Use of Borate Complexation in Assigning Relative Stereochemistry of Acyclic Polyhydroxylated Compounds

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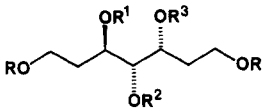
A method is described for determining the relative stereochemistry of acyclic polyhydroxylated compounds. In the experimental procedure borate complexes of the acyclic polyhydroxylated compound are formed, acetylated, and decomposed to diols which are separated and analyzed by ^1H NMR spectroscopy. Analysis of results with 16 known carbohydrates indicates that borate complexes preferentially with *syn*-1,2- and *syn*-1,3-diols rather than with *anti*-1,2- and *anti*-1,3-diols and terminal glycols.

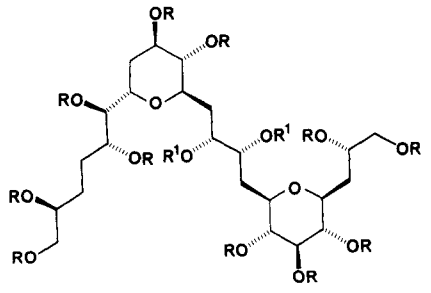
As a result of our studies on the stereochemistry of palytoxin,[1] we have developed a simple chemical procedure which may prove useful in differentiating *syn*- and *anti*-1,2-diol functionalities in complex, acyclic polyhydroxylated compounds. The method is based on the fact that borate complexes preferentially with *syn*-1,2-diols rather than with *anti*-1,2-diols or terminal glycols in acyclic systems.[2,3]

During our ozonolysis studies of *N*-(*p*-bromobenzoyl)-palytoxin we noticed that reductive workup with sodium borohydride, followed by acetylation of the freeze dried reaction mixture with acetic anhydride and pyridine, led to both partially (mostly diols) and fully acetylated products. For example, comparable amounts of **1**[4] and **2**,



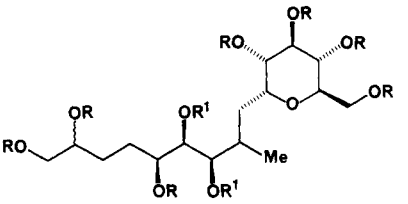
	R	R^1	R^2	R^3
1	Ac	Ac	Ac	Ac
2	Ac	Ac	H	H
3	Ac	H	Ac	H
4	H	H	H	H

which represented C(85)–C(91) in palytoxin, were formed. A small amount of **3** was also produced, but to our surprise other triacetates of the parent pentaol **4** could not be detected. What was even more interesting, comparable amounts of **5**[4] and **6**, which represented C(60)–C(82) in



	R	R^1
5	Ac	Ac
6	Ac	H
7	H	H

palytoxin, were formed, but other undecaacetates of the parent tridecaol **7** could not be found. Comparable amounts of **8**[4] and **9**, which represented C(92)–C(106) in



	R	R^1
8	Ac	Ac
9	Ac	H
10	H	H

palytoxin, were also formed, and at least one other heptaacetate (not identified) of the parent nonaol **10** appeared to have been produced. Presumably exposure of the polyhydroxylated ozonolysis products to boric acid in the reductive workup procedure had produced certain borate esters which had survived the acetylation reaction. During the chromatography of the acetylated complexes on silica, however, these borate esters had decomposed to diols. Although we did not recognize the structural significance and value of this borate complexation at the time our assignments of stereochemistry for palytoxin were made, it is now clear that the structures of these partially acetylated ozonolysis products indicated the positions of *syn*-1,2-diol functionalities in the acyclic portions of the palytoxin molecule.

The discovery that only acyclic *syn*-1,2-diols were being produced as major products prompted us to examine simpler systems, such as alditols, aldoses, ketones, and certain disaccharides of known stereochemistry. In this paper we present some preliminary results of this study.

Borate Complexation. In our study each polyhydroxylated compound (Table I), e.g., alditol, aldose, ketose, or disaccharide, was first exposed to sodium borohydride in water. In this step a reducing sugar was converted to alditol. Acetic acid was then added to decompose the remaining borohydride to boric acid and the mixture was evaporated to dryness. Borate esters of the alditol were formed during the evaporation. The borate complexes were next acetylated with acetic anhydride and pyridine and then the acetylated borate esters were decomposed by transesterification with methanol.[5] The resulting mixture of fully acetylated and partially acetylated alditol (mostly diol) was separated by HPLC on silica. Generally *syn*-1,2-diols were the first diols to be eluted, followed successively by *anti*-1,2-diols, *syn*-1,3-diols,

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(2) Dale, J. *J. Chem. Soc.* **1961**, 910.

(3) This is analogous to the preferred cleavage of *syn*-1,2-diols rather than *anti*-1,2-diols and terminal glycols by periodate. Hutson, D. H.; Weigel, H. *J. Chem. Soc.* **1961**, 1546.

(4) Moore, R. E.; Bartolini, G. *J. Am. Chem. Soc.* **1981**, *103*, 2491.

(5) (a) Abdel-Akher, M.; Hamilton, J. K.; Smith, F. *J. Am. Chem. Soc.* **1951**, *73*, 4691. (b) Reid, E. B.; Siegel, J. R. *J. Chem. Soc.* **1954**, 520.

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Table I. Partially Acetylated Alditols Obtained via Borate Complexation

starting material	diol compd	method, % A	B
D-arabinose	D-arabitol		
	1,4,5-triacetate (**11a**)		88
	1,2,5-triacetate (**11b**)		2
	1,3,5-triacetate (**11c**)		10
D-ribose	ribitol		
	1,4,5-triacetate (**12a**)		30
	1,3,5-triacetate (**12b**)		70
D-xylose	xylitol		
	1,3,5-triacetate (**13a**)		77
	1,4,5-triacetate (**13b**)		23
2-deoxy-D-galactose	2-deoxy-D-*lyxo*-hexitol		
	1,3,6-triacetate (**14a**)		81
	1,5,6-triacetate (**14b**)		6
	1,4,6-triacetate (**14c**)		13
2-deoxy-D-*xylo*-hexitol	2-deoxy-D-*xylo*-hexitol		
	1,5,6-triacetate (**15a**)		40
	1,3,6-triacetate (**15b**)		30
	1,4,6-triacetate (**15c**)		30
2-deoxy-D-*ribo*-hexitol	2-deoxy-D-*ribo*-hexitol		
	1,4,6-triacetate (**16a**)		>95
2-deoxy-D-glucose	2-deoxy-D-*arabino*-hexitol		
	1,5,6-triacetate (**17a**)		80
	1,3,6-triacetate (**17b**)		13
	1,4,6-triacetate (**17c**)		7
D-galactose	galactitol		
	1,4,5,6-tetraacetate (**18a**)		90
	1,3,5,6-tetraacetate (**18b**)		10
D-mannitol	D-mannitol		
	1,2,5,6-tetraacetate (**19a**)	70	78
	1,3,4,6-tetraacetate (**19b**)	1	1
	1,4,5,6-tetraacetate (**19c**)	6	3
	1,3,5,6-tetraacetate (**19d**)	22	17
	2,4,5,6-tetraacetate (**19e**)	1	1
sorbitol	sorbitol		
	1,2,5,6-tetraacetate (**20a**)	57	30
	1,3,5,6-tetraacetate (**20b**)	30	50
	1,4,5,6-tetraacetate (**20c**)	13	20
perseitol	D-*glycero*-D-*galacto*-heptitol		
	1,2,3,6,7-pentaacetate (**21a**)	57	65
	1,4,5,6,7-pentaacetate (**21b**)	11	22
	1,2,4,6,7-pentaacetate (**21c**)	15	6
	1,2,3,5,7-pentaacetate (**21d**)	12	3
	1,3,5,6,7-pentaacetate (**21e**)	4	2
D-*gluco*-heptose	D-*glycero*-D-*gluco*-heptitol		
	1,2,5,6,7-pentaacetate (**22a**)	37	29
	1,2,4,6,7-pentaacetate (**22b**)	56	70
	1,3,4,6,7-pentaacetate (**22c**)	4	
	1,2,3,4,7-pentaacetate (**22d**)	3	1
D-*manno*-heptulose	L-*glycero*-D-*galacto*-heptitol		
	1,2,3,6,7-pentaacetate (**23a**)		66
	1,2,4,6,7-pentaacetate (**23b**)		8
	1,3,5,6,7-pentaacetate (**23c**)		4
	1,2,3,5,7-pentaacetate (**23d**)		4
	pentaacetates of perseitol (**21a–e**)		18
3-deoxy-D-*lyxo*-hexitol	3-deoxy-D-*lyxo*-hexitol		
	1,5,6-triacetate (**24a**)		>90
gentiobiose	6-*O*-β-D-glucopyranosyl-D-glucitol		
	1,2,5,2′,3′,4′,6′-heptaacetate	60	
	1,3,5,2′,3′,4′,6′-heptaacetate	33	
	1,4,5,2′,3′,4′,6-heptaacetate	5	
lactose	4-*O*-β-D-galactopyranosyl-D-glucitol		
	1,5,6,2′,3′,4′,6′-heptaacetate	50	
	1,2,6,2′,3′,4′,6′-heptaacetate	50	

anti-1,3-diols, and terminal glycols. *syn*-1,2-Diols and *syn*-1,3-diols were almost always the predominant products, but *anti*-1,3-diols were sometime formed in appreciable amounts. Only very small to nil amounts of *anti*-1,2-diols and terminal 1,2- and 1,3-diols were produced.

The total yield of diol varied considerably. Most of the carbohydrates examined (Table I) produced diol in 20–50% yield, but lactose consistently gave a lower yield of diol (5–10%). The yield of diol was greater if the acetylation was carried out at 55–60 °C in acetic anhydride and pyridine containing small amounts of water and acetic acid to dissolve the borate complexes (Method A), rather than at room temperature in dry acetic anhydride and pyridine in which the borate complexes were only sparingly soluble (Method B). The composition of the diol complement, however, appeared to be somewhat different for the two methods. The yields of *anti*-1,3-diols, for example, appeared to be higher with Method A.

Chart I. Acetylation Products from Perseitol

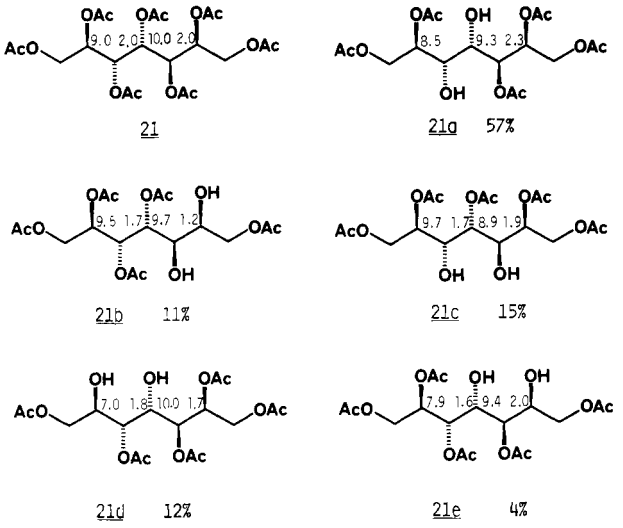
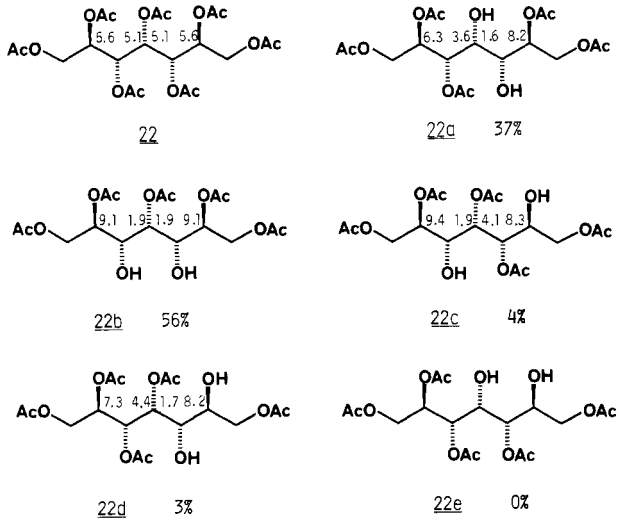


Chart II. Acetylation Products from D-*gluco*-Heptose



The *syn*-1,2-diol **19a** was the major constituent and the *anti*-1,3-diol **19d** was a minor constituent in the mixture of diols produced from mannitol. Only a very small amount of the *anti*-1,2-diol **19a** was formed.

Sorbitol produced the *syn*-1,2-diol **20a** as the major product, along with large quantities of the *syn*-1,3-diol **20b** and the *syn*-1,2-diol **20c**. *anti*-1,2-Diols and *anti*-1,2-diols could not be detected.

syn-1,2-Diols were the major partially acetylated products from perseitol, D-glucoheptose, D-mannoheptulose, gentiobiose, and lactose (Charts I–V). Interestingly, the *syn*-1,2-diols **20a**, **21a**, **22a**, **23a**, and **25a** were formed in much higher yield than the *syn*-1,2-diols **20c**, **21b**, **25c**, and **26a**, suggesting that borate complexation was occurring much more readily with *syn*-1,2-diol functionalities nearer the center of the carbon chain than the termini. This was probably because of more restricted C–C bond rotations

Table II. Proton–Proton Coupling Constant Data for Acetylated Alditols[a,b]

compd	coupling constants, Hz							
	1,2	2,3	3,4	4,5	5,6	6,7	geminal	OH, CH[c]
D-arabitol pentaacetate (**II**)	7.1[d]	2.4	8.4	4.8			−11.6 (1,1)	
	4.8			2.7			−12.5 (5,5)	
1,4,5-triacetate (**11a**)	5.4	1.3	8.8	5.3			−11.5 (1,1)	5.6 (2)
	7.1			2.5			−12.3 (5,5)	8.7 (3)
1,2,5-triacetate (**11b**)	7.1	1.4		2.4			−11.8 (1,1)	
	5.1			4.0			−11.9 (5,5)	
1,3,5-triacetate (**11c**)	7.3	2.2	7.3				−11.6 (1,1)	5.9 (2)
	4.6							3.7 (4)
ribitol pentaacetate (**12**)	6.1	5.5	5.5	6.1			−12.2 (1,1)	
	3.4			3.4			−12.2 (5,5)	
1,4,5-triacetate (**12a**)	5.9	6.4	5.5	5.8			−11.9 (1,1)	
	3.3			3.1			−12.4 (5,5)	
1,3,5-triacetate (**12b**)	5.1	6.4	6.4	5.1			−11.4 (1,1)	4.4 (2)
	3.5			3.5			−11.4 (5,5)	4.4 (4)
xylitol pentaacetate (**13**)	6.0	5.3	5.3	6.0			−12.0 (1,1)	
	4.3			4.3			−12.0 (5,5)	
1,3,5-triacetate (**13a**)		3.1	3.1					5.1 (2)
								5.1 (4)
1,4,5-triacetate (**13b**)	6.4	3.5	4.5	6.4			−11.8 (1,1)	5.6 (2)
	4.9			4.1			−12.1 (5,5)	7.2 (3)
2-deoxy-D-*lyxo*-hexitol pentaacetate (**14**)		10.0	6.7	3.8	6.7		−11.8 (6,6)	
		3.4			5.1			
1,3,6-triacetate (**14a**)	5.3, 6.0[e]	9.2	8.0	1.7	6.2		−14.8 (2,2)	8.9 (4)
	5.3, 8.1	3.8			6.2			5.0 (5)
1,5,6-triacetate (**4b**)		9.2	7.9	1.9	7.1		−11.1 (1,1)	4.2 (3)
	5.4, 8.3	2.5			5.1		−14.5 (2,2)	8.1 (4)
							−11.7 (6,6)	
1,4,6-triacetate (**14c**)	5.0, 5.7	10.1	6.2	2.2	7.0		−11.2 (1,1)	
	4.6, 9.2	2.8			5.0		−14.6 (2,2)	
							−11.5 (6,6)	
2-deoxy-D-*xylo*-hexitol pentaacetate (**15**)	6.2, 6.2		5	6	5.8		−12.0 (6,6)	
	6.2, 6.2				3.9			
1,5,6-triacetate (**15a**)		7.5	4.3	4.1	6.7		−12.0 (6,6)	
		5.2			4.3			
1,3,6-triacetate (**15b**)	6.3, 6.3	6.9	4.4	3.5	6.7		−11.7 (6,6)	
	6.3, 6.3	6.3			4.7			
1,4,6-triacetate (**15c**)	5.0, 5.5	9.3	2.9	2.9			−11.4 (1,1)	5.2 (3)
	5.0, 8.6	3.7					−14.3 (2,2)	4.5 (5)
2-deoxy-D-*ribo*-hexitol pentaacetate (**16**)	5.2, 6.0	9.2	3.9	6.4	6.0		−11.3 (1,1)	
	5.6, 8.4	3.9			2.8		−12.3 (6,6)	
1,4,6-triacetate (**16a**)	5.0, 5.8	10.0	6.3	6.7	5.5		−11.4 (1,1)	4.7 (5)
	4.8, 9.2	2.7			3.4		−14.5 (2,2)	4.5 (3)
							−11.8 (6,6)	
2-deoxy-D-*arabino*-hexitol pentaacetate (**17**)		4.6	2.6	8.5	4.9		−12.5 (6,6)	
		8.9			2.7			
1,5,6-triacetate (**17a**)	6.2, 4.8	3.7	1.7	8.6	5.4		−11.1 (1,1)	7.3 (4)
	8.5, 5.3	9.4			2.5		−14.6 (2,2)	
							−12.3 (6,6)	
1,3,6-triacetate (**17b**)	7.5, 4.7	4.3	1.2	9.4	2.1		−14.6 (2,2)	7.2 (4)
	7.5, 4.7	9.5			4.0		−12.1 (6,6)	
1,4,6-triacetate (**17c**)		4.5	2.2	7.0			−11.4 (1,1)	
	8.2, 5.5	9.1						
galactitol hexaacetate (**18**)	7.5	2.2	10.0	2.2	7.5		−11.6 (1,1)	
	4.8				4.8		−11.6 (6,6)	
1,4,5,6-tetraacetate (**18a**)	6.3	1.2	9.5	2.1	7.2		−11.5 (6,6)	6.0 (2)
	6.3				5.7			8.3 (3)
1,3,5,6-tetraacetate (**18b**)	7.4	2.0	9.4	1.9	6.7		−11.7 (1,1)	
	4.2				6.1		−11.5 (6,6)	
D-mannitol hexaacetate (**19**)	5.1	9.2	2.4	9.2	5.1		−12.5 (1,1)	
	2.8				2.8		−12.5 (6,6)	
1,2,5,6-tetraacetate (**19a**)	5.5	8.7	1.2	8.7	5.5		−12.3 (1,1)	7.6 (3)
	2.6				2.6		−12.3 (6,6)	7.6 (4)
1,3,4,6-tetraacetate (**19b**)	2.4	9.2		9.2	2.4		−11.9 (1,1)	
	4.7				4.7		−11.9 (6,6)	
1,4,5,6-tetraacetate (**19c**)				8.3	4.2		−12.5 (6,6)	
					2.3			
1,3,5,6-tetraacetate (**19d**)		7.2	1.7	9.7	3.2			5 (4)
					3.2			
2,4,5,6-tetraacetate (**19e**)	3.3	9.5	1.6	8.3	4.5		−13.1 (1,1)	
					2.6		−12.4 (6,6)	
sorbitol hexaacetate (**20**)	6.1	6.3	4.4	6.7	5.3		−12.1 (1,1)	
	4.0				3.6		−12.4 (6,6)	
1,2,5,6-tetraacetate (**20a**)	6.4	5.5	1.6	8.4	4.9		−12.1 (1,1)	5.7 (3)
	3.8				2.8		−12.5 (6,6)	7.4 (4)
1,3,5,6-tetraacetate (**20b**)	6.8	3.4	1.8	9.4	3.3		−11.5 (1,1)	4.6 (2)
	3.9				3.3			4.9 (4)
1,4,5,6-tetraacetate (**20c**)	6.7	3.7	2.7	6.9	5.3		−11.8 (1,1)	4.8 (2)
	4.5				2.4		−12.4 (6,6)	7.9 (3)

Table II (Continued)

compd	coupling constants, Hz 1,2	2,3	3,4	4,5	5,6	6,7	geminal	OH, CH[c]
D-*glycero*-D-*galacto*-heptitol heptaacetate (**21**)	7.2	2.0	10.0	2.0	9.0	5.2	−11.7 (1,1)	
	4.9					2.9	−12.5 (7,7)	
1,2,3,6,7-pentaacetate (**21a**)	7.1	2.3	9.3		8.5	5.5	−11.5 (1,1)	7.7 (4)
	5.7					2.5	−12.3 (7,7)	7.7 (5)
1,4,5,6,7-pentaacetate (**21b**)	6.2	1.2	9.7	1.7	9.5	4.3	−12.6 (7,7)	5.8 (2)
	6.2					2.6		7.4 (3)
1,2,4,6,7-pentaacetate (**21c**)	6.4	1.9	8.9	1.7	9.7	2.8	−11.5 (1,1)	7.6 (3)
	6.4					3.6	−12.6 (7,7)	7.6 (5)
1,2,3,5,7-pentaacetate (**21d**)	7.9	1.7	10.0	1.8	7.0		−11.8 (1,1)	5.7 (4)
	4.3							
1,3,5,6,7-pentaacetate (**21e**)	7.3	2.0	9.4	1.6	7.9	6.1	−11.7 (1,1)	7.8 (2)
	4.1					2.8	−12.5 (7,7)	6.5 (4)
D-*glycero*-D-*gluco*-heptitol heptaacetate (**22**)[f]	5.4	5.6	5.1	5.1	5.6	5.4	−12.2 (1,1)	
	4.3					4.3	−12.2 (7,7)	
1,2,5,6,7-pentaacetate (**22a**)	4.9	8.2	1.6	3.6	6.3	5.6	−12.4 (1,1)	8.2 (4)
	2.8					2.5	−12.4 (7,7)	7.3 (3)
1,2,4,6,7-pentaacetate (**22b**)	3.1	9.1	1.9	1.9	9.1	3.1	−12.5 (1,1)	4.1 (3)
	3.1					3.1	−12.5 (7,7)	4.1 (5)
1,3,4,6,7-pentaacetate (**22c**)	4.1	8.3	4.1	1.9	9.4	4.3	−12.4 (7,7)	8.0 (5)
	4.1					2.7		5.1 (2)
1,2,3,4,7-pentaacetate (**22d**)		8.2	1.7	4.4	7.3	5.2	−12.3 (7,7)	5.7 (2)
						3.1		7.8 (3)
L-*glycero*-D-*galacto*-heptitol heptaacetate (**23**)[f]	7.6	3.3	8.6	2.4	8.8	5.2	−12.1 (1,1)	
	3.2					2.7	−12.5 (7,7)	
1,2,3,6,7-pentaacetate (**23a**)	7.5	2.7	8.7	1.0	8.9	5.4	−12.1 (1,1)	7.8 (5)
	3.4					2.6	−12.4 (7,7)	8.2 (4)
1,2,4,6,7-pentaacetate (**23b**)	5.7	6.7	5.4	1.7	9.7	2.6	−12.3 (1,1)	7.3 (3)
	3.1					3.5	−12.7 (7,7)	6.4 (5)
1,3,5,6,7-pentaacetate (**23c**)		5.0	8.9	1.6	7.5	5.9	−12.5 (7,7)	4.6 (2)
						2.6		6.7 (4)
1,2,3,5,7-pentaacetate (**23d**)	7.9	2.6	9.7	1.7	7.2		−12.3 (1,1)	7.8 (4)
	3.4							4.1 (6)
3-deoxy-D-*lyxo*-hexitol pentaacetate (**24**)	5.5	6.5	6.5	4.0	6.6		−12.0 (1,1)	
	3.6	6.5	6.5		4.4		−11.8 (6,6)	
1,5,6-triacetate (**24a**)	7.5			3.6	6.9		−12.0 (1,1)	2.2
	3.3				4.5		−11.8 (1,1)	3.6
6-*O*-β-D-glucopyranosyl-D-glucitol nonaacetate (**25**)[g]	6.1	4.8	6.1	4.8	5.4		−12.0 (1,1)	
	3.9				4.7		−11.0 (6,6)	
1,2,5,2′,3′,4′,6′-heptaacetate (**25a**)	6.6	5.7	1.5	8.0	4.7		−12.2 (1,1)	6.7 (3)
	3.6				3.5		−10.6 (6,6)	8.2 (4)
1,3,5,2′,3′,4′,6′-heptaacetate (**25b**)		3.3	2.0	8.7	2.9		−11.1 (6,6)	4.8
					3.5			4.8
4-*O*-β-D-galactopyranosyl-D-glucitol nonaacetate (**26**)[h]	3.5	7.3	3.3	6.0	5.7		−12.4 (1,1)	
	4.3				3.0		−12.3 (6,6)	
1,5,6,2′,3′,4′,6′-heptaacetate (**26a**)	4.9	2.2	4.7	4.0	7.3		−11.4 (1,1)	6.5 (3)
	7.0				2.9		−12.4 (6,6)	5.7 (2)
1,2,6,2′,3′,4′,6′-heptaacetate (**26b**)	6.0	4.6	4.7	4.7	7.0		−12.0 (1,1)	6.5 (5)
	4.2				3.3		−11.7 (6,6)	5.4 (3)
3-deoxy-D-*arabino*-hexitol pentaacetate (**27**)	5.5	10.5	3.5	3.1	6.9		−11.9 (1,1)	
	3.4	3.5	10.5		2.8		−14.5 (3,3)	
							−12.1 (6,6)	
3-deoxy-L-*xylo*-hexitol pentaacetate (**28**)	5.6	10.5	3.5	3.8	7.1		−11.9 (1,1)	
	3.6	3.5	10.5		4.2		−14.5 (3,3)	
							−11.9 (6,6)	
3-deoxy-L-*ribo*-hexitol pentaacetate (**29**)	5.7	6	6	4.8	6.3		−12.0 (1,1)	
	3.6	6	6		3.5		−12.2 (6,6)	

[a] Spectra determined in $CDCl_3$ at 300 MHz. [b] Coupling constants between magnetically equivalent protons were obtained from carbon-13 satellite peaks. [c] Number in parentheses refers to carbon position for OH group. [d] Entry at top is coupling constant associated with methylene proton at highest field; entry at bottom is associated with methylene proton at lowest field. The same format is used throughout this table. [e] Entry at top left is the coupling constant between the C-1 proton at highest field and the C-2 proton at highest field; entry at top right is the coupling constant between the C-1 proton at highest field and the C-2 proton at lowest field. Similarly the entry at bottom left refers to J between C-1 H at lowest field and C-2 H at highest field; entry at bottom right is J between C-1 H at lowest field and C-2 H at lowest field. The same format is used throughout this table. [f] Obtained by simulation of spectrum using the coupling constants and chemical shifts reported in this table and supplementary material. [g] Coupling constants for *O*-β-glucopyranosyl group: 1′,2′ = 8.0; 2′,3′ = 9.5; 3′,4′ = 9.5; 4′,5′ = 9.9; 5′,6′ = 2.5 and 4.5; 6′,6′ = −12.4. Values for diols vary ±0.1 ppm. [h] Coupling constants for *O*-β-galactopyranosyl group: 1′,2′ = 7.9; 2′,3′ = 10.5; 3′,4′ = 3.4; 4′,5′ = 0.9; 5′,6′ = 6.5 and 6.5. Values for diols vary ±0.1 ppm.

at the center of the carbon chain compared with relatively unhindered rotation at the terminal positions, the result being fewer molecules with oxygen atoms of a terminal *syn*-1,2-diol group in a position favorable for complexing. The yields of compounds with terminal *syn*-1,2-diol groups were probably lower also because transesterification of the borate esters with acetate would be expected to proceed more readily at the less hindered terminal positions, leading not only to a lower yield of terminal *syn*-1,2-diols but to the virtual absence of terminal glycols.

In the case of D-mannoheptulose, some stereoselectivity was observed in the bobohydride reduction of the ketose,

Chart III. Acetylation Products from D-*manno*-Heptulose

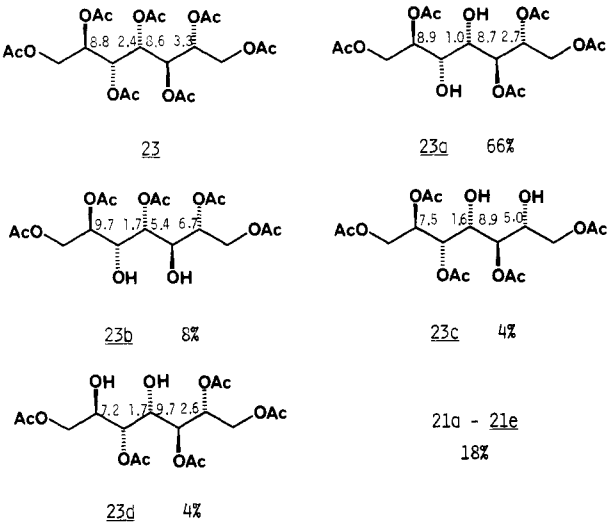


Chart IV. Acetylation Products from Gentiobiose

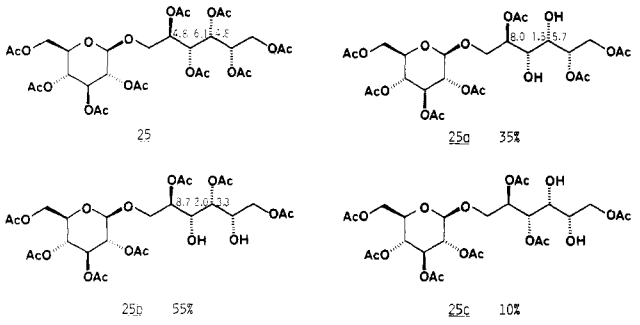
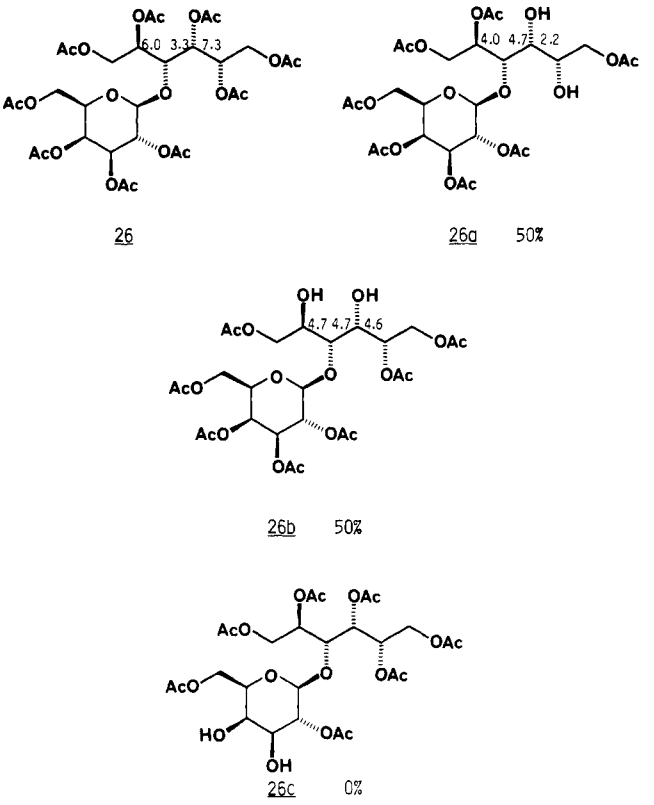


Chart V. Acetylation Products from Lactose



as pentaacetates of L-*glycero*-D-*galacto*-heptitol comprised about 80% of the diol complement, the remaining 20% being pentaacetates of perseitol.

A striking feature of the complexation reaction with gentiobiose and lactose, as well as with the ozonolysis products of palytoxin, was the total absence of cyclic diols, even the *cis*-1,2-diol **26c** from lactose.

NMR Analysis. The structures of all the partially acetylated alditols obtained in this study were deduced in a straightforward manner from ^{1}H NMR data. No difficulty was encountered in differentiating *syn*-1,2-protons from *anti*-1,2-protons since the stereochemistries of all the alditols were known. For the analysis of unknowns, it was important to find out whether the stereochemistry implied from the borate complexation could be corroborated by NMR analysis.

From our palytoxin structure work it was clear that the relative stereochemistry of acyclic polyhydroxylated compounds could not be deteremined reliably from analysis of coupling constatnt data of fully acetylated derivatives alone.[1] Coupling constant data could be correlated with relative stereochemistry of fully acetylated alditols when none of the acetoxyl substituents on methine carbons 1,3 to each other were eclipsed in the fully extended conformations of the compounds. Arabinitol pentaacetate (**11**), galactitol hexaacetate (**18**), mannitol hexaacetate (**19**), and perseitol heptaacetate (**21**), for example, showed large coupling constants of 8.4–10.0 Hz for *anti*-1,2-methine protons and small coupling constants of 2.0–2.4 Hz for *syn*-1,2-methine protons. The large and small couplings reflected the preferred, zig–zag conformations for these molecules in solution. This was consistent with X-ray crystallographic representations of arabinitol, galactitol, and mannitol which showed that these molecules were planar and fully extended in the solid state.[6]

There were exceptions. 3-Deoxy-D-*arabino*-hexitol pentaacetate (**27**) and 3-deoxy-L-*xylo*-hexitol pentaacetate (**28**), for example, both showed a small coupling constant (3.1 and 3.8 Hz, respectively) for $J_{4,5}$.

Most of the fully acetylated alditols with *syn*-1,3-acetoxy groups, such as ribitol pentaacetate (**12**), xylitol pentaacetate (**13**), **15**, **16**, sorbitol hexaacetate (**20**), **22**, **23**, and **25** showed coupling constants in the 4–7 Hz region. These medium-sized coupling constants were the direct consequence of eclipsed acetoxy groups in the fully extended conformers, resulting in increases in populations of nonextended conformers (sickle forms) and hence coupling constants between those for pure anti-1,2 and pure syn-1,2 stereochemistry. X-ray crystallographic studies of ribitol, xylitol, allitol, sorbitol, D-iditol, and D-altritol had shown that the carbon chains of these carbohydrates are bent in the solid state.[6] The steric interaction of the eclipsed acetoxyl groups could be considered analogous to the 1,3-interaction of two axial acetoxy groups on an unstrained, six-membered ring.

The coupling constants for several fully acetylated alditols and various partially acetylated alditols isolated via borate complexation are shown in Table II. A perusal of the data indicates that, in systems possessing eclipsed acetoxy groups, coupling constants for vicinal methine protons generally become larger for *anti*-1,2-protons and smaller for *syn*-1,2-protons when partially acetylated alditols are compared with fully acetylated alditols. Sorbitol hexaacetate (**20**), for example, shows coupling constants of 6.3, 4.4, and 6.7 Hz for $J_{2,3}$, $J_{3,4}$, and $J_{4,5}$. For the diols

(6) Jeffrey, G. A.; Kim, H. S. *Carbohyd. Res.* **1970**, *14*, 207.

20a–c, $J_{2,3}$, $J_{3,4}$, and $J_{4,5}$ are on the average 4.2, 2.0, and 8.2 Hz, respectively, in accord with syn,syn,anti stereochemistry for these compounds. Similarly compound **25** shows coupling constants of 4.8, 6.1, and 4.8 Hz, for $J_{2,3}$, $J_{3,4}$, and $J_{4,5}$ whereas diols **25a,b** exhibit average coupling constants of about 4.5, 1.7, and 8.3 Hz, respectively, in agreement with the syn,syn,anti stereochemistry for these compounds. Heptaacetate **23** shows coupling constants of 3.3, 8.6, 2.4, and 8.8 Hz for $J_{2,3}$, $J_{3,4}$, $J_{4,5}$, and $J_{5,6}$, respectively, similar in magnitude to those shown by **21**. Diols **23b** and **23c**, however, exhibit average coupling constants of 5.9, 7.2, 1.7, and 8.6 Hz for $J_{2,3}$, $J_{3,4}$, $J_{4,5}$, and $J_{5,6}$, respectively, in line with anti,anti,syn,anti stereochemistry for these compounds. 4-*O*-β-Galactopyranosyl-D-glucitol, however, which possesses a sugar moiety instead of an acetoxyl group on C-4 of the sorbitol residue, is an exception and does not show the same coupling constant trends on comparison of the fully acetylated compound **26** and the diols **26a,b**, at least for $J_{3,4}$ and $J_{4,5}$.

Experimental Section

Ozonolysis of Palytoxin. *N*-(*p*-Bromobenzoyl)palytoxin (28 mg) in 40 mL of 70% aqueous EtOH at 0 °C was treated with excess ozone for 2 min. The solution was purged with argon for 10 min to remove ozone and then 52 mg of sodium borohydride in 2 mL EtOH was added. The mixture was allowed to stand for 1 h at 0 °C. The excess borohydride was then destroyed with 2 mL of 0.5 M phosphate buffer, the solution was concentrated in vacuo to a small volume to remove EtOH, and the concentrate was freeze dried. The residue was treated with 10 mL of 6:1 acetic anhydride/pyridine under argon at room temperature overnight. The excess reagents were evaporated in vacuo and the residual oil was distributed between EtOAc and H_2O. The EtOAc layer was evaporated to give 27 mg of material which was subjected to HPLC on silica (Whatman Partisil M9 10/50 column) to give the fully acetylated compounds **1**, **8**, and **5** followed by the diols **6**, **9**, **2**, and **3**.

Compound **1**: ^{1}H NMR ($CDCl_3$) δ 5.268 (ddd, C-3 H), 5.153 (dd, 6.5 and 3.5 Hz, C-4 H), 5.082 (ddd, C-5 H), 4.057 (br t, 2 H on C-7), 4.048 (t, 2 H on C-1), 2.130 (s, OAc), 2.047 (s, OAc) 2.032 (s, OAc), 2.025 (s, 2 OAc), 1.90 (m, 2 H on C-6), 1.841 (m, 2 H on C-2).

Compound **2**: FDMS, *m/e* 307 (MH); ^{1}H NMR ($CDCl_3$) δ 4.859 (ddd, 9.8, 7.9, and 3.0 Hz, C-5 H), 4.249 (dt, C-1 H), 4.187 (dt, C-1 H), 4.137 (m, C-7 H), 4.107 (m, C-7 H), 3.592 (ddd, 9.6, 3.8, and 1.9 Hz, C-3 H), 3.323 (dd, 7.9 and 1.9 Hz, C-4 H), 2.252 (m, C-6 H), 2.11 (s, OAc), 2.045 (s, OAc) 2.04 (s, OAc), 1.937 (m, C-2 H), 1.927 (m, C-6 H), 1.761 (m, C-2 H).

Compound **5**: FDMS, *m/e* 1106 (M^+); ^{1}H NMR ($CDCl_3$) δ 5.404 (dd, 9.0 and 2.4 Hz, C-18 H), 5.15 (m, C-2 H and C-11 H), 5.107 (t, 9.3 Hz, axial H on C-6), 5.05 (m, J(10,11) = 5.1 Hz, C-10 H and C-22 H), 4.957 (ddd, 9.9, 8.2, and 4.4 Hz, axial H on C-15), 4.883 (br dt, 9.9 and 2.4 Hz, C-19 H), 4.806 (t, 9.6 Hz, axial H on C-5), 4.777 (t, 9.6 Hz, axial H on C-7), 4.704 (t, 8.2 Hz, axial H on C-14), 4.292 (dd, −12.0 and 3.5 Hz, C-1 H), 4.245 (dd, −11.9 and 3.3 Hz, C-23 H), 4.058 (dd, −12.0 and 5.3 Hz, C-1 H), 4.029 (dd, −11.9 and 6.6 Hz, C-23 H), 3.955 (ddd, 8.3, 5.1, and 3.4 Hz, equatorial H on C-17), 3.764 (ddd, 9.5, 8.2, and 2.6 Hz, axial H on C-13), 3.453 (td, 9.6 and 2.3 Hz, axial H on C-4), 3.312 (m, axial H on C-8), 2.090 (s, OAc), 2.070 (s, OAc), 2.066 (s, OAc), 2.049 (s, OAc), 2.044 (s, 2 OAc), 2.029 (s, 2 OAc), 2.021 (s, 2 OAc), 2.0 (ddd, equatorial H on C-16), 1.996 (s, OAc), 1.992 (s, OAc), 1.975 (s, OAc), 1.790 (ddd, −14.7, 10.1, and 2.6 Hz, C-12 H), 1.763 (ddd, −14.5, 8.8, and 2.3 Hz, C-3 H), 1.690 (ddd, −13.8, 9.9, and 5.1 Hz, axial H on C-16), 1.672 (m, 2 H on C-21), 1.667 (ddd, −14.7, 9.6, and 2.3 Hz, C-12 H), 1.618 (ddd, −14.5, 9.6, and 4.2 Hz, C-3 H), 1.610 (m, 2 H on C-20), 1.59 (m, 2 H on C-9).

Compound **6**: FDMS, *m/e* 1023 (MH); ^{1}H NMR ($CDCl_3$) δ 5.532 (dd, C-18 H), 5.350 (m, C-2 H), 5.141 (t, C-6 H), 5.06 (m, C-19 H and C-22 H), 4.875 (ddd, C-15 H), 4.839 (t, C-5 H), 4.812 (t, C-7 H), 4.764 (t, C-14 H), 4.233 (dd, C-23 H), 4.185 (dd, C-1 H), 4.015 (dd, C-1 H), 4.008 (m, C-16 H), 4.00 (dd, C-23 H), 3.937 (ddd, C-17 H), 3.73 (ddd, 11, 5, and 2 Hz, C-10 H), 3.573 (td, C-8 H), 3.565 (m, C-11 H), 3.313 (td, C-4 H), 2.123 (s, OAc), 2.086 (s, OAc), 2.073 (s, OAc), 2.053 (s, 3 OAc), 2.041 (s, 2 OAc), 2.013 (s, OAc), 2.0 (m, equatorial H on C-16), 1.990 (s, OAc), 1.977 (s, OAc), 1.722 (ddd, axial H on C-16), 1.698 (ddd, C-3 H), 1.683 (br dd, C-12 H), 1.66 (br m, 4 H on C-20 and C-21), 1.633 (br dd, −14 and 11 Hz, C-9 H), 1.588 (ddd, C-3 H), 1.512 (br dd, C-12 H), 1.425 (br ddd, −14, 12, and 2 Hz, C-9 H).

Compound **8**: FDMS, *m/e* 762 (M^+); ^{1}H NMR ($CDCl_3$) δ 5.254 (t, C-4 H), 5.204 (dd, 6.5 and 4.3 Hz, C-10 H), 5.034 (dd, C-5 H), 4.99 (m, C-11 H), 4.99 (m, C-14 H), 4.941 (t, C-3 H), 4.921 (dd, 6.5 and 4.3 Hz, C-9 H), 4.260 (dd, −12.3 and 4.9 Hz, C-1 H), 4.243 (m, C-6 H), 4.193 (dd, −12.0 and 3.5 Hz, C-15 H), 4.077 (dd, −12.3 and 2.9 Hz, C-1 H), 3.983 (dd, −12.0 and 6.4 Hz, C-15 H), 3.800 (ddd, C-2 H), 2.128 (s, OAc), 2.082 (s, OAc), 2.076 (s, OAc), 2.075 (s, OAc), 2.058 (s, OAc), 2.057 (s, OAc), 2.047 (s, OAc), 2.029 (s, OAc), 2.020 (s, OAc), 1.95 (m, C-7 H), 1.87 (m, C-8 H), 1.6 (br m, 4 H on C-12 and C-13), 1.23 (m, C-7 H), 0.915 (d, Me on C-8).

Compound **9**: FDMS, *m/e* 660 ($M - H_2O$), 678 (MH); ^{1}H NMR ($CDCl_3$) δ 5.35 (t, C-4 H), 5.04 (dd, C-5 H), 4.95 (t, C-3 H), 3.62 (dd, 6.5 and 1.5 Hz, C-9 H), 3.25 (dd, 8.5 and 1.5 Hz, C-10 H), 0.965 (d, 6.8 Hz, Me on C-8).

Borate Complexation Procedure. Method A. To an ice cold solution of the alditol or aldose (0.25 mmol) in water (1.5 mL) was added sodium borohydride (15–25 mg, 0.4–0.65 mmol) in water (0.5 mL). For a ketose 40 mg (1 mmol) of borohydride was used. After 1 h at 0 °C, glacial acetic acid (1.3 mL) was added and the solution was evaporated at 30–35 °C in vacuo to give a mixture of borate esters. This material was dissolved in water (0.3 mL) and glacial HOAc (0.9 mL), the solution was warmed quickly to 55–60 °C and acetic anhydride:pyridine (2:1) (5 mL) prewarmed to 55–60 °C was added all at once. After 2 h at 55–60 °C the reaction mixture was allowed to stand at room temperature overnight and then evaporated under reduced pressure. The residue was treated with methanol containing 1% HOAc (10 mL) and evaporated to dryness again. The methanol treatment was repeated four more times to ensure that the borate complexes were decomposed and the boric acid removed as the volatile methyl ester. The resulting residue was distributed between water (2 mL) and dichloromethane (4 × 1 mL) and the combined dichloromethane layers were dried and evaporated to give an oil. Separation of the fully and partially acetylated products in the oil was achieved by HPLC on a Whatman M-9 10/50 Partisil column by using EtOAc/hexane, sometimes containing 0.1% HOAc and/or 1–5% EtOH, as the eluant. Additional fully acetylated product was obtained from the water layer above by acetylation of the freeze dried residue with acetic anhydride and pyridine and conventional workup.

Method B. The procedure was exactly the same as Method A except that the acetylation of the borate esters was carried out in acetic anhydride:pyridine (2:1) entirely at room temperature overnight in the absence of water and acetic acid.

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Supplementary Material Available: Chemical shift data of fully and partially acetylated alditols (Tables III and IV) (6 pages). Ordering information is given on any current masthead page.