

carbons (distance 3.55 Å). These, the shortest intermolecular contacts in the structure, show up most clearly in the *ac* Fourier (Fig. 1). Molecules within a layer are at contact along $x = 1/2$, for here the methylene carbon of one aziridine ring is separated from the corresponding carbon of another ring by a distance of only 3.96 Å. The crystal has sizable "holes" on the non-hydrogen-bonded sides of the aziridine rings, *i.e.*, in the lower left and upper right portion of the cell face pictured in Fig. 2.

As is evident from Fig. 3, the view down *a*, the structure may be regarded alternatively as a stack of hydrogen-bonded sheets parallel to *bc*. Each sheet consists of a series of macrocyclic rings hav-

ing 22 atoms (including hydrogen) but, in effect, is only one molecule thick. Since only van der Waal's forces exist between sheets, preferential cleavage of the crystal occurs parallel to the surface of the sheets.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING, STANFORD UNIVERSITY, STANFORD CALIFORNIA]

Deuterium Isotope Effects During Acid Catalyzed Anomerization and C1 Acetoxy Exchange Reactions of Acetylated D-Aldopyranoses¹

BY WILLIAM A. BONNER

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C1 Inversion and C1 acetoxy exchange rates have been measured for penta-*O*-acetyl-D-glucose and tetra-*O*-acetyl-D-xylose anomers both in systems containing AcOH-Ac₂O-H₂SO₄ and containing AcOD-Ac₂O-D₂SO₄, in order to investigate the deuterium isotope effect in the anomerization reaction. In deuteriated anomerization environments the rates of both inversion and C1 acetoxy exchange were approximately 1.7 times greater than those observed in environments lacking deuterium. A qualitative explanation for these observations is given, and the data are discussed with reference to an S_N1 mechanism for the anomerization reaction.

Introduction

Recently we have reported² comparative data for the C1 inversion rates and C1 acetoxy exchange rates prevailing during sulfuric acid catalyzed anomerizations of acetylated aldopyranoses at 25% in 1:1 mixtures of acetic acid and acetic anhydride. Our findings were that those acetylated aldopyranose anomers having a *cis* disposition of acetoxy groups at C1 and C2 showed inversion and exchange rates essentially identical, while those anomers having *trans* C1-C2 acetoxy groups showed C1 exchange rates some 3 to 14 times greater than their corresponding inversion rates. These data could be interpreted mechanistically in two ways, either in terms of an S_N2 displacement 2 of the C1 conjugate acid of the acetylated aldose by acetic anhydride or acetic acid or by an S_N1 ionic process such as 3, either following initial formation 1 of the C1 conjugate acid of the acetylated aldose. In terms of either mechanism the enhanced rate of C1 acetoxy exchange over inversion for *trans* C1-C2 anomers was explainable as a result of the C2 acetoxy participation process 4, an explanation previously offered and well documented by Lemieux and his students.³

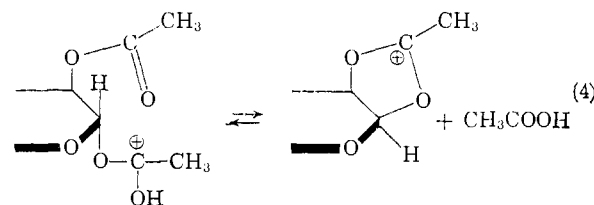
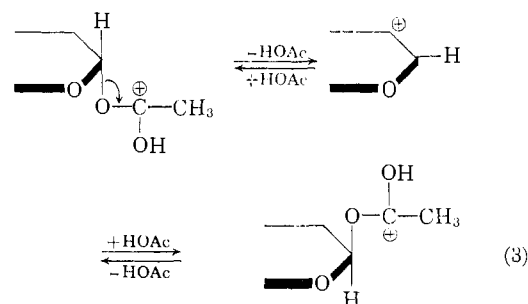
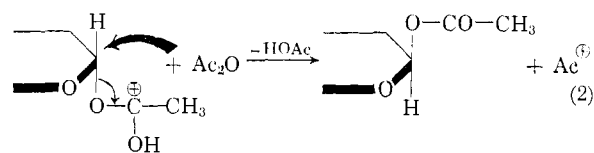
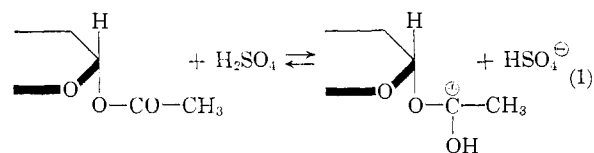
Because of the mechanistic ambiguity inherent in the above and previous⁴ studies of the anomerization reaction, an ambiguity occasioned by the complication of the C2 acetoxy participation process 4, we have more recently turned our attention⁵

(1) We are grateful to the Quaker Oats Company for their generous support of a portion of this research.

(2) W. A. Bonner, *J. Am. Chem. Soc.*, **81**, 5171 (1959).

(3) R. U. Lemieux and coworkers, *Can. J. Chem.*, **30**, 295 (1952); **33**, 109, 120, 134, 148 (1955).

(4) W. A. Bonner, *J. Am. Chem. Soc.*, **73**, 2659 (1951); E. B. Painter, *ibid.*, **75**, 1137 (1953); **81**, 5696 (1959).



to anomerization and C1 acetoxy exchange experiments employing the anomers of tetra-*O*-acetyl-2-

(5) W. A. Bonner, *ibid.*, **83**, 962 (1961).

TABLE I
ANOMERIZATION AND C1 ACETOXY EXCHANGE RATES FOR ACETYLATED D-ALDOPYRANOSIDES UNDER VARIOUS EXPERIMENTAL CONDITIONS

No.	Acetylated D-Aldopyranose	Solvent	Catalyst	Catalyst conc., M	A $k_{\alpha} + k_{\beta}$, min. ⁻¹	B k_{β} , min. ⁻¹	C k_{α} , min. ⁻¹	D $k_{\text{exch-}\beta}$, min. ⁻¹	E $k_{\text{exch-}\alpha}$, min. ⁻¹
1	Glucose	AcOH-Ac ₂ O ^a	H ₂ SO ₄	0.50	0.0337 ^{b,c}	0.0296 ^{b,c}	0.0041 ^{b,c}	0.433 ^{e,d}	0.00422 ^e
2	Glucose	AcOD-Ac ₂ O	D ₂ SO ₄	.50	.0577	.0507	.0070	0.757 ^d	0.0068 ^e
3	Xylose	AcOH-Ac ₂ O	H ₂ SO ₄	.05	.0703 ^f	.0551 ^f	.0152 ^f
4	Xylose	AcOD-Ac ₂ O	D ₂ SO ₄	.05	.1225	.0962	.0263
5	Glucose	Ac ₂ O	H ₂ SO ₄	.50	.590	.519	.071
6	Glucose	Ac ₂ O	D ₂ SO ₄	.50	.790	.695	.095
7	Glucose	Ac ₂ O	H ₂ SO ₄	.05	.0725	.0639	.0086	0.310 ^d
8	Glucose	AcOH	H ₂ SO ₄	.50	.00430	.00378	.00052	0.0470 ^d	0.0004 ^f

^a 1:1 mixture in each case. ^b Average of all values from past work. ^c Ref. 2. ^d Obtained using tetra-*O*-acetyl- β -D-glucopyranosyl acetate-1-C¹⁴ (ref. 2). ^e Obtained using tetra-*O*-acetyl- α -D-glucopyranosyl acetate-2-C¹⁴ (ref. 2). ^f Ref. 7.

deoxy-D-glucopyranose,⁶ a system in which such C2 acetoxy participation is precluded. In these studies it was found that for both anomers the rates of C1 acetoxy exchange were 1.8 to 3.7 times as rapid as the rates of C1 inversion, a fact which is in qualitative accord with the predictions of an S_N1 mechanism such as (3) and which precludes the S_N2 process 2. Furthermore, on application of steady-state treatment to the rate equations applying to the ionic mechanism 3, it was possible⁵ to predict with reasonable accuracy the $k_{\text{exch}}/k_{\text{inv}}$ ratio for each of the anomers in question, thus adding weight to the validity of mechanism 3.

We have now undertaken a study of the deuterium isotope effect observed during anomerization and C1 acetoxy exchange reactions of several acetylated aldopyranose anomers, with the hope of obtaining additional data bearing on the validity of our demonstration⁵ of an ionic mechanism for the anomerization process.

Methods and Results

Penta-*O*-acetyl- β -D-glucopyranose and tetra-*O*-acetyl- β -D-xylopyranose have been anomerized at 25° in the solvents and with the catalysts listed in Table I. The polarimetrically determined anomerization rate for each experiment is given in Column A of Table I. Individual inversion rate constants applying to each anomerization have been calculated by combining the data of Column A with the anomerization equilibrium data which we have reported⁷ in a recent study of the generality of anomerization reaction. These specific inversion rates are listed in Columns B and C of Table I. The rates of C1 acetoxy exchange under several of the anomerization environments employed in Table I have been measured by following as a function of time the loss of radioactivity from the appropriate anomer of tetra-*O*-acetyl-D-glucopyranosyl acetate-C¹⁴. These C1 acetoxy exchange rate data are listed in Columns D and E of Table I. The precision of the data in Table I proved to be comparable with those reported in earlier studies^{2,4,7,8} of a similar sort. In Table II are recorded the numerical values of significant ratios of the various specific rate constants listed in Table I.

(6) W. A. Bonner, *J. Org. Chem.*, **26**, 908 (1961).

(7) W. A. Bonner, *J. Am. Chem. Soc.*, **81**, 1448 (1959).

(8) W. A. Bonner, *ibid.*, **80**, 3372, 3697 (1958).

TABLE II
SIGNIFICANT RATIOS OF SPECIFIC RATE CONSTANTS IN TABLE I

No.	Acetylated D-aldopyranose	Solvent ^a	Ratio	Items in Table I	Value
1	β -Glucose	A	$(k_{\text{exch-}\beta}/k_{\beta})_{\text{H}}$	1D/1B	14.6
2	β -Glucose	A	$(k_{\text{exch-}\beta}/k_{\beta})_{\text{D}}$	2D/2B	15.6
3	α -Glucose	A	$(k_{\text{exch-}\alpha}/k_{\alpha})_{\text{H}}$	1E/1C	1.03
4	α -Glucose	A	$(k_{\text{exch-}\alpha}/k_{\alpha})_{\text{D}}$	2E/2C	0.97
5	β -Glucose	A	$(k_{\alpha} + k_{\beta})_{\text{D}}/(k_{\alpha} + k_{\beta})_{\text{H}}$	2A/1A	1.71
6	β -Glucose	A	$(k_{\text{exch-}\beta})_{\text{D}}/(k_{\text{exch-}\beta})_{\text{H}}$	2D/1D	1.75
7	β -Glucose	A	$(k_{\beta})_{\text{D}}/(k_{\beta})_{\text{H}}$	2B/1B	1.71
8	α -Glucose	A	$(k_{\text{exch-}\alpha})_{\text{D}}/(k_{\text{exch-}\alpha})_{\text{H}}$	2E/1E	1.6
9	α -Glucose	A	$(k_{\alpha})_{\text{D}}/(k_{\alpha})_{\text{H}}$	2C/1C	1.71
10	β -Xylose	A	$(k_{\alpha} + k_{\beta})_{\text{D}}/(k_{\alpha} + k_{\beta})_{\text{H}}$	4A/3A	1.74
11	β -Glucose	B	$(k_{\alpha} + k_{\beta})_{\text{D}}/(k_{\alpha} + k_{\beta})_{\text{H}}$	6A/5A	1.34
12	β -Glucose	B	$(k_{\text{exch-}\beta}/k_{\beta})_{\text{H}}$	7D/7B	4.85
13	β -Glucose	C	$(k_{\text{exch-}\beta}/k_{\beta})_{\text{H}}$	8D/8B	12.4
14	α -Glucose	C	$(k_{\text{exch-}\alpha}/k_{\alpha})_{\text{H}}$	8E/8C	0.8

^a A, 1:1 mixtures of either Ac₂O-AcOH or Ac₂O-AcOD; B, 100% Ac₂O; C, 100% AcOH.

Discussion

Examination of the various ratios listed in Table II leads to some interesting generalizations regarding anomerization and C1 acetoxy exchange phenomena and permits, we believe, certain mechanistic conclusions to be made. In the first place both the anomerization (No. 5) and inversion (No. 7,9) rates for glucose and xylose (No. 10) acetates as well as the C1 acetoxy exchange rates for α -D-glucose (No. 8) and β -D-glucose (No. 6) acetates are approximately 1.7 times greater in 1:1 AcOD-Ac₂O with D₂SO₄ catalyst than in 1:1 AcOH-Ac₂O containing H₂SO₄ catalyst. This observation is in accord with the more general parallel observation that the rates of most acid-catalyzed reactions are more rapid, for example, in D₂O than in H₂O.⁹ In terms of the ionic mechanism 3 under consideration, the rate increases noted for the deuterium-containing systems are explainable in terms of a shift of the rapid equilibrium 1 to the right when D₂SO₄ is substituted for H₂SO₄. This

(9) Cf. K. Wiberg, *Chem. Revs.*, **55**, 718 (1955), for numerous examples and a discussion of this generalization for both aqueous and non-aqueous systems.

equilibrium shift increases the concentration of the common conjugate acid of the acetylated aldose, thus increasing the rates of both reactions 3 and 4 to comparable extents. The latter steps, involving no O-H bond fission, should not be subject to a deuterium isotope effect. It is interesting to note that the anomerization rate isotope effect in pure acetic anhydride (No. 11) is only about 78% as great as the corresponding isotope effect (No. 5) in 1:1 acetic acid-acetic anhydride, an observation which suggests that acetic anhydride is more basic than acetic acid to H₂SO₄.

The essentially similar rates of C1 exchange and C1 inversion for 1,2-*cis* anomers (No. 3) as well as the enhanced rate of exchange over inversion for 1,2-*trans* anomers (No. 1) find their parallels in the present deuterated systems (Nos. 4 and 2, resp.) to practically equivalent extents. More significant mechanistically are the similarities in values for the deuterium isotope effects in all C1 acetoxy inversion and exchange rates. Table II reveals that the kinetic isotope effects for $k_{\text{exch-}\beta}$ (No. 6), k_{β} (No. 7), $k_{\text{exch-}\alpha}$ (No. 8) and k_{α} (No. 9) are all identical within experimental error¹⁰ under similar environmental conditions. To us these similarities argue strongly for a common type of conjugate acid precursor, that of the acetylated aldose, in both the C1 exchange and inversion reactions. This observation is thus in accord with mechanism 3 but, in itself, does not exclude mechanism 2.

The similarities in the values of $(k_{\text{exch-}\beta}/k_{\beta})_{\text{H}}$ in 1:1 acetic acid-acetic anhydride (No. 1) and 100% acetic acid (No. 14) suggest that this ratio is not particularly sensitive to changes in solvent composition. With the limited data at hand,

(10) Cf. Ref. 7 for a discussion of the errors involved, particularly with respect to specific rate constants for inversion.

however, it is not possible to determine if the rather different value for this ratio in 100% acetic anhydride (No. 12) is due to a difference in solvent composition or in catalyst concentration.

Experimental

Deuterio-Sulfuric Acid.—Liquid sulfur trioxide (Sulfam) (10.092 g.) was weighed into a small glass-stoppered flask. The stopper was replaced by a rubber stopper equipped with a small vent slit and a hypodermic syringe. The flask was chilled in an ice-bath and the calculated volume (2.34 ml.) of 99.5% deuterium oxide was added to the sulfur trioxide through the hypodermic needle very slowly with swirling and cooling. The resulting deuterio-sulfuric acid, having d^{20} 1.868 was used directly in the anomerization and exchange experiments described below. As a control, unlabeled sulfuric acid, d^{20} 1.834, was made in an identical fashion by the action of water on sulfur trioxide. Use of this sulfuric acid as catalyst in anomerization experiments gave results identical within experimental error to those obtained with commercial C.P. sulfuric acid.^{2,4}

Deuterio-acetic acid was prepared typically as follows. Acetic anhydride (15.6 ml.) was treated with a drop of the above deuterio-sulfuric acid. The calculated volume of 99.5% deuterium oxide (3.08 ml.) was added dropwise with swirling and cooling. After standing in a glass-stoppered vessel for several days the mixture was treated with anhydrous sodium acetate (ca. 1 g.) and the product was distilled through a small Claisen head, b.p. 117°.

Anomerization experiments were conducted at 25° under the solvent and catalyst conditions listed in Table I in the manner fully described previously.^{2,4,7} Equilibrium constant data previously published^{4,7} have been used to calculate the individual inversion rate constants given in Table I.

C1 acetoxy exchange experiments were performed at 25° under the indicated solvent and catalyst conditions in Table I according to the procedures which we have described previously.² For these exchange experiments the anomers of tetra-*O*-acetyl-D-glucopyranosyl acetate-C¹⁴, prepared as described before,² were employed. The exchange rate constants shown are the averages of those calculated on the basis of products isolated from 4 to 6 aliquots taken at different times from each reaction mixture. The precision in the exchange rate constants in Table I was about the same as that previously reported.²

[CONTRIBUTION FROM THE RESEARCH LABORATORY, NATIONAL ENGINEERING SCIENCE COMPANY, PASADENA, CALIFORNIA]

B¹¹ N.m.r. Chemical Shifts. II. Amine-borate Ester Complexes, Alkoxydifluoroborane Trimers and Tetrahaloborate Ions^{1,2}

BY HERBERT LANDESMAN AND ROBERT E. WILLIAMS

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The B¹¹ nuclear magnetic resonance spectra of BF₂Cl and BCIF₂ have been obtained but no B¹¹-F¹⁹ spin coupling could be observed. Some amine addition compounds of triethyl and triallyl borates have been prepared and the B¹¹ chemical shifts are found to be dependent on reactant concentrations. Thus borate-amine exchange is taking place. Evidence that the compounds produced from the reaction of one mole of various borate esters and two moles of boron trifluoride are alkoxydifluoroborane cyclic trimers rather than the previously suggested coordination complexes is presented. Chemical shifts for tetrahalo and tetrapseudohalo borate ions prepared in nitrobenzene are presented.

In the previous paper,¹ B¹¹ chemical shifts for a large variety of boron compounds were presented and correlations were made between shift values and bonding in the compounds. Another group of compounds has been reported by Phillips and co-workers³ and where there was overlap there is reasonably good agreement.

(1) Paper I; T. P. Onak, H. Landesman, R. E. Williams and I. Shapiro, *J. Phys. Chem.*, **63**, 1533 (1959).

(2) This paper was presented at the 138th Meeting of the American Chemical Society, New York, September 1960.

(3) W. D. Phillips, H. C. Miller and E. L. Muettterties, *J. Am. Chem. Soc.*, **81**, 4496 (1959).

Additional B¹¹ shift values (δ) are shown in Table I. There is noted a large shift to high field in the change from sp² bonding in boron triethyl to sp³ in boron triethyl dimethyl amine complex. Also of interest is the effect of phenyl groups in triphenyl boron as compared to triethyl boron. Here the resonance effect of the phenyl groups permits greater shielding and a shift to higher field. Shifts for the complexes of boron triiodide are at highest field yet observed for boron compounds.

Boron-Fluorine Coupling.—Boron-fluorine spin coupling in B¹¹ spectra has not been observed either