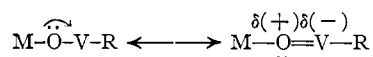


though both are reduced completely to the divalent state under these conditions,³ is probably due to the presence of the oxygen ligand in the latter case. Resonance forms such as



would effectively decrease the electron attracting power of the vanadium center and the observed

lower relative reactivity of propylene with this system (*vs.* VCl₄) is in accord with the preceding analysis.

Acknowledgments.—The authors are indebted to Mr. J. J. Smith, Miss O. M. Garty and Dr. G. W. Phillips for many stimulating discussions, and to the Union Carbide Plastics Research Department Analytical Group for assistance with some of the analyses.

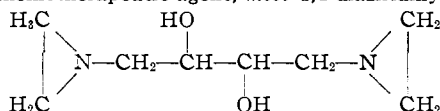
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, STANFORD RESEARCH INSTITUTE, MENLO PARK, CALIFORNIA]

The Crystal Structure of *meso*-1,4-Diaziridinyl-2,3-butanediol¹

BY EDWIN S. GOULD AND R. A. PASTERNAK

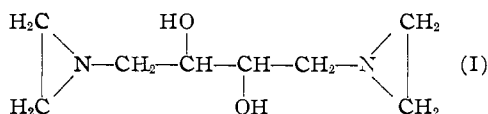
RECEIVED OCTOBER 10, 1960

The crystal structure of the cancer chemotherapeutic agent, *meso*-1,4-diaziridinyl-2,3-butanediol



has been determined. The space group is $P2_1/c-C_{2h}^5$ with two molecules in the unit cell. The diol molecules form a layer-structure perpendicular to the *b*-plane with hydrogen bonds connecting each -OH group in one layer to a nitrogen atom of an adjacent layer. In common with other structures having three-membered rings, the observed C-C bond length (1.46 Å.) is considerably less than the usual C-C bond length.

The compound 1,4-diaziridinyl-2,3-butanediol,²



(I) besides exhibiting marked anti-tumor activity, has several features which might warrant structural study. First, no compound having the ethyleneimine (aziridine) ring system appears to have been studied in the solid state,³ and it seemed likely that the C-C and C-N bond lengths and the exocyclic bond angles associated with this highly strained ring might be significantly different from the usual values existing in unstrained compounds. The nature of the hydrogen bonding in this diol was also of interest, for two modes of intramolecular hydrogen bonding and two more modes of intermolecular hydrogen bonding were possible. Finally, the compound has been assumed,² from the manner of its formation from *meso*-1,2,3,4-diepoxybutane, to be the *meso*, rather than the *d,l* form of the diol, but confirmation of this assignment was desirable.

Experimental

The diol (Fwt. 172.2) crystallizes from ethylene glycol monomethyl ether in platelets. Weissenberg photographs, using Cu K α radiation, established the monoclinic cell dimensions (Å.)

(1) This research was sponsored by the Research Committee of the Division of Physical and Biological Sciences of Stanford Research Institute. The support of this committee is gratefully acknowledged.

(2) This diol was first prepared by L. Vargha, L. Toldy and E. Kasztreiner, *Acta Chim. Acad. Sci. Hung.*, **19**, 295 (1959). It is described in greater detail by E. J. Reist, I. Junga, M. E. Wain, O. P. Crews, L. Goodman and B. R. Baker, *J. Org. Chem.*, in press (1961).

(3) However, microwave studies of gaseous ethyleneimine have been reported by T. E. Turner, V. C. Fiora and W. M. Kendrick, *J. Chem. Phys.*, **23**, 1966 (1955).

$$a = 8.71 \quad b = 6.98 \quad c = 7.59 \quad (\text{each} \pm 0.01 \text{ \AA}) \quad \beta = 95.4^\circ \\ V = 460 \text{ \AA}^3$$

The observed density (obtained by flotation) was 1.25 g./cc., corresponding to 1.99 molecules per unit cell. The plane of the plates corresponds to the *bc* plane of the cell.

The systematic absences were: $h0l$ if *l* is odd, and $0k0$ if *k* is odd. These establish the centrosymmetric space group $P2_1/c-C_{2h}^5$. The molecule must have a center of symmetry, and the asymmetric unit contains four carbons, a nitrogen, an oxygen and eight hydrogen atoms. The observed space group is consistent with the *meso* form of the diol but not with the *d,l*-form.

Zero and upper layer data were taken with multiple films for rotation about the three major axes. For rotation about *a*, 8 layers were taken; for rotation about *b*, 6 layers; and for rotation about *c*, 7 layers. In effect, data were taken in triplicate except for a small number of reflections having high values of $\sin \theta$. Intensities were measured by visual comparison with intensity strips. Separate intensity strips were used for each rotation axis since a different crystal was used for each axis. Lorentz and polarization corrections were made in the usual way, and the corrected intensities were normalized to a single scale by cross correlation between the various sets of films. Absorption corrections were not made. For the most part, intensities obtained from rotation about *b* were given preference in the determination of the structure, but with reflections having *k* values of 6, 7 or 8, intensities obtained from rotation about the *a* and/or *c* axes were used.

Determination of the Structure

Reflections for which (*k* + *l*) is even were found to be much stronger than those for which (*k* + *l*) is odd, thus indicating that the structure approaches an "a-face-centered" one. Moreover, relative intensities of the corresponding reflections on the $h0l$, $h2l$ and $h4l$ photographs were very similar; the same was true of the corresponding reflections on the $h1l$, $h3l$ and $h5l$ photographs. This distribution indicates a layer-structure with the layers perpendicular to *y*, separated by the distance *b*/2. In accordance with this picture, the 020 reflection is much more intense than any of the others. Sixty-one intensities were available for the $h0l$ projection. The sharpened Patterson projection⁴ along *y* was calculated. This showed three well-resolved peaks close to the origin. These peaks were used for application of the superposition

(4) A. L. Patterson, *Z. Krist.*, **90**, 517 (1935).

method.⁵ This approach, in conjunction with the consideration of molecular models, led to a reasonable trial structure.

Structure factors for the reflections in the $h0l$ zone were determined from the provisional parameters, and an electron density projection calculated. Four successive Fourier summations were carried out. The last included all 61 reflections and did not result in any additional sign changes. The final $h0l$ Fourier map is shown in Fig. 1.

Further refinement of the $h0l$ projection involved three successive structure-factor least square cycles; in the least-squares treatment, only the diagonal terms of the normal equations were calculated. During these cycles, individual isotropic temperature factors for each atom were evaluated; these were about 3 \AA^2 for the chain carbons (C_1 and C_2), about 4 \AA^2 for the ring carbons and only about 2 \AA^2 for the oxygen and nitrogen atoms. The value of the correlation factor R , where R is defined by the equation

$$R = \frac{\sum_{N} \|F_{\text{obsd.}}\| - \|F_{\text{calcd.}}\|}{\sum_{N} \|F_{\text{obsd.}}\|}$$

was 0.18 at this stage of the determination.

Due to the near-planarity of the molecule, the $hk0$ and the $0kl$ Patterson projections were very poorly resolved and could not be used to determine y -parameters for the atoms. Instead, estimates were made using the observed projected bond lengths in the ac projection and known "standard" bond lengths, *i.e.*, C-C 1.53 \AA , C-N 1.49 \AA and C-O 1.44 \AA . The N-C-C-C-C-N chain was assumed to be "kinked," but the projected values for the C-O bond and the bonds in the ring lay close enough to the usual bond lengths so that both the ring and the C-O bond were taken, as a first approximation, to lie parallel to the ac plane. These preliminary y -parameters were refined by least-squares while keeping the x and z parameters constant and using initially only the $h1l$, then both the $kl1$ and the $h2l$ data. The parameters converged rapidly; after three iterations with both layer-data, the shifts were less than 0.02 \AA . The subsequent refinement of all parameters based on the complete data converged after another three iterations.

For the final stages of refinement, the eight hydrogen atoms were included. Their approximate parameters were calculated assuming normal C-H and O-H bond lengths and appropriate interbond angles⁶ around the heavy atoms. Each hydrogen atom was assumed to have an isotropic temperature factor of 4.0 \AA^2 . Temperature anisotropies for the carbon, nitrogen and oxygen atoms were taken into account by introducing six anisotropic temperature factors for each of these atoms. These temperature factors were of the form

$$T_i = \exp(-\alpha_i h^2 - \beta_i k^2 - \gamma_i l^2 - \delta_i hk - \epsilon_i hl - \eta_i kl)$$

In the least-squares refinement cycles, reflections having $F_{\text{obsd.}}$ greater than 4.0 were weighted in inverse proportion to $F_{\text{obsd.}}$. Those having $F_{\text{obsd.}}$ lying between 4.0 and the minimum observed value were given unit weight. Nine of the very intense reflections having very low values of $\sin \theta$ were omitted, for here extinction effects were especially pronounced. After two iterations, slight adjustments of the scaling factors of some of the layers were carried out by multiplying each observed intensity in the layer by the ratio $\Sigma F_{\text{calcd.}} / \Sigma F_{\text{obsd.}}$ for the layer.⁷ After three additional cycles, the indicated parameter shifts were less than 0.005 \AA , in contrast to the average standard errors of 0.008 \AA in the

(5) M. J. Buerger, *Acta Cryst.*, **3**, 87 (1950); **4**, 531 (1951). For a more detailed description of the application of this method, see R. A. Pasternak, *ibid.*, **9**, 341 (1956).

(6) The H-C-H bond angles at the ring carbons were assumed to be 116° (see C. A. Coulson and W. E. Moffitt, *J. Chem. Phys.*, **15**, 151 (1947)). The other interbond angles involving hydrogen atoms were taken as 109° .

(7) Since these ratios did not show a systematic trend, this procedure appeared preferable to improving agreement merely by adjustment of temperature factors in the y direction; nevertheless, the β -values for the atoms must be regarded as somewhat less reliable than the α - and γ -values. Those very intense reflections omitted from the least-squares refinement were omitted also from the ratios used in these adjustments of scale factors.

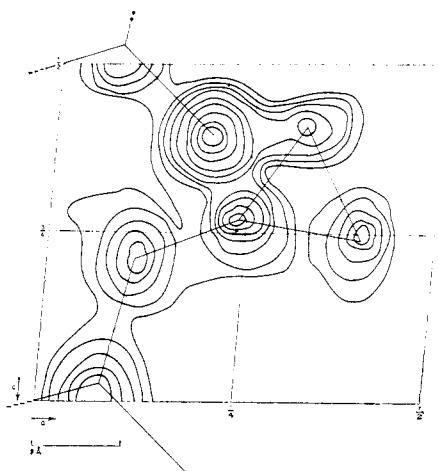


Fig. 1.—Electron density projection of one half molecule of *meso*-1,4-diaziridinyl-2,3-butanediol on (010). Contours are at approximately $1 \text{ e.}\text{\AA}^{-2}$ intervals, beginning with $1.0 \text{ e.}\text{\AA}^{-2}$. Intersections of the "bonds" mark the positional parameters resulting from the final 3-dimensional refinement.

parameters. The final R value, with 482 observed reflections included,⁸ was 0.126.

Table I lists the final positional parameters for each of the atoms in the asymmetric unit, together with the standard deviations calculated using the weighted residuals from the least-squares treatment. Table II lists the final temperature parameters. Table III gives the bond distances, together with estimated standard deviations,⁹ and the interbond angles. The average deviation of about 0.010

TABLE I

FINAL POSITION PARAMETERS FOR *meso*-1,4-DIAZIRIDINYL-2,3-BUTANEDIOL

	x	y	z
C_2	0.0734 ± 0.0008	0.0532 ± 0.0010	0.9747 ± 0.0008
C_1	$.1161 \pm .0008$	$.9807 \pm .0010$	$.7989 \pm .0008$
$C\alpha$	$.3233 \pm .0010$	$.0011 \pm .0011$	$.5930 \pm .0012$
$C\beta$	$.3964 \pm .0009$	$.0171 \pm .0011$	$.7743 \pm .0011$
N	$.2423 \pm .0006$	$.1010 \pm .0007$	$.7347 \pm .0008$
O	$.1997 \pm .0005$	$.0164 \pm .0006$	$.1073 \pm .0006$
H_1 (O)	0.215	0.167	0.151
H_2 (C_2)	.048	.204	.938
H_3 (C_1)	.032	.036	.696
H_4 (C_1)	.155	.840	.777
H_5 ($C\alpha$)	.341	.117	.537
H_6 ($C\alpha$)	.286	.891	.510
H_7 ($C\beta$)	.425	.135	.837
H_8 ($C\beta$)	.460	.909	.815

TABLE II

ANISOTROPIC TEMPERATURE FACTORS FOR *meso*-1,4-DIAZIRIDINYL-2,3-BUTANEDIOL

	α_i	β_i	γ_i	δ_i	ϵ_i	η_i
C_2	0.015	0.023	0.018	-0.001	0.005	0.000
C_1	.014	.029	.017	-.004	.006	-.009
$C\alpha$.022	.033	.022	.002	.012	-.006
$C\beta$.012	.030	.025	.000	.007	-.005
N	.012	.029	.015	.004	.008	.007
O	.014	.026	.018	.000	-.005	.003

(8) A list of all calculated and observed structure factors for this structure has been deposited as Document No. 6556 with the ADI Auxiliary Publications Project, Photoduplication Service, Library of Congress, Washington 25, D. C., U. S. A. A copy may be secured by citing the Document number and remitting \$1.25 for photoprints or \$1.25 for 35 mm. microfilm in advance by check or money order payable to Chief, Photoduplication Service, Library of Congress.

(9) G. A. Jeffrey and D. W. J. Cruickshank, *Quart. Rev.*, **VII**, 369 (1953).

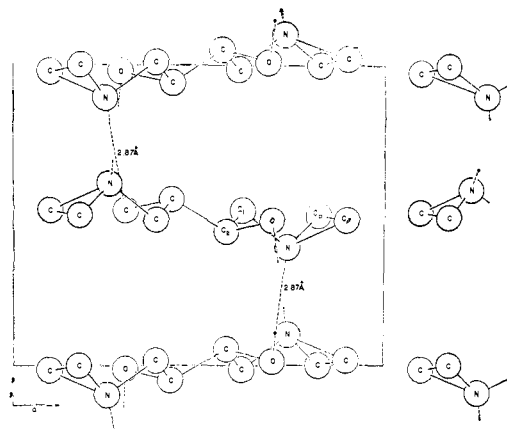


Fig. 2.—A view of the structure perpendicular to the *ab* face.

Å. in the bond lengths corresponds to an error of about 1.5° in the bond angles.

TABLE III

BOND DISTANCES AND BOND ANGLES			
Bond	<i>d</i> (Å.)	Angle	(°)
C ₂ -C ₂	1.558 ± 0.014	C ₂ -C ₂ -C ₁	108.5
C ₁ -C ₂	1.505 ± .010	C ₂ -C ₂ -O	108.9
C ₂ -O	1.442 ± .008	C ₁ -C ₂ -O	107.9
C ₁ -N	1.501 ± .010	C ₂ -C ₁ -N	109.4
C _α -N	1.510 ± .011	C ₁ -N-C _α	116.3
C _β -N	1.468 ± .010	C ₁ -N-C _β	110.8
C _α -C _β	1.463 ± .012	C _α -N-C _β	58.9
O-H...N	2.874 ± .006	N-C _α -C _β	59.1
		N-C _β -C _α	58.9

Discussion

Of the interatomic distances listed, the C-O bond and the O-H...N distance in the intermolecular hydrogen bond are close to the conventional values¹⁰ and require little comment. The others may be considered on the basis of numerical significance levels suggested by Cruickshank,¹¹ who feels that the difference between two bond lengths is unequivocally significant only if the observed values differ by more than $2.33\sqrt{\sigma_1^2 + \sigma_2^2}$, where σ_1 and σ_2 are the standard errors in the bond lengths being compared.

By this criterion, the C_α-C_β bond in the ring is significantly shorter than the C-C bonds in the chain, but its length agrees well with the C-C bonds in the three-membered ring compounds, ethyleneimine⁸ (1.48 Å.), ethylene sulfide¹² (1.49 Å.), ethylene oxide¹² (1.47 Å.), spiropentane¹³ (1.48 Å.) and cyclopropanecarbohydrazide¹⁴ (1.48, 1.49 and 1.51 Å.). This shortening is presumably a consequence of the inability of the orbitals of the carbon atom to rehybridize to about 60°, the angle between atoms in the ring. The area of greatest orbital overlap lies well outside the ring, and for the necessary bonding the carbons must approach

(10) For a summary of O-H...N- bond lengths, see G. C. Pimentel and A. L. McClellan, "The Hydrogen Bond," Freeman and Co., Inc., San Francisco, 1960, p. 285.

(11) D. W. J. Cruickshank, *Acta Cryst.*, **2**, 65 (1949); **3**, 72 (1960).

(12) G. L. Cunningham, A. W. Boyd, R. J. Myers and W. D. Gwinn, *J. Chem. Phys.*, **19**, 676 (1951).

(13) J. Donohue, G. L. Humphrey and V. Schomaker, *J. Am. Chem. Soc.*, **67**, 332 (1945).

(14) D. B. Chesnut and R. E. Marsh, *Acta Cryst.*, **11**, 413 (1958).

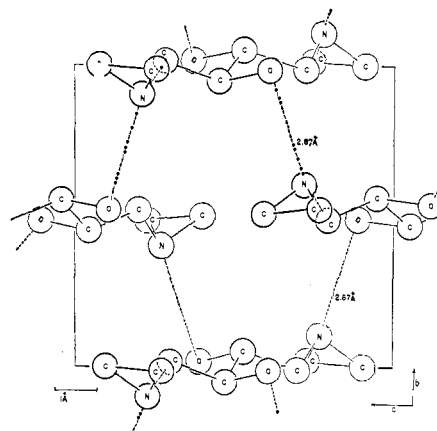


Fig. 3.—A view of the structure perpendicular to the *bc* face.

each other more closely than do the carbon atoms in an aliphatic chain where orbital overlap is greatest along the line of centers.¹⁵ Even with the close approach, however, the C-C bonds in three-membered rings are weaker than those in normal aliphatic and alicyclic systems.

In the four-carbon chain, the C-C bond at the center (1.56 Å.) is significantly longer than the C-C bonds on either side of it (1.51 Å.). This type of "short-long-short" arrangement has been observed on a more extended scale for the aliphatic chains of a number of compounds,¹⁶ although it is by no means general.

Perhaps the most disturbing feature of the structure is the apparent difference in length between the two C-N bonds in the ring (1.51 vs. 1.47 Å.). By the Cruickshank standard,¹¹ which presupposes randomness of errors, this difference is significant. We believe, however, that it is much more likely an artifact arising from some type of systematic error in our experiments. If such a difference were real, it would indicate that the bonds in the aziridine ring were extraordinarily sensitive to dissymmetry of crystal environment. In view of the relatively high temperature factor of C_α, a check on this difference by a low temperature study of the diol would be desirable.

The layer-like structure of the solid diol is evident from Fig. 2, the view down *c*. The intermolecular hydrogen bonds (length 2.87 Å.) holding the layers together are indicated by dashed lines. The C-O...N angle (involving the hydrogen bond) is 96.8°; hence the OH bond deviates by only about 13° from the O...N vector. The intramolecular O...N distance is 2.96 Å., but hydrogen bonding at this location is excluded by the very small angle C₂-O-N (56°).

The oxygen atom of one layer contacts the aziridine ring of the next, not only through the hydrogen bond to nitrogen, but also at one of the

(15) This question has been discussed by J. E. Kilpatrick and R. Spitzer, *J. Chem. Phys.*, **14**, 463 (1946). See also Coulsen and Moffitt, ref. 6.

(16) See, for example, the structures of: sebacic acid (J. D. Morrison and J. M. Robertson, *J. Chem. Soc.*, 993 (1949)); *N,N'*-diacetylhexamethylenediamine (M. Bailey, *Acta Cryst.*, **8**, 575 (1955)); 11-aminoundecanoic acid hydrobromide (G. A. Sim, *ibid.*, **8**, 833 (1955)); and tetradecanamide (J. Turner and E. C. Lingafelter, *ibid.*, **8**, 551 (1955)).

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.

Acknowledgment.—The authors gratefully acknowledge the extensive help to Mr. Graham Wallace in programming the machine calculations, and they are indebted to Dr. Richard Marsh of the California Institute of Technology for supplying a program for calculations of structure factors and for least-squares refinement of data. They also wish to thank Dr. Leon Goodman and Mrs. Irene Junga for a generous supply of the crystalline diol.

[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

RECEIVED OCTOBER 29, 1960

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

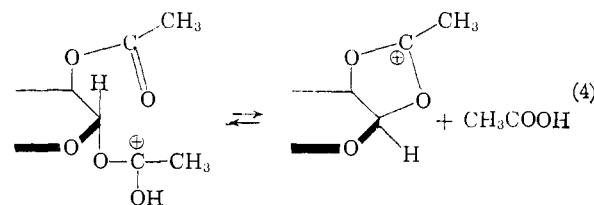
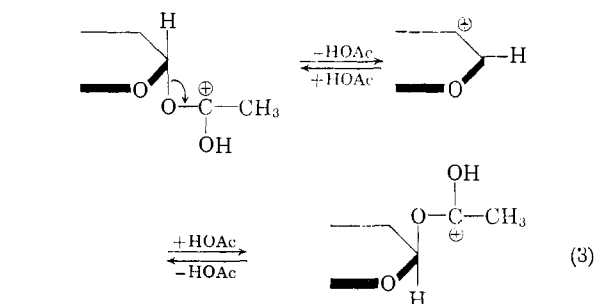
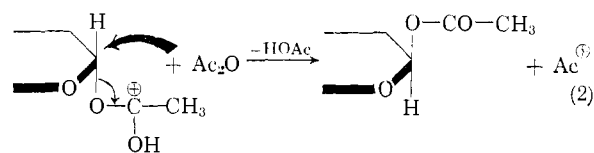
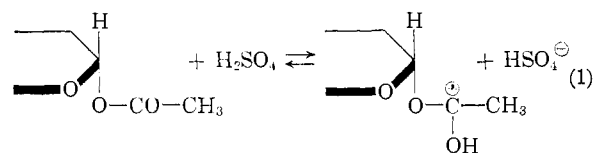
Because of the mechanistic ambiguity inherent in the above and previous⁴ studies of the anomerization reaction, an ambiguity occasioned by the complication of the C2 acetoxy participation process 4, we have more recently turned our attention⁵

(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).