formulation the n.m.r. spectrum of each of the five alkaloids has peaks at δ = ~4.4 (1 H, m) and 4.93 p.p.m. (1 H, d of d, J = 1.5, 7 c.p.s.) which are not removed by hydrogenation. These signals are assigned, respectively, to protons on the α- and β-carbon atoms of the isocaproic chain bearing, respectively, a nitrogen and an oxygen atom, the nitrogen atom being assigned the α-position on biogenetic grounds. Chemical confirmation of an α,β-disubstituted isocaproic acid fragment was provided by sulfuric acid hydrolysis of ceanothine-B to yield α-ketoisocaproic acid isolated as the *syn*- and *anti*-2,4-dinitrophenylhydrazones, identical with authentic specimens.

Joining of these expanded fragments of the C_{14} unit leads to a unique structure containing the nine-membered ring in I. Although the enamide double bond is formally conjugated with the aromatic ether and would be expected to have λ_{max} 319 mμ (ϵ ~8000),[8] ceanothine-B has no ultraviolet absorption beyond 300 mμ. The explanation is clear from a Dreiding model which shows that the plane of the double bond is held almost perpendicular to the plane of the aromatic ring, as in IV, and hence the ultraviolet spectrum is merely the superposition of the enamide and *o*-alkyl phenol ether chromophores. In agreement with this formulation for the C_{14} unit, there are strong peaks at *m/e* 134 and 135 attributed to the ions V and VI (or equivalents) in the mass spectra of each of the alkaloids but not of dihydroceanothine-B. Attachment of the two amino acid residues to the C_{14} unit being possible in only one sense, ceanothine-B, therefore, has the complete structure I.

Of the four asymmetric carbon atoms present, the three α-amino carbon atoms are assumed to have the L configuration. The coupling constants of the δ 4.93 p.p.m. doublet of doublets indicates the *threo* configuration for the β-carbon of the aryloxyleucine. The shift in position of the N-methyl group from δ_{CDCl_3} 1.97 to 2.15 p.p.m. on hydrogenation of ceanothine-B is understandable if this apparently distant group is actually held close to one face of the double bond by intramolecular hydrogen bonding of the amide groups (see dotted lines in I).

Since all five of the ceanothus alkaloids examined have the same basic ultraviolet spectrum which undergoes the same change on hydrogenation, and since all five contain the discernible n.m.r. peaks of the C_{14} unit, this unit is probably present in all of these bases. The ceanothus alkaloids have certain features relating them to the other recently discovered peptide alkaloids in which there is considerable current interest.[8-10]

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(8) E. Zbiral, E. L. Ménard, and J. M. Müller, *Helv. Chim. Acta*, **48**, 404 (1965).
(9) M. Païs, X. Monseur, X. Lusinchi, and R. Goutarel, *Bull. soc. chim. France*, 817 (1964).
(10) M. Païs, J. Mainil, and R. Goutarel, *Ann. pharm. françs.*, **21**, 139 (1963).
(11) Fellow of the Alfred P. Sloan Foundation.

E. W. Warnhoff,[11] J. C. N. Ma, P. Reynolds-Warnhoff
Department of Chemistry
University of Western Ontario, London, Canada
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Nucleophilic Assistance in the Acid-Catalyzed Reactions of Acetals and Glycosides[1]

Sir:

The possibility that in certain enzymically catalyzed hydrolyses of glycosides the enzyme provides nucleophilic assistance to the rupture of the glycosidic bond has frequently been considered,[2] but there has been little evidence to substantiate or refute the occurrence of such a process. One obvious argument that can be used against the proposal that the enzyme provides nucleophilic assistance is based on the mechanism of the acid-catalyzed hydrolysis of acetals and glycosides being invariably A1 without nucleophilic participation by water in the rate-determining step.[3] It would therefore be of interest if any simple acid-catalyzed reactions of acetals and glycosides which did not proceed by an A1 mechanism could be found. To this end the reactions of the acyclic dimethyl acetals of glucose and galactose in dilute aqueous hydrochloric acid were studied. Under these conditions, besides undergoing hydrolysis to glucose and galactose, these acetals also yield a mixture of the α- and β-furanosides by a concurrent ring closure.[4] The products and rates of these reactions are shown in Table I. Two mechanisms

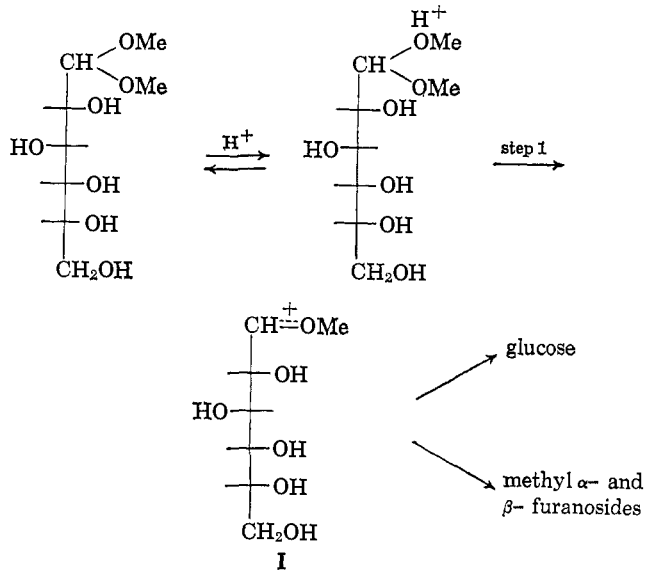
Table I. Kinetically Controlled Products and Rate Constants for the Reactions of Some Acyclic Aldose Acetals in 0.05 *M* HCl at 35°

Dimethyl acetal of	Products, % Aldose	Furanosides	Pyranosides	$10^4 k_{total}$, sec.$^{-1}$
D-Glucose	<2	>98	<0.5	17
D-Galactose	29	71	<0.5	1.58

are possible for the ring closure to furanosides. In mechanism 1 a carbonium ion (I), of the type normally postulated to intervene in the hydrolysis of acetals,[3] is competed for by water and the internal hydroxyl group. In mechanism 2 the ring closure is synchronous with the rupture of the acetal bond. With mechanism 1 the total rate of reaction is the rate of ionization (step 1), and this should be independent of the configuration of carbon 4, but with mechanism 2 the rate of ring closure, and hence the total rate, could well depend on this configuration. The observation that k_{total} for the glucose acetal is about ten times greater than for the galactose acetal and that the product from the glucose acetal contains a much higher proportion of furanosides therefore supports mechanism 2. The anchimeric assistance associated with the ring closures is indicated by the results given in Table II. The rate of

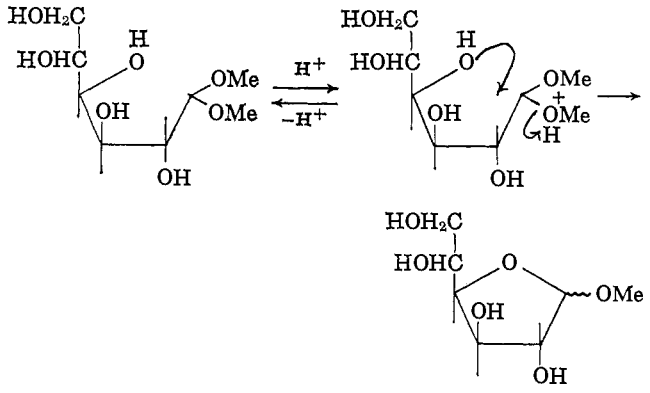
(1) This work was supported by the Department of Scientific and Industrial Research and the Royal Society.
(2) D. E. Koshland in "The Mechanism of Enzyme Action," W. D. McElroy and B. Glass, Ed., The Johns Hopkins Press, Baltimore, Md., 1954, p. 608; E. H. Fisher and E. A. Stein, *Enzymes*, **4**, 313 (1960); M. L. Bender and R. Breslow in "Comprehensive Biochemistry," Vol. 2, M. Florkin and E. H. Stotz, Ed., Elsevier Publishing Company, Amsterdam, 1962, p. 38; K. Wallenfels and O.P. Malhotra, *Advan. Carbohydrate Chem.*, **16**, 239 (1961); F. C. Mayer and J. Larner, *J. Am. Chem. Soc.*, **81**, 188 (1959).
(3) See L. L. Schaleger and F. A. Long, *Advan. Phys. Org. Chem.*, **1**, 27 (1963).
(4) The hydrolysis of these acetals was first investigated by M. L. Wolfrom and S. W. Waisbrot, *J. Am. Chem. Soc.*, **61**, 1410 (1939), who concluded that the products were the free aldoses and pyranosides. However, we have been unable to detect any pyranosides by paper chromatography.

Mechanism 1



I

Mechanism 2



ring closure of the glucose acetal is 340 times and the galactose acetal 29 times greater than the estimated unassisted rate of ionization of a pentahydroxyhexanal acetal based on the $\rho^*\sigma^*$ relationship. The rates of ring closure are also substantially greater than the observed rate of hydrolysis of D-glyceraldehyde dimethyl acetal. Since hydroxyl substituents cause a decrease in the rate of hydrolysis of acetals through their inductive effect, the rate constant of this latter reaction sets an upper limit on the unassisted rate of ionization for the glucose and galactose acetals. It is therefore concluded that the ring closure of the glucose and galactose acetals involves a nucleophilic attack synchronous with the rupture of the acetal bond.

Nucleophilic attack synchronous with the acid-catalyzed rupture of a glycosidic bond possibly occurs also in the hydrolysis of aldofuranosides. In Table III are given the entropies of activation for the acid-catalyzed hydrolysis of a series of furanosides and the corresponding pyranosides. The contrast between the two sets of results is striking, and the simplest explanation of the negative values for the furanosides is that they react by an A2 mechanism, which would not be too surprising in view of the generally observed greater ease of nucleophilic attack on five-membered compared with six-membered rings.[5] The possibility that these negative entropies of activation result from an intramolecular nucleophilic attack by one of the hydroxyl groups is excluded by the observation that the entropy of activation for the hydrolysis of methyl α-D-galactofuranoside (II) is similar to the others. With this furanoside, nucleophilic attack with inversion of configuration by the hydroxyl groups at positions 2, 5, and 6 to form a three-, five-, or six-membered ring is prevented sterically. Thus the criterion of mechanism based on entropy of activation supports an A2 mechanism, but clearly confirmation of this by another criterion is desirable.

Table II. Second-Order Rate Constants for the Acid-Catalyzed Hydrolysis and Ring Closure of Some Dimethyl Acetals at 25°

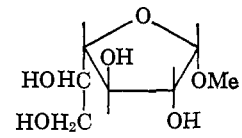
Reaction	10^4k l. mole^{-1} sec.$^{-1}$	$10^4 \cdot k_{calcd}$[a]	k/k_{calcd}
Hydrolysis of D-glyceraldehyde acetal	1.77	2.48	.71
Ring closure of D-glucose acetal	110	.324	340
Ring closure of D-galactose acetal	9.3	.324	29

[a] Calculated rate of ionization using Taft's $\rho^*\sigma^*$ equation based on a value for the second-order rate constant for the hydrolysis of acetaldehyde dimethyl acetal of 2.74×10^{-1} l. mole^{-1} sec.$^{-1}$ (Tables of Chemical Kinetics, National Bureau of Standards Circular 510, 1951, p. 22). ρ^* was assumed to be −3.65 and σ^* for the first hydroxymethyl group to be 0.555 (M. M. Kreevoy and R. W. Taft, *J. Am. Chem. Soc.*, **77**, 5590 (1955)). σ^* values for the other hydroxyl groups were calculated from this, assuming an attenuation factor of 0.5 for each additional carbon atom between the hydroxyl group and the reaction center (J. C. McGowan, *J. Appl. Chem.*, **10**, 312 (1960)).

Table III. Entropies of Activation (cal. deg.$^{-1}$ mole^{-1}) for the Hydrolysis of Some Glycosides

	Furanosides, 1 *M* $HClO_4$ at 25°	Pyranosides,[a] 1 *M* HCl at 60°
Methyl α-D-gluco-	−11.1	+14.8
Methyl β-D-gluco-	−9.0[b]	+16.5
Methyl α-D-galacto-	−9.4	+17.7
Methyl β-D-galacto-	−8.7	−13.3
Methyl α-D-xylo-	−8.3	+15.7
Methyl β-D-xylo-	−8.8	+17.5

[a] Results of W. G. Overend, C. W. Rees, aud J. S. Sequeira. *J. Chem. Soc.*, 3429 (1962). [b] Unpublished result of A. A'Court.



(II)

(5) See E. L. Eliel in "Steric Effects in Organic Chemistry," M. S. Newman, Ed., John Wiley and Sons, Inc., New York, N. Y., 1956, p. 121.

Brian Capon, David Thacker
Department of Chemistry, Birkbeck College
London W.C.1, England
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On the Mechanism for the Pyrolysis of Diborane

Sir:

Nearly all of the reactions of diborane have been interpreted in terms of a mechanism involving the dissociation of diborane into two borane (BH_3) molecules which are postulated as being the active species.[1]

(1) S. H. Bauer, *J. Am. Chem. Soc.*, 78, 5775 (1956).