of this research. We thank Priya Kumar for performing preliminary work.

Registry No. La(L)$^{3+}$, 125897-09-8; Eu(L)$^{3+}$, 138606-01-6; Gd(L)$^{3+}$, 125897-21-4; Tb(L)$^{3+}$, 138606-02-7; Lu(L)$^{3+}$, 138606-03-8; ApUp, 1985-21-3; poly(adenylic acid), 24937-83-5; RNase, 9001-99-4.

Exo and Endo Activation in Glycoside Cleavage: Acetolysis of Methyl α- and β-Glucopyranosides[1]

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The mechanism of glycoside cleavage is of fundamental importance for the chemical manipulation of sugars[3] and for an understanding of biochemical processes which involve glycosyl transfer.[4,5] This manuscript describes experiments designed (a) to elucidate the preferred site of activation in cleavage of α- and β-glucopyranosides by trapping the oxo-carbenium intermediate(s) arising thereby and (b) to determine the final products arising from the alternate pathways.

The site of anomeric activation in glycoside cleavage is a contentious issue of long standing.[3,6] Early key experiments[7] (appeared to!) establish that activation occurs at the exocyclic oxygen, thereby leading to a cyclic oxo-carbenium ion **1** rather than to the acyclic counterpart, **4**; however, the latter has continued to resurface in a wide range of circumstances.[8]

Central to the question of the activation site is the issue of the relative basicities of the exo and endo oxygens, which is related, in turn, to the anomeric effect(s).[9,10] The FMO rationalization for the latter phenomenon invokes nσ* donation from the oxygen(s) to the C1-O bond.[11] That oxygens which are involved in nσ* donation should be less basic than those not so engaged is a seminal intuitive contribution by Deslongchamps.[12] An ab initio study of dimethoxymethane, carried out in this laboratory,

Scheme I

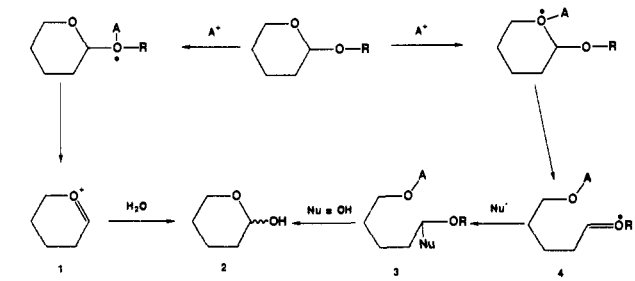

Chart I

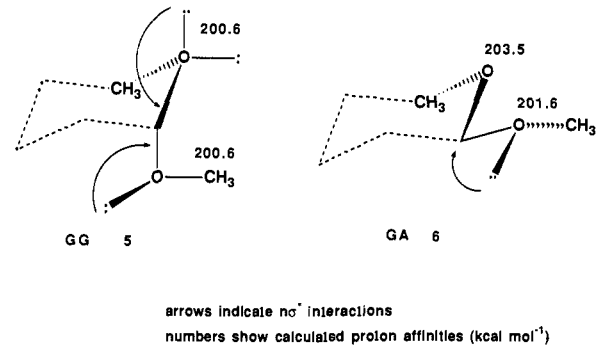

Table I. Percent Distribution of Products in Acetolysis Reaction Mixtures[a-c]

		products[d,e]			
entry	starting material	**7**	**8**	**9**	**10**
i	methyl α-D-glucopyranoside	73	18	8	tr
ii	methyl β-D-glucopyranoside	19	5	48	23
iii	acyl acetal **11a** (epimeric)	2	tr	46	52
iv	acyl acetal **11a** (1*S*)	2	tr	46	52
v	acyl acetal **11a** (1*R*)	2	tr	47	51
vi	dimethyl acetal **11b**			66	34

[a] A 0.1 M solution of anhydrous ferric chloride in acetic anhydride was prepared. The "starting material" was dissolved in this solution to obtain 0.1 M concentration. It was found that addition of one drop of concentrated sulfuric acid reduced the reaction time from 3 to 1.5 h without altering the product composition, and this was done routinely. [b] The composition remained unchanged after standing for 7 days. [c] The composition of each reaction mixture was determined by GLC. [d] Compounds **7-10** were synthesized by known procedures. **7**: Wolfram, M. L.; Thompson, A. *Methods in Carbohydrate Chemistry, II*; Academic Press: New York, **1963**; Vol. 2, p 212. **8**: Moore, J. A.; Dalrymple, D. L.; Rodig, O. R. In *Experimental Methods in Organic Chemistry*; Saunders College Publishing: New York, **1982**; p 32. **9**: Backinowsky, L. V.; Nepogod'ev, S. A.; Shashkov, A. S.; Kochetkov. N. K. *Carbohydr. Res.* **1985**, *135*, 144. **10** was isolated by column chromatography of the product from acetolysis of the β-glucoside and identified by spectral (^{1}H NMR, MS) data. [e] The ^{1}H NMR signals for H-1 of the compounds **7-9** are clearly resolved at 300 MHz: **7** δ 6.30 (d, $J_{1,2}$ = 3.6 Hz), **8** 5.68 (d, $J_{1,2}$ = 8.1 Hz), **9**α 6.42 (d, $J_{1,2}$ = 3.6 Hz), **9**β 6.09 (s), **10** 6.85 (d, $J_{1,2}$ = 5.0 Hz).

has provided support for that postulate by determining the proton affinities for oxygens in the GG and GA rotamers to be as shown in **5** and **6** (Chart I).[13] As indicated by the broken lines, these rotamers correspond to axial and equatorial glycosides, respectively, and as noted by Lemieux,[14] the nσ* donations in **5** are in competition. Accordingly, Praly and Lemieux found that for β-glycosides (i.e., **6**) the exo anomeric effect was stronger than in α-glycosides.[15]

In view of these differences in oxygen basicities, a β-glycoside might be expected to be activated on the ring oxygen and react

(1) We are grateful to the National Science Foundation (CHE 8920033) and the National Institutes of Health (GM 41071) for financial support for this work.

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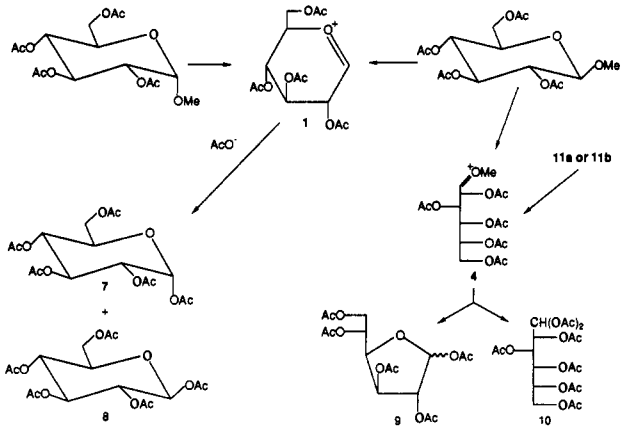
Scheme II



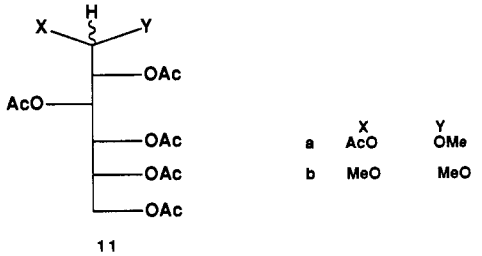
through an acyclic oxo-carbenium ion **4**, whereas an α-glycoside would be activated on *both* oxygens and, in the ideal case, react equally through cyclic and acyclic ions (**1** and **4**). In the case of hydrolysis, this difference is untestable since both ions, **1** and **4**, lead to the same product **2**. With a nucleophile other than water, however, it might be possible to trap each ion and therefore quantify the contribution of the acyclic species (e.g., **3**, Nu = OH).

Our experimental approach for examining these issues took advantage of the recent report of Dasgupta on the acetolysis of methyl α-D-glucopyranoside with anhydrous ferric chloride in acetic anhydride.[16] The products obtained were the peracetylated pyranose and furanose (isolated as a mixture) and the acyclic derivative. In this medium, the activator is the acetylium ion and the nucleophile is acetate (i.e., in Scheme I, A = CH_3CO^+, Nu = CH_3COO^-). Thus, use of this mild medium would allow us (a) to intercept the intermediates produced from α- or β-glycosides and (b) to determine their precise fates as they progress toward products.

First, we repeated the work of Dasgupta[16] on methyl α-D-glucopyranoside using a modified acetolysis medium (see Table I). Independent analysis by gas chromatography and ^1H NMR spectroscopy established that peracetylated α- and β-pyranoses **7** and **8** (Scheme II) accounted for 91% of the product mixture (entry i).

For the β-D-glucoside, the same four components were present but in very different amounts, with the major constituents (Table I, energy ii) being the furanosyl acetate **9** and the acyclic heptaacetate **10**. (Scheme II).

With respect to the acyclic oxo-carbenium ion **4**, trapping by acetate ion would lead to the acyl acetal **11a**, a type of derivative that has been isolated by Hudson from acetolysis of methyl arabinosides,[17] but never from a hexoside. A synthesis of **11a** was



	X	Y
a	AcO	OMe
b	MeO	MeO

11

therefore undertaken. Our approach was facilitated by the recent procedure described by Keith,[18] whereby dimethyl acetal **11b**[19] was converted into **11a** as a 1:1 mixture of diastereomers. Acetolysis of **11a** was complete in 0.75 h, and the product (Table I, entry iii) was comprised of furanose and acyclic peracetates. The 1(*R*) and 1(*S*) diastereomers of **11a** could be isolated by column chromatography, and acetolysis of each under similar conditions was found to give the same product mixture (Table I, entries iv and v).

The results in entries i and ii establish clearly that the α- and β-glucopyranosides react through different intermediates. Notably, the ratio of the α- and β-pyranosyl acetates is 4:1 in both entries, and thus it can be concluded that the cyclic oxo-carbenium ion **1** is produced from both anomers and is trapped by acetate ion to give **7** and **8**.

*The result in entry iii shows that the acyl acetal intermediate (and hence **4**) gives rise to furanose and acyclic products almost exclusively.* The differences in ratio of **9** and **10** in entries ii and iii suggest that **11a** may be reacting through additional intermediates. Nevertheless, the validity of ion **4** was further verified by exposing the *dimethyl acetal **11b** to the reaction conditions, whereupon **9** and **10** were produced in 2:1 ratio with no evidence of **7** and **8**.*

Contrary to what may be expected on the sole consideration of oxygen basicities (vida supra), it is the β, not the α, anomer that gives rise to both cyclic and acyclic ions. Clearly, therefore, there are factors other than oxygen basicities that are determining the course of glycoside hydrolysis. A search for these is underway and will be reported in due course.

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A General, Catalytic, and Enantioselective Synthesis of α-Amino Acids

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In recent years, much research has been directed toward the development of enantioselective syntheses of α-amino acids[1] and the use of α-amino acids as key starting materials for the synthesis of complex chiral molecules.[2] Interest in synthetic, unnatural α-amino acids has also increased sharply because of emerging therapeutic and biological possibilities. This communication reports a new, practical, and very general approach to α-amino acids which is based on the use of a robotlike catalyst for enantioselective reduction of ketones.[3]

Many types of trichloromethyl ketones are available by synthesis either from the reaction of aldehydes with nucleophilic trichloromethide reagents followed by oxidation[4] or from the reaction of nucleophilic carbon reagents with trichloroacetyl chloride. Most trichloromethyl ketones can be reduced by catecholborane[3f] (1.5 equiv) in the presence of the (*S*)-oxazaborolidine catalyst **1** (0.1 equiv) in toluene or CH_2Cl_2 to form (*R*) secondary alcohols (**2**) with greater than 97:3 enantioselectivity, as indicated in Table

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