α-D-glucose pentaacetate, m. p. 109–110°, $[\alpha]^{25}\text{D}$ 97.0° (*c*, 0.63, chloroform); mixed m. p. 109–110°. The original aqueous layer from each reaction had rotations of 1.12, 0.90, 0.92, 0.07°, respectively, in a four-decimeter tube. Duplicate bromine analyses applied to products from reactions similar to 3 and 4 in Fig. 1 were 4.48, 4.57% and 4.95, 5.10%, respectively.

The following observations in a one-decimeter tube are of interest by contrast to the rapid mutarotations in Fig. 1. A 10% solution of acetobromoglucose mutarotated from 18.30 to 17.95° in twenty-four hours, and acetobromoglucose was recoverable in 88% yield by processing as above. One gram of acetobromoglucose and 3 ml. of acetic anhydride diluted to 10 ml. with acetic acid mutarotated from 18.47 to 18.28° in twenty-one hours. One gram of acetobromoglucose in 10 ml. of acetic acid containing five equivalents hydrogen bromide mutarotated from 18.65 to 18.35° in twenty-four hours.

Mutarotations of Acetobromoglucose with Other Substances

Lithium Acetate.—One gram of acetobromoglucose was dissolved in 10 ml. of a solution containing five equivalents of lithium acetate. The mutarotation was more gradual than with lithium bromide, changing from 19.09 to 17.85° per decimeter in 655 minutes. Processing the equilibrium mixture (5.35°) as before gave 0.47 g. of crude sirup containing no bromine. This was crystallized from 2-propanol and shown to be impure β-D-glucose pentaacetate, m. p. 128.5–129°, mixed m. p. 130–131°.

Lithium Perchlorate.—Five molecular equivalents were used in an experiment as above, the rotation per decimeter changing from 19.82 to 12.55° in 1373 minutes. The mixture darkened badly and the product was not isolated.

Perchloric Acid.—Sixty per cent. perchloric acid (5 equiv.) was treated with 10% excess acetic anhydride and cooled. One gram of acetobromoglucose was added in the mixture diluted to 10 ml. Mutarotation from 19.70 to 16.31° per decimeter was observed in 2477 minutes.

Mutarotation Accompanying Hydrolysis of Acetobromoglucose.—Several qualitative experiments showed the effect of lithium salts on enhancing the rate of reaction of acetobromoglucose in acetic acid with small amounts of water. In general, 1.00 g. of acetobromoglucose was dissolved in acetic acid containing five equivalents of the salt, 0.5 ml. or 1.5 ml. of water was added, the solution diluted to 10 ml. with acetic acid, and mutarotation followed in a one-decimeter tube. The data are summarized in Figs. 2 and 3.

Summary

The reaction of acetobromoglucose with lithium bromide in acetic acid medium has been found to be a second order process. The sirups from the reaction, however, are more complex than predicted by a simple Walden inversion involving bromide ion. Hydrolysis and acetolysis of the acetobromoglucose are apparently competing reactions.

Lithium salts have been found to enhance the rate of hydrolysis of acetobromoglucose in dilute acetic acid.

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RECEIVED NOVEMBER 10, 1948

[CONTRIBUTION FROM THE NATIONAL BUREAU OF STANDARDS]

Orthoester Reactions of Sugar Acetates with Ammonia[1]

BY HORACE S. ISBELL AND HARRIET L. FRUSH

I. Introduction

In 1940 there was pointed out the importance of the opposite-face mechanism in replacement reactions of the carbohydrates.[2] The formation of orthoesters, of anhydro compounds and of similar products was explained on the basis that in these reactions a neighboring nucleophilic group approaches the face of a carbon atom opposite a replaceable group and combines with inversion of configuration, releasing electrons to the replaceable group. This concept was based in part on the experimental work of Isbell and Frush which was published later.[3] Subsequently, the role of neighboring groups in replacement reactions has been emphasized, especially by Winstein and co-workers,[4] who have done much brilliant research in the field. In continuation of the subject we have presented explanations for many reactions which had seemed somewhat peculiar.[5] This paper concerns some reactions of acetyl sugars with ammonia, and their significance in relation to orthoester formation, and the role of neighboring groups.

The migration of acyl groups from one carbon to another has been known for many years. In 1920, Fischer[6] suggested that the migration of an

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[1] Presented before the Organic Division of The American Chemical Society at the Washington meeting August 30, 1948.

[2] H. S. Isbell, *Ann. Review of Biochem.*, **9**, 65 (1940).

[3] H. L. Frush and H. S. Isbell, *J. Research, Natl. Bur. Stand.*, **27**, 413 (1941).

[4] S. Winstein and R. E. Buckles, THIS JOURNAL, **64**, 2780 (1942); **65**, 613 (1943); S. Winstein and D. Seymour, *ibid.*, **68**, 119 (1946).

[5] H. S. Isbell, *J. Research N. B. S.*, **32**, 45 (1944); H. L. Frush and H. S. Isbell, *ibid.*, **35**, 111 (1945); H. S. Isbell, *Ann. Review of Biochem.*, **12**, 205 (1943).

[6] E. Fischer, *Ber.*, **53**, 1621 (1920).