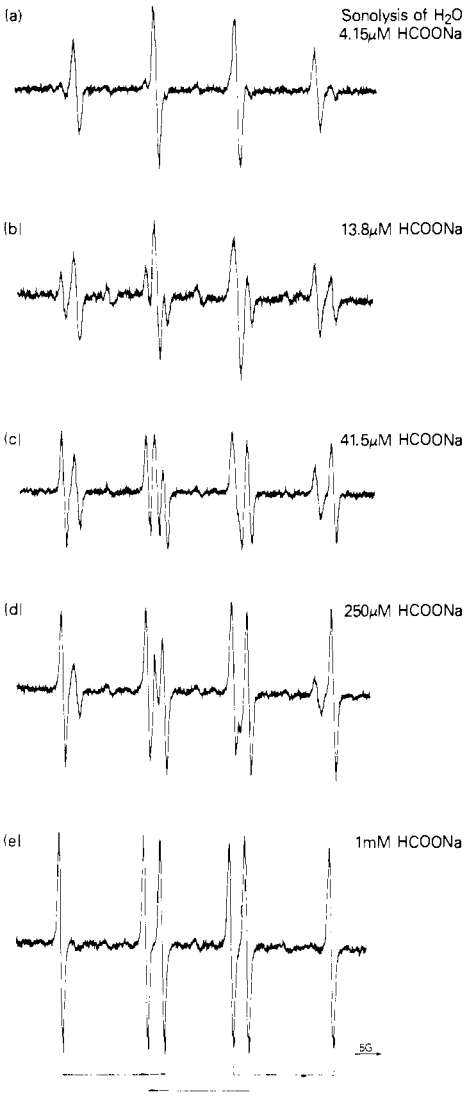

Figure 2. ESR spectra of sonicated (3 min) argon-saturated aqueous solutions containing DMPO (250 μM) and various sodium formate concentrations. At this DMPO concentration the H–DMPO spin adduct signal is negligible. A stick diagram for the CO_2^-–DMPO spin adduct is shown.

O^-.[41,42] Similarly, when aqueous POBN solutions containing sodium formate were sonicated, a decrease of the H–POBN adduct and an increase of the CO_2^-–POBN adduct were observed with increase in formate concentration. Analogous evidence was obtained with the formation of $CH_3CH(OH)$ adducts[28] when ethanol was used as a scavenger in the presence of DMPO or POBN. Since ethanol does not react with e_{aq}^-,[39] this result suggests that the H adducts are formed from ·H. Further support for this result was obtained when aqueous POBN solutions (25 mM) containing $CdSO_4$ (300 μM), a well-known e_{aq}^- scavenger,[39] were sonicated. The signal intensity of H–POBN adduct was not decreased, indicating no formation of e_{aq}^-. The effects of various volatile and nonvolatile radical scavengers and of dissolved gases on the radical yields will be the subject of forthcoming publications.

Registry No. H·, 12385-13-6; HO·, 3352-57-6; OH-DMPO spin adduct, 55482-03-6; H-DMPO spin adduct, 40936-29-6; OH-PYBN spin adduct, 69397-28-0; H-PYBN spin adduct, 69397-35-9; H-POBN spin adduct, 81616-73-1.

(41) $k_{DMPO+\cdot OH} = 4.3 \times 10^9$ M^{-1} s^{-1}, $k_{POBN+\cdot OH} = 3.5 \times 10^9$ M^{-1} s^{-1}: P. Neta, S. Steenken, E. G. Janzen, and R. V. Shetty, *J. Phys. Chem.*, **84**, 532 (1980).

(42) The observed changes in the ESR spectra occur when the product, $k_{HCOO^-+\cdot OH}[HCOO^-]$, is comparable to $k_{DMPO+\cdot OH}[DMPO]$.

Reductive Cleavage of Glycosides

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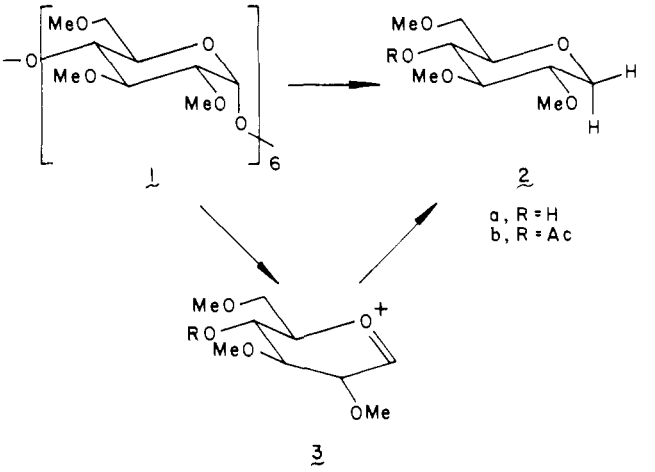
The technique of "methylation analysis" is routinely employed in the structural characterization of complex carbohydrates as a means to establish the linkage positions of the constituent monosaccharides. This method is based on the ability to fractionate and characterize the partially methylated monosaccharides generated via hydrolysis of the fully methylated polysaccharide, which is accomplished most conveniently by combined gas–liquid chromatography/mass spectrometry of their alditol acetate derivatives.[1] This method suffers the disadvantage, however, that hydrolysis of the fully methylated polysaccharide permits furanose–pyranose equilibration in many of the resultant partially methylated monosaccharides and therefore the loss of the desired structural information. On the basis of methylation analysis, for example, one cannot distinguish between a 4-linked *aldohexopyranose* residue and a 5-linked *aldohexofuranose* residue, as both give the same partially methylated sugar (2,3,6-tri-*O*-methylhexose) after hydrolysis of the glycosidic linkage. The same problem is encountered with 4- and 5-linked aldopentose residues and 5- and 6-linked ketohexose residues.

Although methods are available for distinguishing between furanose and pyranose residues in polysaccharides,[2-4] their application is laborious and in some cases inconclusive, especially in cases where both ring forms are present in substantial proportions. We therefore sought to develop a method, based on methylation analysis, that would allow us to simultaneously determine the position of linkage *and* the ring form of each monosaccharide residue in a polysaccharide. A route involving cleavage of the glycosidic carbon–oxygen bond by a hydride equivalent, as in the conversion of **1** to **2a** would be particularly



advantageous because (1) the ring form of the monosaccharide residue would be preserved, (2) a stable anhydroalditol would be generated, and (3) for aldoses at least, a mixture of anomers would not be formed. Ionic hydrogenation with triethylsilane in trifluoroacetic acid, which has been shown to effect the reduction of other acetals and ketals,[5] seemed to potentially be an attractive means of accomplishing this type of conversion. Treatment of

† Recipient of Faculty Research Award 143 from the American Cancer Society.

(1) H. Björndal, B. Lindberg, and S. Svensson, *Carbohydr. Res.*, **5**, 433–440 (1967).

(2) F. Smith and J. W. Van Cleve, *J. Am. Chem. Soc.*, 77, 3091–3096 (1955).

(3) I. J. Goldstein, G. W. Hay, B. A. Lewis, and F. Smith, "Methods in Carbohydrate Chemistry", Vol. 5, Academic Press, New York, pp 361–377.

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(5) D. N. Kursanov, Z. N. Parnes, and N. M. Loim, *Synthesis*, 633–651 (1974).

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Table I. Yields of Products Obtained in the Reductive Cleavage of Some Model Glycosides

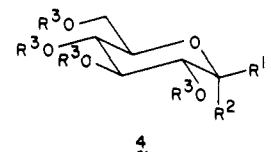
compd	product	yield,[a] %
4a	4d	97
4b	4d	91
4c	4d	96
4e	4f	92[b]
5a	5b	100
6a	6b	95
6c	6d	98
7a	4d	48[c]
	7b	40[c]
	7c	10[c]

[a] Based on gas chromatographic analysis. [b] Isolated yield. [c] Theoretical yields for 4d and (7b + 7c) are 50%.

permethylated cyclohexaamylose[6] (**1**) with triethylsilane and trifluoroacetic acid under the conditions known to reduce hemiacetals[7] or other acetals,[5] however, failed to produce **2a**. Small amounts of **2a** were formed if the reaction was carried out at elevated temperature (70 °C), but these conditions led to rapid decomposition of triethylsilane, as expected.[8]

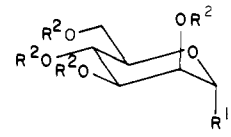
The conversion of **1** to **2a** was readily accomplished, however, with a modification[9] of the procedure developed by Doyle, et al.[10] for the boron trifluoride assisted organosilane reduction of aldehydes and ketones. The ^{1}H NMR spectrum of the crude product was identical with the spectrum of authentic **2a**,[11] and analysis of the crude product after acetylation by gas–liquid chromatography[12] demonstrated that **2b** was present in >95% yield. Silica gel chromatography of the product under the conditions previously described for authentic **2a**[11] gave pure **2a** in 73% yield.[13] The reductive depolymerization of **1** could also be accomplished in the presence of acetic anhydride to give **2b** directly,[14] which conveniently provides derivatives suitable for GC/MS analysis in a single step.

The formation of anhydroalditols **2a** and **2b** in the boron trifluoride assisted reduction of **1** with triethylsilane reflects hydride trapping of the presumed intermediate *cyclic* oxonium ion **3**. Although the isolated yield of **2a** was good (73%), the formation of significant amounts of products reflecting trapping of *acyclic* oxonium ion intermediates in the reduction of **1** cannot be excluded, since the resultant nonvolatile polyetherial products would not have been observed by GC analysis. So that the possibility that acyclic alditols were formed under the conditions of the cleavage reaction could be explored, model glycosides were chosen for study that would yield only volatile reduction products. All of the compounds examined (Table I), however, gave high yields of anhydroalditols arising from reduction of *cyclic* oxonium ion intermediates. Only in the reduction of methyl 2,3,5-tri-*O*-methyl-β-D-ribofuranoside (**6a**) was a significant amount (5%) of an acyclic product observed.[15]



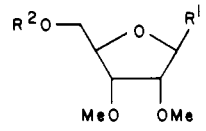
4

a, R^1=H, R^2=OMe, R^3=Me
b, R^1=OMe, R^2=H, R^3=Me
c, R^1,R^2=H,OH, R^3=Me
d, R^1=R^2=H, R^3=Me
e, R^1=OMe, R^2=H, R^3=$CH_2C_6H_5$
f, R^1=R^2=H, R^3=$CH_2C_6H_5$
g, R^1=R^2=R^3=H



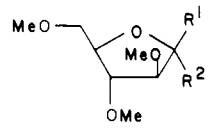
5

a, R^1=OMe, R^2=Me
b, R^1=H, R^2=Me



6

a, R^1=OMe, R^2=Me
b, R^1=H, R^2=Me
c, R^1=OMe, R^2=H
d, R^1=R^2=H



7

a, R^1=OMe_4-α-D-Glc_p, R^2=CH_2OMe
b, R^1=H, R^2=CH_2OMe
c, R^1=CH_2OMe, R^2=H

So that the applicability of the method to the cleavage of 5-linked furanosyl residues could be investigated, the model furanoside (**6c**) was chosen because structurally simple, well-characterized furanose-containing polysaccharides are not readily available. In particular, methyl 2,3-di-*O*-methyl-β-D-ribofuranoside (**6c**) was chosen because the free C-5 hydroxyl group provides the opportunity for intramolecular trapping of the cyclic oxonium ion and subsequent rearrangement to other products. Treatment of **6c** with triethylsilane, trifluoroacetic acid, and boron trifluoride etherate, however, gave the expected 1,4-anhydroalditol (**6d**) in >98% yield, as judged by gas–liquid chromatography[12] of its acetate.[16]

The reductive cleavage of glycosides also appears to have synthetic utility as a means of preparing anhydroalditols. Treatment of methyl 2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranoside (**4e**) under the conditions already described[9] gave **4f** in 92% yield. Catalytic hydrogenolysis of **4f**, to remove the benzyl protecting groups, gave crystalline 1,5-anhydro-D-glucitol (**4g**) in 63% overall yield.[17]

In these reactions, the ratios and amounts of reagents were not optimized; on the contrary, large excesses of reagents were used in order to ensure completion of the reactions as well as to more closely approximate the analytical conditions under which the reactions would be used. The reactions could be carried out with

(6) J. Boger, R. J. Corcoran, and J.-M. Lehn, *Helv. Chim. Acta*, **61**, 2190–2218 (1978).

(7) M. P. Doyle, D. J. DeBruyn, and D. A. Kooistra, *J. Am. Chem. Soc.*, **94**, 3659–3661 (1972).

(8) K. A. Andrianov, S. A. Igonina, and V. I. Sidorov, *J. Organomet. Chem.*, **128**, 43–55 (1977).

(9) Permethylated cyclohexaamylose (**1**) was suspended in 30 molar equiv of triethylsilane at 0 °C, and boron trifluoride etherate (30 equiv) and trifluoroacetic acid (12 equiv) were sequentially added. The reaction mixture was allowed to warm to room temperature and after 16 h was diluted with 95% ethanol (5 volumes) and deionized by passage through a column of excess mixed-bed ion-exchange resin (Dowex AG501-X8). The eluate was evaporated to dryness, and the residue was evaporated several times from MeOH–HCl (500:1 v/v) to remove borate.

(10) M. P. Doyle, C. T. West, S. J. Donnelly, and C. C. McOsker, *J. Organomet. Chem.*, **117**, 129–140 (1976).

(11) R. E. Brandon, L. R. Schroeder, and D. C. Johnson, "Cellulose Technology Research", American Chemical Society, Washington, D.C., 1975, pp 125–146.

(12) 10% OV 17 on Chromosorb W ($^1/_8$ in. × 8 ft), 150 °C, 5 min, then 5 °C/min to 250 °C.

(13) **2a**: ^{1}H NMR (D_2O) δ 3.39, 3.49, 3.62 (three s, 9 H, methoxyl), 3.17–3.79 (complex, 7 H, H-1a, 2, 3, 4, 5, 6), 4.19 (dd, J = 4.7, 11.5 Hz, 1 H, H-1e); $[\alpha]^{25}_D$ +51° (*c* 2.0, H_2O) [lit.[10] $[\alpha]^{25}_D$ +53.8°].

(14) Compound **1**, triethylsilane, boron trifluoride etherate, and trifluoroacetic acid were mixed in the proportions already given,[9] and the mixture was cooled to 0 °C prior to the dropwise addition of acetic anhydride (12 equiv). After this warmed to room temperature, a homogeneous solution was obtained. After being kept for 24 h at room temperature, the reaction mixture was diluted with $CHCl_3$, extracted with cold aqueous $NaHCO_3$, dried over anhydrous Na_2SO_4, and evaporated to dryness to give **2b** in 81% yield: ^{1}H NMR ($CDCl_3$) δ 2.11 (s, 3 H, acetoxy), 3.36, 3.48, 3.53 (three s, 9 H, methoxyl), 3.11–3.67 (complex, 6 H, H-1a, 2, 3, 5, 6), 4.12 (dd, J = 5.2, 11.0 Hz, 1 H, H-1e), 4.82 (t, J = 9.4 Hz, 1 H, H-4); $[\alpha]^{25}_D$ +30° (*c* 2.3, $CHCl_3$).

(15) The acyclic product was identified after acetylation as 1,2,3,5-tetra-*O*-methyl-4-*O*-acetylribitol by GC/MS analysis.[1] The presence or absence of acyclic products in the other reactions was established similarly.

(16) The ^{1}H NMR spectra of the product and its 5-*O*-acetyl derivative were identical with the spectra of authentic **6d** and its 5-*O*-acetyl derivative, respectively. Authentic **6d** was prepared from 1,4-anhydro-D-ribitol [D. D. Heard, B. G. Hudson, and R. Barker, *J. Org. Chem.*, **35**, 464–467 (1970)] by successive tritylation, methylation [S. Hakomori, *J. Biochem. (Tokyo)*, **55**, 205–208 (1964)], and detritylation [G. R. Barker and D. C. C. Smith, *J. Chem. Soc.*, 1323–1326 (1955)]. **6d**: ^{1}H NMR ($CDCl_3$) δ 2.20 (br s, 1 H, hydroxyl), 3.44, 3.46 (two s, 6 H, methoxyl), 3.00–4.00 (complex, 7 H, H-1, 2, 3, 4, 5). Acetyl derivative: δ 2.07 (s, 3 H, acetyl), 3.43 (s, 6 H, methoxyl), 3.00–4.50 (complex, 7 H, H-1, 2, 3, 4, 5).

(17) Identified by comparison with an authentic sample [G. R. Gray and R. Barker, *J. Org. Chem.*, **32**, 2764–2768 (1967)]. GC/MS analysis indicated that **4g** was formed in 87% overall yield from **4e**.

equally satisfactory results in the absence of trifluoroacetic acid, in fact, but we feel that trifluoroacetic acid may, in some cases, be advantageous as a solvent for high molecular weight permethylated polysaccharides. Analysis of all reactions after workup by GC/MS demonstrated in each case that reductive cleavage was virtually quantitative. In each reaction the product of reductive cleavage was identical with the authentic anhydroalditol derivative as judged by electron impact mass spectrometry, chemical ionization mass spectrometry, ^{1}H NMR spectroscopy, gas–liquid chromatography, and optical rotation.

We conclude from these results that reductive cleavage of glycosides is potentially an attractive method for polysaccharide structure determination. Moreover, the reaction conditions described herein are synthetically useful as a means to prepare anhydroalditols, which have proven to be very useful analogues for the study of the mechanisms of carbohydrate-requiring enzymes.

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On the Concept of Graph-Theoretical Individual Ring Resonance Energies

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Hückel molecular orbital theory has been reexamined and redefined in terms of graph-theoretical concepts.[1,2] Graph-theoretical definitions of resonance energies (GTRE) have arisen out of this work,[3-6] and the applications of these definitions comprise a sizable part of the chemical graph-theoretical literature. Recent papers have stressed the point that GTRE's can be divided among the individual rings of polycyclic π molecular graphs. Both individual ring aromaticies[5,9,10] and the theory of London diamagnetism[11,12] have been interpreted on this basis.

The purpose of this communication is to point out that the principal definition[7-10,12] for individual ring aromaticies is based on polynomial equations that have *imginary roots* in several key, nontrivial cases. The roots of these polynomials must be taken to correspond to energy levels, and the existence of imaginary roots therefore obviates the use of these GTRE's in discussing ring aromaticities or susceptibilities due to individual ring currents. This failing of the GTRE definition, when added to other, less formal types of difficulties,[13-19] should lead to caution in the use of the GTRE concept.

The details of a GTRE calculation are as follows. The coefficients of the HMO secular polynomial $P^{HMO}(G)$ can be written by using graph theory since each term is a prescribed function of the number of bonds (edges), rings (cycles), and atoms (vertices) in the molecular graph.[20-23] The polynomial for a hypothetical cyclic resonance-free reference system $P^{ref}(G)$ is obtained by deleting all cyclic component terms from the original polynomial.[3-6,23]

$$P^{ref}(G) = P^{HMO}(G) - \sum(\text{ring terms}) \quad (1)$$

The ordered set of the roots of $P^{HMO}(G)$ and $P^{ref}(G)$ allow one to define GTRE as

$$\text{GTRE} = E(P^{HMO}) - E(P^{ref}) = \sum_i g_i(x_i^{HMO} - x_i^{ref}) \quad (2)$$

where g_i is an occupation number and the sum is over all i occupied levels.[24]

In a polycyclic π molecular graph, it is presumed[7-10,12] that the GTRE can be divided among the various rings by defining individual ring reference polynomials

$$P^{ref}(G/R_n) = P^{HMO}(G) - (\text{ring terms})(R_n) \quad (3)$$

where $P^{ref}(G/R_n)$ refers to the polynomial with algebraic terms for the individual ring R_n deleted. The use of eq 2 with the roots of eq 3 gives individual ring resonance energies.

The interested reader can check all calculations by using standard computer programs that determine the eigenvalues of the adjacency matrix of a graph (HMO programs). This follows because the HMO polynomial can be written as the product function

$$P^{HMO}(G) = \prod_{\substack{G \\ (k \text{ levels})}} (x - x_k) \quad (4)$$

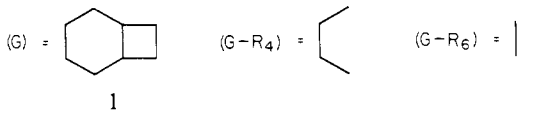
where the x_k are the k HMO eigenvalues. In addition, each set of ring terms is given by

$$(\text{ring terms})(R_n) = -2P^{HMO}(G - R_n) \quad (5)$$

where $G - R_n$ is the molecular graph with the individual ring deleted.[8,11,20] Therefore, all reference polynomials are obtainable in terms of HMO secular polynomials for the graph and subgraphs of the original system.[23]

$$P^{ref}(G/R_n) = P^{HMO}(G) + 2P^{HMO}(G - R_n) = \prod_G (x - x_k) + 2 \prod_{\substack{G-R_n \\ l \text{ levels}}} (x - x_l) \quad (6)$$

These definitions are illustrated in the following by using the π molecular graph of benzocyclobutadiene (**1**).



1

$$P^{HMO}(G) = x^8 - 9x^6 + 22x^4 - 16x^2 + 1 \quad (7)$$

R_4 terms $= -2(x^4 - 3x^2 + 1)$ $\quad$ R_6 terms $= -2(x^2 - 1)$

R_8 terms $= -2$

$$P^{ref}(G/R_4) = x^8 - 9x^6 + 24x^4 - 22x^2 + 3 \quad (8)$$

$$P^{ref}(G/R_6) = x^8 - 9x^6 + 22x^4 - 14x^2 - 1 \quad (9)$$

$$P^{ref}(G/R_8) = x^8 - 9x^6 + 22x^2 - 16x^2 + 3 \quad (10)$$

Equations 8–10 are fourth-degree equations in the variable x^2. According to Descartes' rule of signs,[25] $P^{ref}(G/R_6)$ (eq 9) has

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(24) Gutman[13] and Aihara[17] show that there may not be a continuous one-to-one mapping of the roots of the HMO polynomial with those of the reference polynomial. The occupation numbers g_i then refer to the occupied eigenlevels in the case of the original π molecular system but are taken to correspond to the $n/2$ (n = number of electrons) most negative roots in the case of the reference polynomial.

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