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The nitrile oxide–isoxazoline approach to 11-carbon monosaccharides. Conversion of 3-(tetritol-1-yl)-5-(tetrofuranos-4-yl)-2-isoxazolines into 6-deoxyundecoses☆

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Abstract

Hydrogenolysis of (5*R*)-3-(1,2:3,4-di-*O*-isopropylidene-D-*arabino*-tetritol-1-yl)-5-(3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-*xylo*-tetrofuranos-4-yl)-4,5-dihydroisoxazole afforded the 7-ulose derivative, from which 6-deoxy-D-*gluco*-D-*gluco*- and D-*manno*-D-*gluco*-undecose derivatives **17** and **18** were prepared by reduction with sodium borohydride or L-Selectride. The configuration of the new stereogenic centre (C-7) in compounds **17** and **18** was established by NMR analysis of their 5,7-*O*-isopropylidene derivatives. 6-Deoxy-L-*manno*-D-*gluco*- and L-*gluco*-D-*gluco*-undecose analogues **19** and **20** were prepared similarly from the isomeric 3-(L-*arabino*-tetritolyl)-4,5-dihydroisoxazole. Removal of the isopropylidene protecting groups from compounds **17** and **20** yielded 3-*O*-benzyl-6-deoxy-D-*gluco*- and L-*manno*-D-*gluco*-undecopyranoses, which were characterised as their octa-acetate derivatives. The corresponding reaction sequence from 3-(D- and L-*arabino*-tetritol-1-yl)-5-(2,3-*O*-isopropylidene-3-*O*-methyl-α-D-*lyxo*-tetrofuranos-4-yl)-4,5-dihydroisoxazoles afforded 6-deoxy-D/L-*gluco*-D-*manno* and D/L-*manno*-D-*manno*-undecose derivatives.

Keywords: 2-Isoxazolines (4,5-dihydroisoxazoles); 6-Deoxyundecos-7-uloses; 6-Deoxyundecoses

1. Introduction

The identification of 11-carbon monosaccharide structural subunits in the hikizimycin [2,3], tunicamycin [4] and herbicidin [5] antibiotics has stimulated widespread interest in the synthesis of such higher-carbon sugars [6]. We are developing a route (Scheme 1) based on nitrile oxide–isoxazoline chemistry [7], which involves chain elongation at the non-reducing terminus of readily accessible ω-unsaturated monosaccharides by 1,3-dipolar cycloaddition with a nitrile oxide, followed by reductive cleavage of the resulting 2-isoxazoline (4,5-dihydroisoxazole) cycloadducts. In the previous paper in this series [8] we reported that the undecose framework could be constructed by cycloaddition of a five-carbon nitrile oxide to a six-carbon alkene, and that such reactions proceeded stereoselectively and in satisfactory yield. For example, isoxazoline **1** was obtained by combination of D-arabinononitrile oxide **2** and the D-Glc-derived alkene **3**. We now de-

☆ For a preliminary description of part of this work, see Ref. [1].

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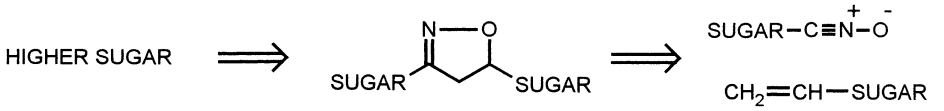
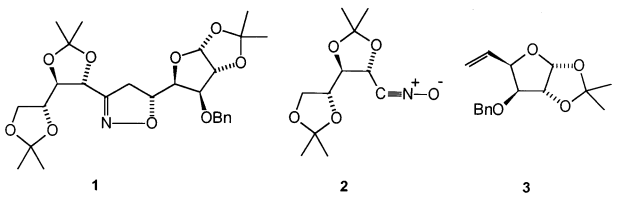


Scheme 1.

scribe the conversion of the isoxazoline cycloadducts into undecose derivatives.



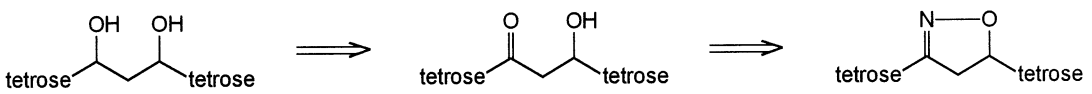
1 2 3

2. Results and discussion

The chemistry of 2-isoxazolines is well documented [7]. They are readily prepared by nitrile oxide/alkene cycloaddition reactions, they are often sufficiently robust as to allow the introduction and/or manipulation of substituents, but under reducing conditions they can undergo cleavage at the N–O bond to afford β-hydroxyimines and products derived therefrom. Of particular relevance to higher-sugar synthesis is their ability to undergo hydrogenolysis to yield β-hydroxyketones [7a], which can subsequently be converted into 1,3-diols, and we have previously exploited this chemistry to provide access from carbohydrate isoxazolines to 7-deoxy-nonoses and -decoses [9]. An isoxazoline, such as compound **1**, can thus be regarded as a masked form of an undecose (Scheme 2).

Isoxazoline ring opening.—Of the various established methods for cleavage of the N–O bond, we selected hydrogenation with a palladium/charcoal or Raney nickel catalyst in the presence of boric acid, methanol and water. This protocol, developed by Curran and others [7], is designed to achieve conversion to the β-hydroxyketone, while minimising epimerisation, retro-aldol reactions, and competing over-reduction to γ-aminoalcohols.

Initial experiments were carried out with isoxazoline **1** using the conditions previously used successfully in the nonose/decose series [9], involving hydrogenolysis over a palladium–charcoal catalyst. However, the reaction proved to be slower in this case and TLC examination after 18 h showed the presence of significant amounts of unreacted starting material as well as a new more polar material that gave a positive stain with Brady's reagent, consistent with the target β-hydroxyketone **4** (Scheme 3). Continuing the reaction for a further 20 h afforded, after preparative TLC, unreacted isoxazoline (51%) and the more polar component (19%), which was identified by its spectroscopic properties as the D-*arabino*-D-*gluco*-6-deoxyundecos-7-ulose **4**. The presence of the carbonyl group was confirmed by an IR peak at 1724 cm^{-1} and a ^{13}C NMR signal at δ_C 210 ppm. In other respects, its NMR spectra (Tables 1–3) are broadly similar to those of the isoxazoline precursor; the only significant variations are associated with the replacement of the isoxazoline moiety by the target β-hydroxyketone. The signals for C-6 and C-8 adjacent to the carbonyl group in the product are shifted to higher frequency, and there are corresponding shifts to lower frequency for C-5 and, in the proton spectrum, for the ABX pattern attributable to H-5 and H-6ab, and for H-8 adjacent to the carbonyl. Proton 5-H shows distinct trans–diaxial and axial–equatorial couplings of 9.1 and 2.6 Hz to H-6a and H-6b, consistent with the target β-hydroxyketone adopting a hydrogen-bonded half-chair conformation (Fig. 1),



Scheme 2.

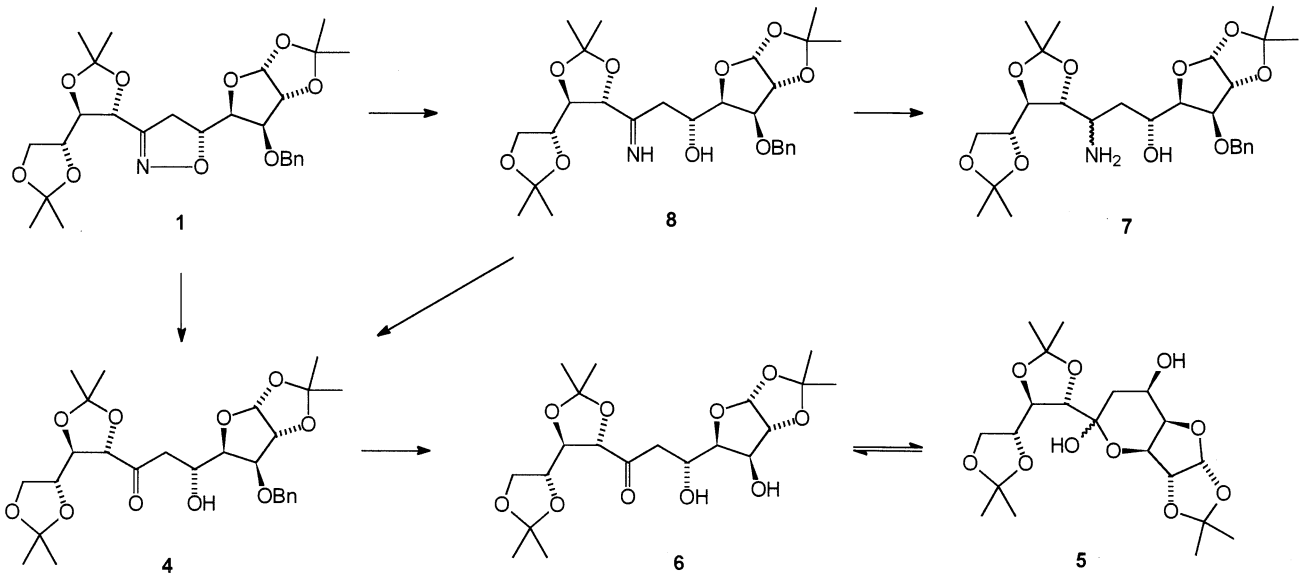
Table 1
^{1}H NMR chemical shifts (δ_H/ppm) [a] for undecos-7-uloses **4**, **5**/**6**, **13**, **15** and **16**, and undecose derivatives **17**–**32**, **35**–**38**

	1-H	2-H	3-H	4-H	5-H	6-H	7-H	8-H	9-H	10-H	11-H	$PhCH_2$ [b]	OMe	OH	Me
4	5.87	4.59	4.07	4.02	4.44	2.89		4.35	4.15	4.12	3.94	4.59		2.91	1.30, 1.33, 1.36
						3.14					4.10	4.70			1.40, 1.43, 1.47
5/**6**	5.91	4.55	3.91–3.98 [c]		4.27	1.77		4.32	4.37	4.05	3.96			2.0	1.30, 1.33, 1.37
						1.86					4.14			3.66	1.40, 1.41, 1.50
13	5.88	4.59	4.08	4.02	4.43	2.91		4.36	4.19	4.15	4.10	4.58		3.03	1.30, 1.32, 1.33
						3.10					3.95	4.69			1.41, 1.43, 1.46
15	4.83	4.53	4.79	3.79	4.42	2.91		4.37	4.17	4.15	3.93		3.27	3.10	1.29, 1.31, 1.36
						3.08					4.08				1.39, 1.42, 1.43
16	4.81	4.50	4.75	3.76	4.38	2.92		4.37	4.18	4.12	4.05		3.24	3.10	1.26, 1.29, 1.30
						2.98					3.91				1.37, 1.40, 1.41
17	5.88	4.58	4.09	3.97	4.22	1.72	4.0 [c]	3.9 [c]	3.9 [c]	4.0 [c]	3.93		4.64	3.0	1.29, 1.32, 1.35
						2.08					4.12		4.70	3.6	1.39, 1.41, 1.46
18	5.93	4.60	4.11	4.07	4.27	1.93	3.97	3.78	3.75	4.07	3.99		4.58	3.11	1.30, 1.33, 1.34
						1.93					4.17		4.70	3.67	1.42, 1.46, n.d. [d]
19	5.90	4.57	4.11	3.98	4.23	1.59	3.92	3.8 [c]	3.8 [c]	4.06	4.17		4.70	2.83	1.29, 1.33, 1.36
						2.29					3.99		4.70	4.06	1.44, 1.47, n.d.
20	5.92	4.60	4.08	4.03	4.27	1.92	4.0 [c]	3.86	3.90	4.0 [c]	4.11		4.52	2.54	1.30, 1.31, 1.34
						1.68					3.92		4.70	2.78	1.37, 1.38, 1.45
21	4.82	4.50	4.78	3.71	4.15	1.71	4.0 [c]	3.9 [c]	3.9 [c]	4.0 [c]	3.91		3.24	3.10	1.28, 1.33, 1.37
						2.03					4.08			3.70	1.43, n.d., n.d.
22	4.85	4.50	4.80	[e]	[e]	1.91	[e]	[e]	[e]	[e]	[e]		3.25	2.09	1.27, 1.30, 1.32
						1.91								[e]	1.39, 1.42, n.d.
23	4.87	4.54	4.82	3.76	[f]	1.64	[f]	[f]	[f]	[f]	[f]		3.30	[f]	1.23, 1.31, 1.34
						2.22									1.35, 1.43, 1.47
24	4.88	4.54	4.81	3.81	4.25	1.93	4.0 [c]	3.9 [c]	3.9 [c]	4.0 [c]	4.11		3.28	2.5	1.29, 1.30, 1.35
						1.79					3.93			3.0	1.39, 1.45, n.d.
25	5.86	4.54	4.0 [c]	4.0 [c]	4.24	1.69	4.0 [c]	3.86	4.0 [c]	4.0 [c]	3.96	4.56			1.28, 1.32, 1.35
						1.77					4.11	4.63			1.36, 1.37, 1.38
															1.45, n.d., n.d.
26	5.88	4.55	4.00	[g]	4.24	2.19	[g]	[g]	3.78	[g]	[g]	4.55			1.29, 1.33, 1.34
						1.87						4.63			1.37, 1.40, 1.47

Table 1 (Continued)
^{1}H NMR chemical shifts (δ_H/ppm) [a] for undecos-7-uloses **4**, **5**/**6**, **13**, **15** and **16**, and undecose derivatives **17**–**32**, **35**–**38**

	1-H	2-H	3-H	4-H	5-H	6-H	7-H	8-H	9-H	10-H	11-H	$PhCH_2$ [b]	OMe	OH	Me
27	5.88	4.55	4.03	3.96	4.23	1.53 1.92	[g]	[g]	3.81	4.13	4.06 3.95	4.57 4.64			1.29, 1.33, 1.35 1.36, 1.37, 1.41 1.46, n.d.
28	5.88	4.54	3.99	4.08	4.25	2.16 1.84	[g]	[g]	[g]	4.03	4.12 3.93	4.55 4.63			1.29, 1.32, 1.33 1.36, 1.38, 1.48 n.d., n.d.
29	4.80	4.48	4.69	3.71	4.20	1.62 1.73	3.96 [c]	3.88	4.03 [c]	4.10	3.96 [c] 4.03 [c]		3.24		1.28, 1.30, 1.31 1.37, 1.38, 1.40 n.d., n.d.
30	4.82	4.49	4.67	3.79	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.		3.26		1.26–1.40
31	4.81	4.49	4.70	3.68	n.d.	n.d. 1.85	n.d.	n.d.	n.d.	n.d.	n.d.		3.26		1.22–1.47
32	4.82	4.50	4.69	3.80	4.17	2.16 1.75	3.92	3.97	3.91	4.03	4.12 3.93		3.25		1.27, 1.32, 1.33 1.36, 1.37, 1.39 1.41, n.d.
35	6.23	4.98 [c]	3.90	4.85	3.94	1.74 1.85	5.03	5.23	5.32	4.97 [c]	4.13 4.13	4.59 4.67			1.95, 1.97, 2.00 2.01, 2.04, 2.10 2.09, n.d.
36	5.56	5.08	3.67	4.87	3.61	1.81 [c]	5.07	5.25	5.36	4.98	4.15	4.56			1.93, 1.98, 1.99 2.02, 2.03, 2.05 2.09, n.d.
37	6.17	4.99	3.87	4.86	3.66	1.59 1.69	5.18 [c]	5.18 [c]	5.37	5.01	4.04 4.19	4.58 4.67			1.95, 1.91, 2.00 2.01, 2.03, 2.05 2.09, 2.12
38	5.51	5.07	3.66	4.89	3.46	[h]	5.17 [c]	5.17 [c]	5.34	5.02	4.06 4.23	4.55			1.91, 1.97, 1.99 2.00, 2.02, 2.03 2.04, n.d.

[a] Recorded in $CDCl_3$ at 360 or 600 MHz.
[b] Also δ 7.2–7.5 (Ph).
[c] Overlapping multiplets.
[d] n.d., not determined.
[e] 3.68–4.18 (complex multiplet).
[f] 3.70–4.26 (complex multiplet).
[g] 3.91–4.11 (complex multiplet).
[h] 1.63–1.87 (complex multiplet).



Scheme 3.

which allows the bulky furanosyl substituent to occupy the sterically less demanding quasi-equatorial position.

A repeat experiment over a longer period (63 h) yielded unreacted starting material (9%), the 6-deoxyundecos-7-ulose **4** (37%), together with a mixture of more polar compounds, which NMR analysis showed not to contain the benzyl group. The major component of the latter mixture was tentatively assigned, on the basis of its spectroscopic properties, hemiketal structure **5**, which is presumably formed by debenzylation at C-3 yielding β,δ-dihydroxyketone **6**, followed by intramolecular addition of the δ-hydroxyl group to the ketone at C-7. In the ^{13}C NMR spectrum there is a characteristic quaternary peak at 97.3 ppm attributable to the hemiketal carbon (C-7), and one at 33.5 ppm for the adjacent methylene carbon (C-6). Supporting evidence is provided by two OH signals at δ_H 2.0 and 3.66 ppm, and peaks at 1.77 and 1.86 ppm for the methylene protons 6a and 6b. In previous work [9] involving hydrogenolysis of higher-sugar isoxazolines debenzylation was not observed, presumably due to the shorter reaction times.

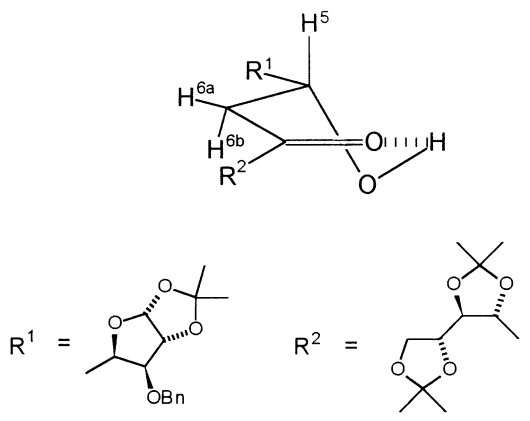


Fig. 1. Half-chair arrangement for β-hydroxyketone **4**.

In order to shorten the reaction times and minimise the debenzylation, the alternative Raney nickel-catalysed procedure was investigated. Isoxazoline **1** was subjected to the same set of standard hydrogenolysis conditions described above, but with Raney nickel in place of the Pd–C catalyst. Complete consumption of the starting material was achieved after only 7 h, and preparative TLC afforded the target β-hydroxyketone **4** in 66% yield, together with an inseparable mixture of γ-aminoalcohols **7** (25%). The latter amines were identified by the characteristic ^{13}C NMR signals for C-7 at 50.7 and 52.3 ppm, as expected [10] for the $CHNH_2$ group; further evidence was provided by high-resolution mass spectrometry and a positive ninhydrin TLC stain. The amino compounds are presumed to arise from hydrogenation of β-hydroxyimine **8**, the putative intermediate on the pathway to the β-hydroxyketone, competing with its hydrolysis (Scheme 3). In an attempt

to increase the proportion of β-hydroxyketone the concentration of boric acid was varied, but with little effect. Indeed, the overriding influence on the yield of product was the nature of the Raney nickel. The best results were achieved when the catalyst had been pre-

Table 2
^{1}H NMR couplings (J_{x-y}/Hz) [a] for undecos-7-uloses **4**, **5**/**6**, **13**, **15** and **16**, and undecose derivatives **17**–**32**, **35**–**38**

	1–2	2–3	3–4	4–5	5–6	6a–6b	6–7	7–8	8–9	9–10	10–11	11a–11b	PhCH_2
4	3.8	<1	3.1	8.6	9.1	18.3			5.8	n.d. [b]	4.5	8.4	11.8
						2.6						7.1	
5/**6**	3.6	n.d.	n.d.	n.d.	5.0	12.5			2.1	3.4	4.8	8.5	
					11.6						6.0		
13	3.8	<1	3.2	8.6	9.1	18.1			5.5	6.6	6.2	8.5	11.8
					2.7						4.5		
15	<1	5.9	3.7	8.5	8.9	17.9			5.6	6.8	4.5	8.5	
					3.0						6.1		
16	<1	5.9	3.7	8.2	7.8	17.4			5.6	6.8	6.2	8.5	
					4.1						4.8		
17	3.8	<1	3.0	8.3	10.2	14.7	10.4	n.d.	n.d.	n.d.	5.0	8.4	11.8
					2.1		2.4				6.0		
18	3.7	<1	3.3	7.7	4.9	n.d.	n.d.	n.d.	7.8	7.3	5.3	8.7	11.7
					7.1						6.2		
19	3.8	<1	3.0	8.3	10.1	14.5	10.1	7.0	n.d.	7.5	6.0	8.4	
					1.7		1.7				5.3		
20	3.8	<1	3.5	8.0	2.7	14.5	10.1	2.6	7.3	7.6	6.0	8.3	11.8
					9.2		2.6				5.1		
21	<1	5.9	3.6	8.4	10.1	14.5	10.1	n.d.	n.d.	n.d.	4.9	8.3	
					2.4		2.4				6.0		
22	<1	5.9	3.7	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	
23	<1	6.0	3.3	8.1	10.1	14.5	10.1	n.d.	n.d.	n.d.	n.d.	n.d.	
					2.2		2.2						
24	<1	6.0	3.7	7.9	2.8	14.5	9.9	n.d.	n.d.	n.d.	6.0	8.3	
					9.1		2.8				4.6		
25	3.7	<1	3.0	8.6	11.6	13.1	11.6	n.d.	n.d.	n.d.	4.2	8.1	11.9
					3.0		3.0				5.7		
26	3.8	<1	3.6	8.5	6.3	13.2	9.6	n.d.	6.7	6.7	n.d.	n.d.	11.7
					8.9		5.9						
27	3.7	<1	2.6	8.7	11.8	13.2	11.8	n.d.	5.3	6.3	6.3	8.3	11.9
					2.5		2.5				5.6		
28	3.8	<1	3.1	8.5	6.3	13.2	9.8	n.d.	n.d.	n.d.	6.2	8.2	11.7
					8.6		5.7				5.3		
29	<1	5.9	3.5	8.4	11.8	12.8	11.8	3.1	6.5	1.9	4.2	n.d.	
					2.6		2.6				8.1		
30	<1	5.9	3.9	8.3	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	
31	<1	5.9	3.5	8.3	11.7	13.0	11.7	n.d.	n.d.	n.d.	n.d.	n.d.	
					2.4		2.4						
32	<1	5.9	3.6	8.5	6.3	13.1	10.0	4.4	6.1	7.9	6.1	8.3	
					9.1		5.8				5.3		
35	3.7	10.0	9.4	10.0	8.9	15.1	8.9	8.0	3.2	8.0	n.d.	n.d.	11.9
					1.9		1.9						
36	8.3	9.4	9.4	9.5	n.d.	n.d.	n.d.	3.9	3.9	7.4	4.1		
											4.1		
37	3.9	10.0	9.3	10.1	10.1	14.0	9.0	n.d.	3.4	7.6	5.2	12.4	11.8
					1.7		<2				3.5		
38	8.3	9.4	9.3	9.6	9.6	n.d.	n.d.	n.d.	4.3	6.7	5.9	12.5	
					2.4						3.1		

[a] Recorded in $CDCl_3$ at 360 or 600 MHz.
[b] n.d., not determined.

Table 3
^{13}C NMR chemical shifts (δ_C/ppm) [a] for undecos-7-uloses **4**, **5**/**6**, **13**, **15** and **16**, and undecose derivatives **17**–**32**

	C-1	C-2–C-4 C-8–C-10	C-5	C-6	C-7	C-11	CMe$_2$	CMe_2	CH$_2$Ph	PhC	PhCH	OMe
4	104.9	76.3, 78.0, 81.1, 81.7, 82.4, 82.9	64.6	43.4	210.2	66.5	109.8, 111.4, 111.6	24.8, 25.9, 26.2, 26.4, 26.5, 26.7	72.3	137.3	127.7, 128.0, 128.5	
5/**6**	105.0	75.0, 76.3, 77.1, 77.9, 84.2, 84.5	63.6	33.5	97.3	67.4	110.1, 111.0, 111.9	25.0, 26.1, 26.3, 26.6, 26.8, 27.9				
13	104.9	76.4, 77.8, 81.1, 81.8, 82.3, 83.0	64.8	43.4	209.9	66.5	109.8, 111.3, 111.6	25.0, 26.0, 26.1, 26.3, 26.6, 26.9	72.2	137.2	127.7, 127.9, 128.4	
15	107.0	76.3, 78.0, 79.4, 81.1, 82.9, 84.7	65.5	43.4	209.1	66.5	109.7, 111.4, 112.5	24.5, 25.0, 25.8, 26.1, 26.3, 26.9				54.4
16	106.9	76.3, 77.7, 79.3, 81.2, 83.0, 84.6	65.7	43.3	208.9	66.5	109.7, 111.2, 112.5	24.5, 24.9, 25.8, 26.1, 26.3, 26.9				54.4
17	104.8	77.0, 77.1, 81.3, 82.3, 82.6, 82.9	69.1 [b]	37.9	71.2 [b]	67.7	109.4, 109.7, 111.5	25.6, 26.1, 26.4, 26.6, 26.9, 27.0	72.3	137.4	127.7, 127.8, 128.4	
18	105.0	76.3, 80.8, 82.0, 82.1, 82.2, 82.9	69.6 [b]	37.9	66.2 [b]	67.7	109.2, 110.0, 111.4	25.0, 26.2, 26.6, 26.7, n.d. [c], n.d.	72.0	137.2	127.7, 127.9, 128.4	
19	104.9	76.1, 80.8, 81.3, 82.5, 82.7, 82.9	69.2 [b]	37.4	73.5 [b]	67.6	109.2, 110.1, 111.5	25.0, 26.2, 26.3, 26.6, 26.8, n.d.	72.3	137.7	127.6, 127.7, 128.4	
20	105.0	77.0, 77.3, 81.6, 82.0, 82.1, 83.0	67.1 [b]	38.2	66.2 [b]	67.6	109.3, 109.6, 111.5	25.1, 26.1, 26.5, 26.7, 26.9, 27.0	71.8	137.0	127.8, 128.1, 128.6	
21	106.8	76.8, 76.9, 79.3, 81.8, 82.9, 84.4	69.8 [b]	37.5	70.9 [b]	67.4	109.3, 109.4, 112.1	24.3, 24.9, 25.7, 26.3, 26.7, 27.0				54.1

Table 3 (Continued)

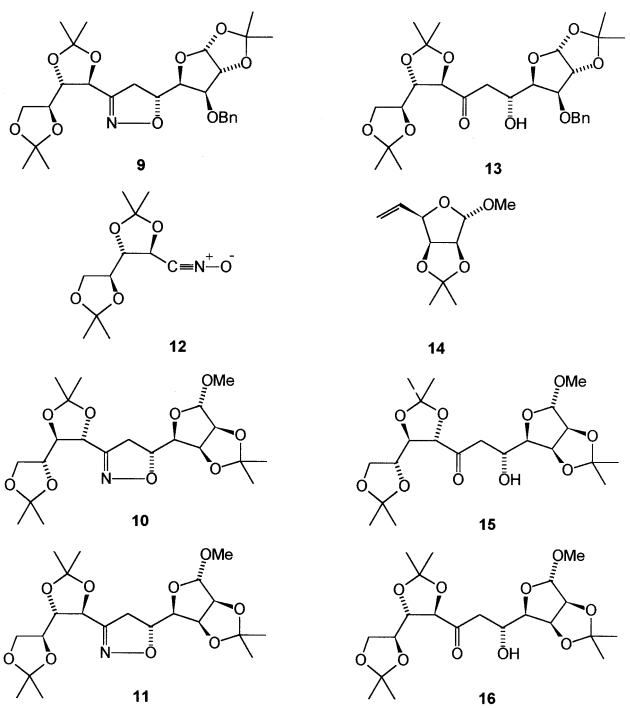
	C-1	C-2–C-4 C-8–C-10	C-5	C-6	C-7	C-11	CMe_2	CMe_2	CH_2Ph	PhC	PhCH	OMe
22	106.6	76.3, 79.9, 80.6, 81.5, 82.8, 84.6	69.8 [b]	37.6	67.1 [b]	67.8	108.8, 109.1, 109.5	25.3, 25.7, 26.5, 26.9, 27.3, 27.4				54.6
23	107.0	76.2, 79.6, 80.2, 81.9, 82.8, 84.6	69.9 [b]	37.3	66.8 [b]	67.3	109.3, 109.6, 112.2	24.9, 25.8, 26.2, 26.7, 26.8, n.d.				54.3
24	106.9	77.0, 77.4, 79.9, 81.5, 83.2, 84.6	67.2 [b]	38.3	67.1 [b]	67.6	109.4, 109.6, 112.5	24.5, 25.1, 25.8, 26.4, 27.0, 27.1				54.4
25	104.8	76.0, 77.4, 80.6, 82.3, 82.8 [d]	67.8 [b]	31.1	65.7 [b]	67.4	98.5, 109.4, 109.5, 111.5	19.7, 25.0, 26.1, 26.4, 26.5, 26.6, 27.3, 29.7	72.2	137.7	127.4, 127.6, 128.2	
26	104.8	76.9, 78.2, 81.2, 81.4, 82.1, 82.8	66.8 [b]	30.3	63.4 [b]	66.9	100.4, 109.4, 110.0, 111.5	24.7, 25.0, 25.2, 26.1, 26.5, 26.7, 27.1, 27.4	72.2	137.5	127.4, 127.7, 128.3	
27	104.9	76.6, 78.5, 80.7, 81.5, 82.3, 83.0	69.8 [b]	30.5	65.6 [b]	66.3	98.4, 104.9, 110.0, 111.7	19.7, 25.2, 26.2, 26.4, 26.7, 27.4, 29.8, n.d.	72.3	137.5	127.5, 127.7, 128.3	
28	104.9	77.1, 77.2, 81.2, 82.0, 82.2, 82.6	65.9 [b]	31.4	63.6 [b]	67.4	100.3, 109.5, 109.7, 111.4	24.9, 25.0, 25.1, 26.1, 26.5, 26.7, 26.8, 27.6	72.2	137.5	127.5, 127.7, 128.3	
29	106.7	76.3, 77.5, 79.1, 81.7, 82.6, 84.7	68.1 [b]	30.7	66.4 [b]	67.5	98.7, 109.4, 112.0	19.4, 24.8, 25.1, 26.0, 26.5, 26.6, 27.5, 29.7				54.2
30	n.d.	64.2, 66.9, 76.8, 78.4, 81.4, 82.0	n.d.	30.7	n.d.	66.7	100.6, 109.4, 110.0, 112.1	24.5–27.5 [d]				54.2
31	106.7	76.5, 78.7, 78.9, 81.3, 81.7, 84.5	69.9 [b]	30.3	66.1 [b]	66.1	98.4, 106.7, 110.0, 111.9	19.3, 24.7, 25.1, 25.8, 26.3, 27.3, 27.5, 29.6				54.0
32	106.8	77.3, 77.4, 79.2, 82.0, 84.7 [b]	66.2 [b]	32.1	64.1 [b]	67.5	106.8, 109.5, 109.7, 112.2	24.2, 24.4, 24.8, 25.1, 25.9, 26.4, 26.8, 27.6				54.2

[a] Recorded in $CDCl_3$ at 50 or 90 MHz.
[b] Alternative assignments.
[c] n.d., not determined.
[d] Overlapping signals.

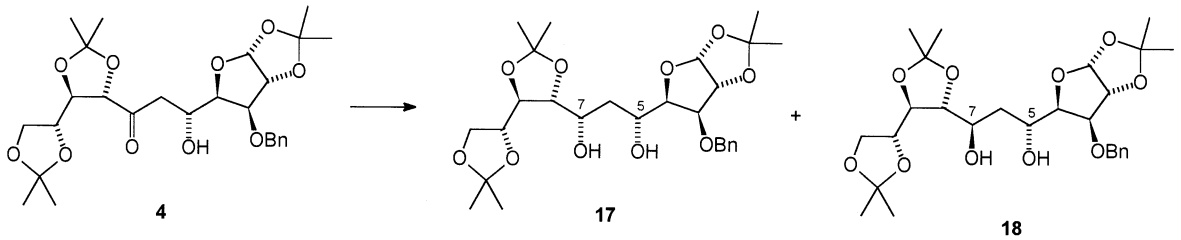
washed with water, as reported by Curran [7a], and stored under methanol at < 0 °C for 3–4 weeks prior to use.

Having established an effective procedure for the conversion of isoxazoline **1** to β-hydroxyketone **4**, the closely related undecose–isoxazolines **9–11** were examined under similar conditions. Isoxazoline **9**, which is derived from alkene **3** and L-arabinononitrile oxide **12**, afforded L-*arabino*-D-*gluco*-6-deoxyundecos-7-ulose **13** (54%), together with 27% of the corresponding γ-aminoalcohol by-products. No evidence for debenzylation was observed for any of the Raney nickel-catalysed reactions. Others [11,12] have achieved similar success in this respect, and the advantages of employing deactivated Raney nickel have also been reported [11]. Similarly isoxazolines **10** and **11**, which were obtained [8] by combination of arabinonitrile oxides **2** and **12** with D-Man-derived hex-5-enofuranoside **14**, yielded D- and L-*arabino*-D-*manno*-6-deoxyundecos-7-uloses **15** (55%) and **16** (52%), respectively (Scheme 4).

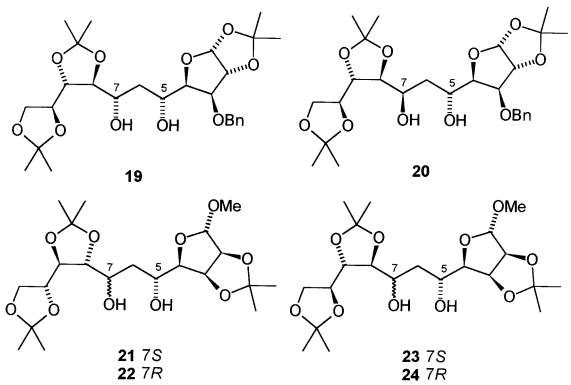
Reduction of 6-deoxyundecos-7-uloses.— The next stage in the sequence from nitrile oxide cycloaddition through to the target higher sugars involves reduction of the carbonyl function of the β-hydroxyketone to provide the corresponding 1,3-diols (Scheme 2). A new asymmetric centre is created in this step at C-7 and, as the D- and L-arabinose-derived undecosuloses have opposite configuration at C-8 adjacent to the carbonyl of the β-hydroxyketone moiety, it was of interest to establish the extent to which this influences the stereochemical outcome. Two reducing agents, sodium borohydride and L-Selectride, were used for this study. Treatment of β-hydroxyketone **4** with sodium borohydride in ethanol–water afforded a mixture of 1,3-diols **17** and **18** in 79% combined yield (Scheme 5). The products were separated by preparative TLC and characterised by ^{1}H and ^{13}C NMR spectroscopy, optical rotation and FABMS. In the carbon spectrum the carbonyl peak at 210 ppm for the starting material is replaced by a CHOH signal at ca. 70 ppm. The isomer ratio (62:38; see Table 4) was measured from the ^{1}H NMR spectrum of the product mixture by comparison of the anomeric proton signals, which are well separated ($\Delta\delta = 0.05$ ppm) despite the remoteness of this nucleus from the centre of asymmetry. β-Hydroxyketones **13**, **15**, **16** reacted similarly yielding mixtures of 1,3-diols **19**/**20**, **21**/**22** and **23**/**24** (72–82%). The borohydride reductions were useful in providing access to both isomers with ratios typically ca. 2:3. Higher yields (76–98%) and greater selectivity, however, were achieved with L-Selectride in THF as reducing agent, with d.e. values ranging from 72 to > 94%. Indeed, except in the case of ketone **13**, the signals attributable to the minor 1,3-diol isomer were on the limits of NMR detection. For all four ketones studied the major product was the same for the two reducing agents. Whereas the D- and L-*arabino*-D-*gluco*-deoxyundecos-7-uloses **4** and **13** afforded chromatographically separable diastereomeric 1,3-diols, the mixtures obtained from D- and L-*arabino*-D-*manno*-deoxyundecos-7-uloses **15** and **16** could not be separated; however, as L-Selectride gave essentially one product, this allowed characterisation of one isomer, and partial ^{1}H and ^{13}C NMR analyses of the minor isomers from the spectra of the mixtures were also obtained.



Scheme 4.



Scheme 5.



The individual 1,3-diols show distinctive splitting patterns for the C-6 methylene protons, which enable the configuration at the new stereogenic centre C-7 to be established. This is illustrated for diols **23** and **24** in Fig. 2, which shows the ^{1}H NMR spectrum for this region. In the major isomer **24** the signals for 6a-H and 6b-H appear as two clearly defined doublet-of-doublet-of-doublets, each with two large and one small coupling. In contrast the spectrum for the minor isomer **23** has two more widely separated doublet-of-triplet patterns, with a small triplet coupling for 6a-H and a large triplet coupling for 6b-H. These observations are consistent with the minor isomer adopting a hydrogen-bonded chair-type conformation (Fig. 3), in which the bulky furanose unit and the L-*arabino*-tetrosyl substituent occupy the least sterically demanding equatorial positions. Conformer **A** has the hydrogen of the 5-OH group in hydrogen bonding, whereas **B** represents the alternative arrangement involving the 7-OH group. In both of these structures 6ax-H would be expected to show two large axial–axial couplings (10–13 Hz), with 6eq-H having two smaller axial–equatorial couplings (2–4 Hz), as observed. On the other hand the corresponding hydrogen-bonded chair-type conformations for the 7R epimer would require one of the bulky substituents to occupy an unfavourable axial position; distortion of the chair is therefore expected, in accord with the observed couplings. Therefore, the major isomer is assigned the 5R,7R configuration **24**, and the minor product is assigned the 5R,7S epimer **23**. Similar characteristic patterns are observed for the C-6 methylene protons of the other pairs of 1,3-diols, and assignment of configuration at C-7 for each isomer was made using the arguments outlined above.

Confirmation of the configuration at C-7.— In order to confirm the structural predictions described above, the 5,7-*O*-isopropylidene ketal derivatives were prepared. By this means the C-5, C-6 and C-7 unit of the undecose is locked in a six-membered 1,3-dioxane ring, for which the vicinal proton–proton coupling constants are predictable when it adopts a chair conformation. Each of the individual 1,3-diols **17**–**20** and the inseparable mixtures

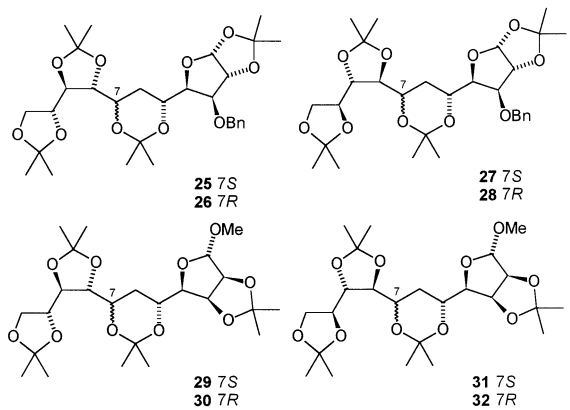


Table 4
Isomer ratios for 1,3-diols

Reducing agent	Isomer ratio			
	17:**18**	**19**:**20**	**21**:**22**	**23**:**24**
$NaBH_4$	62:38	40:60	62:38	37:63
L-Selectride	>97.3	12:88	>95:5	<3:97

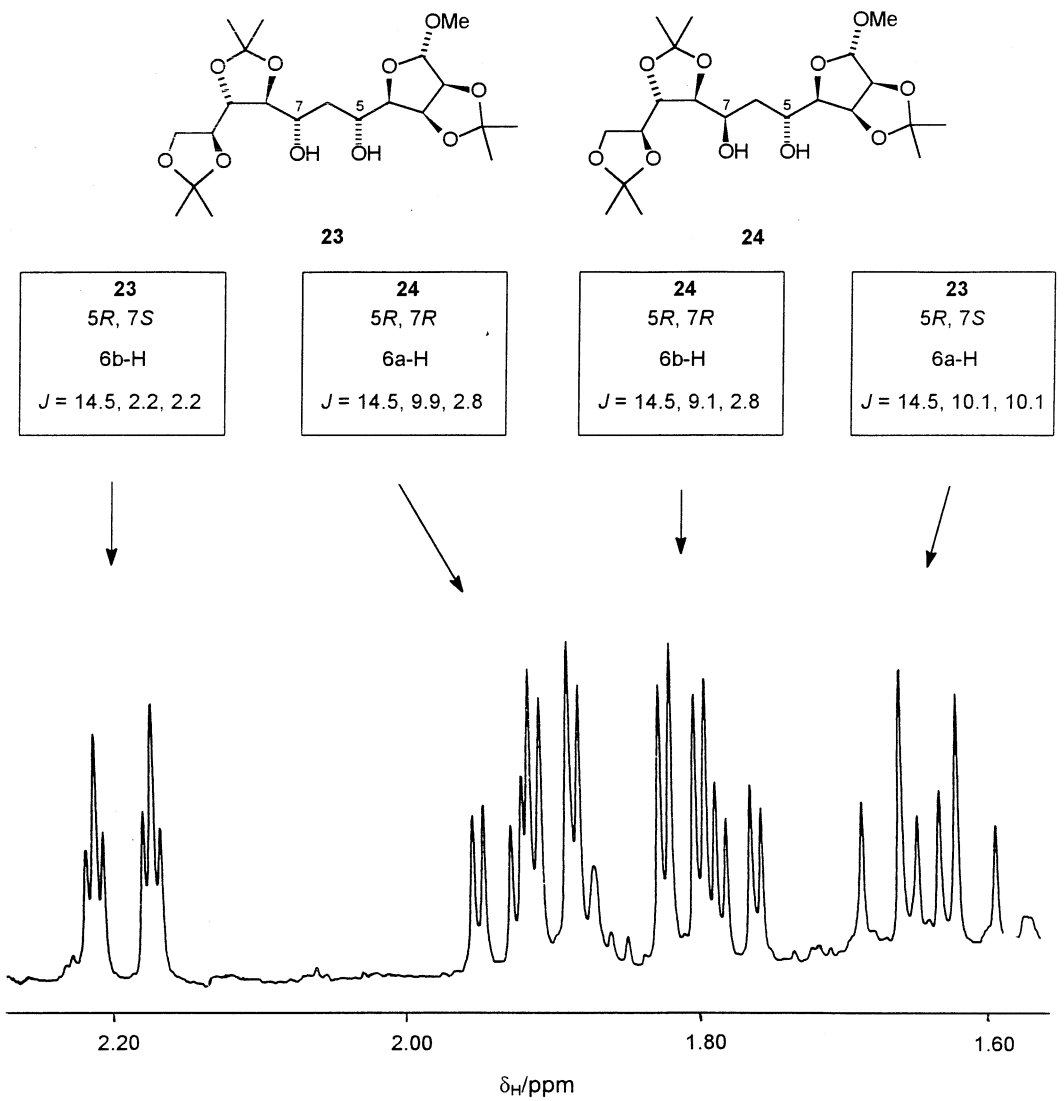


Fig. 2. ^{1}H NMR signals for 6a-H/6b-H for compounds **23** and **24**.

21/**22** and **23**/**24** were treated with acetone and 2,2-dimethoxypropane in the presence of a catalytic amount of *p*-toluenesulfonic acid to afford the corresponding ketals **25**–**32**.

The diol mixtures **21**/**22** and **23**/**24** provided inseparable mixtures of ketals, and it therefore did not prove possible to fully characterise the minor isomers. Examination of the ^{1}H NMR spectra in the region of the C-6 methylene protons for compounds **25** and **26** revealed patterns that closely paralleled those of the diols from which they had been prepared. One isomer has characteristic chair couplings: 6a-H shows two ca. 12 Hz axial–axial couplings, whereas 6b-H has two small (~ 3 Hz) axial–equatorial couplings. Such a chair arrangement (Fig. 4, structure **C**) may be accommodated only by the 5R,7S isomer in which the sugar substituents (R^1 and R^2) can occupy the equatorial positions. The other isomer must therefore have 5R,7R stereochemistry for which a chair structure would necessitate one of these substituents being located in an unfavourable axial position. The *J* values observed for the latter isomer are indeed indicative of a non-chair structure and may best be explained by the 1,3-dioxane ring adopting a twist-boat/skew conformation **D**, which allows both bulky substituents (R^1 and R^2) to occupy pseudo-equatorial positions. Similar spectral features were observed for the other pairs of isomers **27**/**28**, **29**/**30** and **31**/**32**. Further support for these assignments is provided by their ^{13}C NMR data. Distinctive

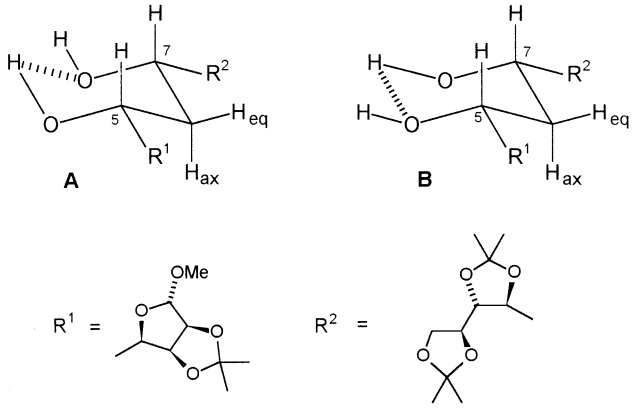


Fig. 3. Hydrogen-bonded chair conformations for compound **23**.

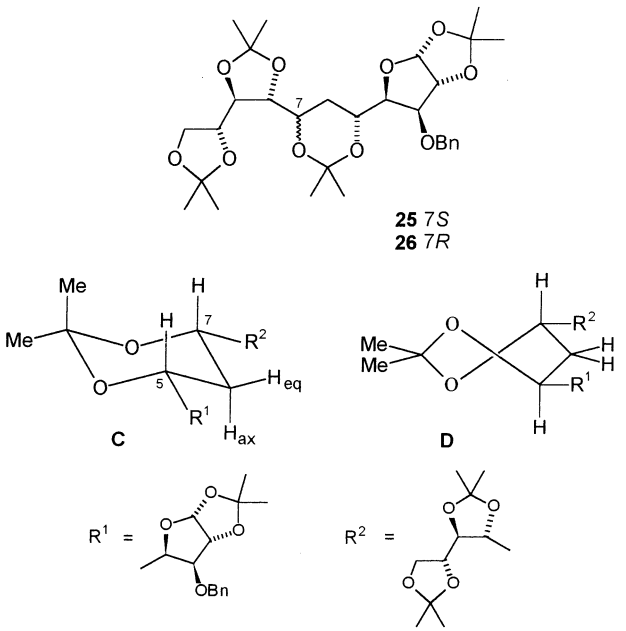
signals are observed for the methyl carbons of the 5,7-*O*-isopropylidene moiety (Table 5). For compounds **25**, **27**, **29** and **31** the axial and equatorial methyl carbon peaks are well separated at 19.3–19.7 and 29.6–29.8 ppm ($\Delta\delta \sim 10$ ppm), whereas for the isomers compounds **26**, **28**, **30** and **32** both fall within the range 24.2–27.6 ppm. The signals for the quaternary CMe_2 are also distinctive: for the chair conformation this carbon absorbs at

Table 5
Characteristic ^{13}C NMR signals for isopropylidene carbons of 1,3-dioxane ring in compounds **25**–**32**

Ketal	Assignment	Conformation	δ_C (ppm)	
			CMe_2	$2\times Me$
25	5R,7S	chair	98.5	19.7, 29.7
27	5R,7S	chair	98.4	19.7, 29.8
29	5R,7S	chair	98.7	19.4, 29.7
31	5R,7S	chair	98.4	19.3, 29.6
26	5R,7R	skew	100.4	24.7–27.4
28	5R,7R	skew	100.3	24.9–27.6
30	5R,7R	skew	100.6	24.5–27.5
32	5R,7R	skew	100.7	24.2–27.6

98.4–98.7 ppm, whereas the corresponding peaks for the skew conformation are at 100.7–100.3 ppm. Previous studies by Buchanan et al. have shown [13] that such values are typical of chair and skew arrangements in 1,3-dioxanes.

Rationalisation of π-facial selectivity.—The following conclusions are evident from the above structural assignments: (a) the predominant 1,3-diol is dependent on the starting β-hydroxyketone and independent of the reducing agent used; (b) L-Selectride provided greatly increased levels of selectivity relative to sodium borohydride; (c) the D-arabinose-derived β-hydroxyketones **4** and **10** provided the 7S isomers predominantly; and (d) the L-arabinose-derived β-hydroxyketones **9** and **11** mainly the 7R isomers. Hence the configu-



Ketal	J/Hz	5-6a	5-6b	6a-6b	6a-7	6b-7
25		11.6	3.0	13.1	11.6	3.0
26		6.3	8.9	13.2	9.6	5.9

Fig. 4. Chair and skew conformations for compounds **25** and **26**.

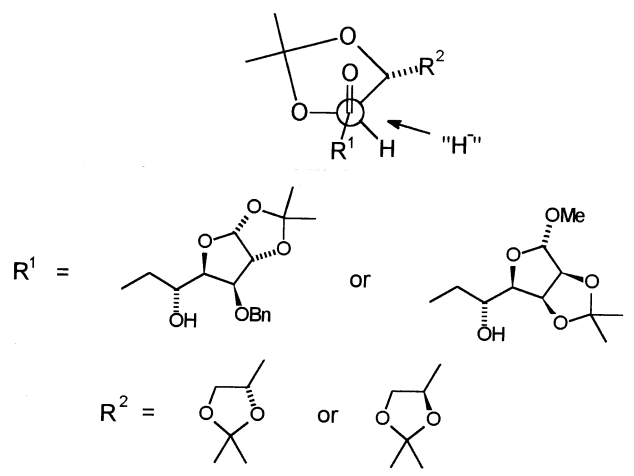
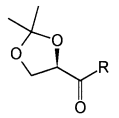


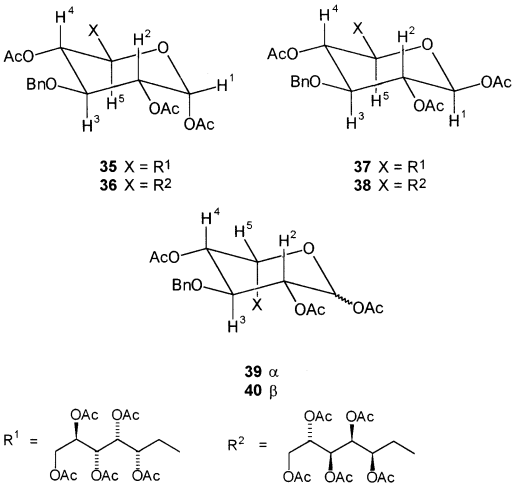
Fig. 5. Felkin–Anh model for reduction of 6-deoxyundecos-7-uloses.

ration at C-8, the position adjacent to the carbonyl function, determines the stereochemistry of major product, which in all cases possesses a threo relationship about the C-7/C-8 bond. In the absence of chelating reagents these results can best be explained in terms of a Felkin–Anh transition-state model [14] (Fig. 5), which involves hydride ion attack on a staggered orientation of substituents with the anti alkoxy group. Similar results have been reported for the related reduction of D-glyceraldehyde-derived compounds **33** and **34** for which the preferential formation of threo/anti products was ascribed to the Felkin–Anh model [15]. The substantially higher levels of selectivity observed for the L-Selectride reductions may be attributed to the greater bulk of this reagent.



33 R = H
34 R = Me

Conversion of 6-deoxyundecofuranoses **17** *and* **20** *into octa*-O-*acetylpyranose derivatives.*—D-*gluco*-D-*gluco*-Undecofuranose **17** was subjected to isopropylidene deprotection (TFA–H_2O) followed by treatment with acetic anhydride–pyridine–DMAP to afford a mixture of α- and β-octaacetylpyranosides **35** and **36**, which were readily separable by chromatography. L-*Gluco*-D-*gluco*-undecofuranoside **20** reacted similarly to yield octa-acetate derivatives **37** and **38**. The ^{1}H NMR spectra of each product showed the same general features (Tables 1 and 2). As reported for penta-*O*-acetyl-D-glucose [16], the α and β forms are readily identified from the anomeric proton resonances; H-1 for the α isomer has the greater chemical shift ($\Delta\delta = 0.06$ ppm) and has smaller $J_{1,2}$ coupling (3.7–3.9 Hz cf. 8.3 Hz for the β isomer). The observed $J_{2,3}$, $J_{3,4}$ and $J_{4,5}$ values (9.3–10.1 Hz) are typical of the axial–axial couplings associated with a pyranose ring of D-gluco configuration. This further reinforces the assignment of R configuration to the chiral centre C-5 in the major adducts formed in the nitrile oxide cycloaddition reactions [8]. In contrast the isoxazoline isomers with opposite configuration at C-5 would yield the corresponding L-idopyranose derivatives **39** and **40**, which would be readily distinguished from the D-gluco products by their ^{1}H NMR parameters.



35 X = R1
36 X = R2

37 X = R1
38 X = R2

39 α
40 β

3. Conclusions

The present work, taken with the results reported in the previous paper in this series [8], demonstrates that nitrile oxide/isoxazoline chemistry is well suited for the construction of 11-carbon monosaccharides. The route is sufficiently flexible as to allow combination of various sugar alkene and sugar nitrile oxides in the cycloaddition step, the resulting isoxazolines can be modified while leaving the heterocyclic ring intact, and their ring-opening reactions can provide access to various functionality including β-hydroxyketones and γ-aminoalcohols. It is anticipated that a wide range of higher monosaccharides and analogues may be accessible by combination of the appropriate sugar alkene and sugar nitrile oxide precursors.

4. Experimental

General methods and materials.—The analytical methods, instrumentation and procedures for preparative chromatography were as previously described [8,9]. The purity of new compounds was established by NMR spectroscopy and by TLC (silica: hexane–Et_2O). (5*R*)-5-(3-*O*-Benzyl-1,2-*O*-isopropylidene-α-

D-*xylo*-tetrofuranos-4-yl)-3-(1,2:3,4-di-*O*-isopropylidene-D-*arabino*-tetritol-1-yl)-2-isoxazoline **1**, (5*R*)-5-(3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-*xylo*-tetrofuranos-4-yl)-3-(1,2:3,4-di-*O*-isopropylidene-L-*arabino*-tetritol-1-yl)-2-isoxazoline **9**, (5*R*)-5-(2,3-*O*-isopropylidene-1-*O*-methyl-α-D-*lyxo*-tetrofuranos-4-yl)-3-(1,2:3,4-di-*O*-isopropylidene-D-*arabino*-tetritol-1-yl)-2-isoxazoline **10**, and (5*R*)-5-(2,3-*O*-isopropylidene-1-*O*-methyl-α-D-*lyxo*-tetrofuranos-4-yl)-3-(1,2:3,4-di-*O*-isopropylidene-L-*arabino*-tetritol-1-yl)-2-isoxazoline **11** were prepared as previously reported [8]. Raney nickel was washed with water (stir and decant × 20) and then stored under MeOH in a freezer for 3–4 weeks prior to use. NMR data for the products are given in Tables 1–3.

Palladium on charcoal-catalysed hydrogenolysis of isoxazoline **1**.—Isoxazoline **1** (100 mg, 0.19 mmol) and boric acid (72 mg, 1.16 mmol) were dissolved in MeOH (15 mL) and water (3 mL). 10% Pd–C (19 mg) was added and the mixture degassed using a water pump, flushed with hydrogen (× 5), and left to stir vigorously under the hydrogen atmosphere for 38 h. The mixture was filtered through a Celite pad and evaporated in vacuo at < 25 °C. MeOH was added and evaporated several times to remove the excess of boric acid as trimethyl borate. Preparative TLC (silica, 60% Et_2O in hexane) afforded, in order of elution, unreacted isoxazoline **1** (52 mg, 51%) and a more polar component, which stained with Brady's reagent and was identified as 3-*O*-benzyl-6-deoxy-1,2:8,9:10,11-tri-*O*-isopropylidene-D-*arabino*-α-D-*gluco*-undecos-7-ulose-(1,4) (**4**) (19 mg, 19%) as a colourless oil; ν_{max}/cm^{-1} (neat): 3490 (OH), 1724 (C=O); HRMS (FAB): Calcd for $C_{27}H_{40}O_{10}$ [M + H]: m/z 524.26213. Found: m/z 524.26217. For NMR data, see Tables 1–3.

A repeat reaction on twice the scale, with THF added to aid dissolution of the isoxazoline, afforded unreacted isoxazoline **1** (17 mg, 9%), undecosulose **4** (74 mg 37%) and a more polar fraction (61 mg), which comprised a mixture of debenzylated compounds, after 63 h. The major component of this mixture was attributed to 6-deoxy-1,2:8,9:10,11-tri-*O*-isopropylidene-D-*arabino*-α-D-*gluco*-undeco-7-ulo-1,4-furanose (**6**) in its hemiketal form **5**. For NMR data, see Tables 1–3.

Raney nickel-catalysed hydrogenolysis of isoxazolines: general procedure.—The isoxazoline (1 M equiv) and boric acid (6 M equiv) were dissolved in a mixture of MeOH and water (5:1) (8–12 mL per 100 mg of isoxazoline) and Raney nickel (three spatula tips per 100 mg of isoxazoline) added. The mixture was degassed, flushed with hydrogen, and left to stir vigorously under a hydrogen atmosphere. Upon completion of the reaction (monitored by TLC), the mixture was filtered through Celite and concd in vacuo at < 25 °C. The excess boric acid was removed by repeated cycles of MeOH addition and evaporation. The resulting oil was purified by preparative TLC on silica (70–90% Et_2O in hexane).

Hydrogenolysis of isoxazoline **1**.—According to the general procedure, isoxazoline **1** (300 mg, 0.56 mmol) yielded undecos-7-ulose-(1,4) (**4**) (194 mg, 66%) after 7 h, and a colourless oil, which gave a positive ninhydrin stain on TLC and was identified as an inseparable mixture (ca. 1:1) of γ-aminoalcohols 7-amino-3-*O*-benzyl-6,7-dideoxy-1,2:8,9:10,11-tri-*O*-isopropylidene-D-*gluco*-and D-*manno*-α-D-*gluco*-undeco-1,4-furanose (**7**) (73 mg, 25%); ^{1}H NMR (200 MHz, $CDCl_3$): 7.39–7.23 (m, 5 H, Ph), 5.87, 5.89 (2 × d overlapping, 1 H, $J_{1,2}$ 3.7, $J_{1,2}$ 3.7 Hz, 1-H), 4.68, 4.79 (2 × d, 1 H, J 11.9 Hz, CH_2Ph), 4.67 (d, s, CH_2Ph), 4.57 (d, ~0.5 H, $J_{2,1}$ 3.8 Hz, 2-H), 4.55 (d, ~0.5 H, $J_{2,1}$ 3.5 Hz, 2-H), 3.54–4.30 (m, 9 H), 3.16–3.28 (m, 1 H), 2.92 (br s, 2 H, NH_2), 2.09–1.71 (m, 2 H, 6-H_2), 1.46, 1.40, 1.39, 1.38, 1.35, 1.33, 1.32, 1.29, 1.28, 1.24 (s, 18 H, 6 × Me); ^{13}C NMR (50 MHz, $CDCl_3$): 138.0, 137.6 (3 × PhC), 128.3, 128.2, 127.6, 127.5 (5 × PhCH), 111.4, 111.3, 109.7, 109.6, 109.1 (3 × CMe$_2$), 105.0, 104.8 (C-1), 84.5, 84.2, 83.5, 82.7, 82.4, 82.0, 81.8, 81.1, 79.9, 77.3, 77.0, 76.9, 69.5, 66.5 (C-2, C-3, C-4, C-5, C-8, C-9, C-10), 72.5, 72.3 (CH_2Ph), 67.8 (C-11), 52.3, 50.7 (C-7), 37.5, 34.6 (C-6), 26.9, 26.8, 26.6, 26.4, 26.1, 25.1, 25.0 (6 × Me); HRMS (FAB): Calcd for $C_{27}H_{42}NO_9$ [M + H]: m/z 524.28593. Found: m/z 524.2859.

Hydrogenolysis of isoxazoline **9**.—According to the general procedure isoxazoline **9** (223 mg, 0.43 mmol) afforded the following compounds after 3 h in order of elution: 3-*O*-benzyl-6-deoxy-1,2:8,9:10,11-tri-*O*-isopropylidene-

L-*arabino*-α-D-*gluco*-undecos-7-ulo-1,4-furanose (**13**) as a clear oil (122 mg, 54%) [ν_{max}/cm^{-1} (neat): 3516 (OH), 1719 (C=O); HRMS (FAB): Calcd for $C_{27}H_{40}O_{10}$ [M + 2H]: *m/z* 524.26213. Found: *m/z* 524.26210; for NMR data, see Tables 1–3] and an oil, which gave a positive ninhydrin stain on TLC and was identified as an inseparable mixture of γ-aminoalcohols 7-amino-3-*O*-benzyl-6,7-dideoxy1,2:8,9:10,11-tri-*O*-isopropylidene-L-*gluco*- and L-*manno*-α-D-*gluco*-undeco-1,4-furanose (60 mg, 27%). ^{1}H NMR (200 MHz, $CDCl_3$): 7.37–7.21 (m, 5 H, Ph), 5.87 (d, 1 H, $J_{1,2}$ 3.7 Hz, 1-H), 4.78–4.59 (m, 2 H, CH_2Ph), 4.56 (d, 1 H, $J_{2,1}$ 3.8 Hz, 2-H), 4.28–3.60 (m, 9 H), 3.31–3.22, 3.13–3.05 (2 × m, 1 H), 2.83 (br s, 2 H, NH_2), 2.26–2.18, 1.91–1.77 (m, 2 H, 6-H_2), 1.44, 1.36, 1.33, 1.31, 1.29 (s, 18 H, 6 × Me); ^{13}C NMR (50 MHz, $CDCl_3$): 138.0, 137.6 (3 × PhC), 128.3, 127.7, 127.5 (5 × PhCH), 111.3, 109.5, 109.1 (3 × *C*Me$_2$), 105.0 (C-1), 85.3, 84.0, 83.5, 82.5, 81.6, 81.3, 79.5, 77.8, 76.9, 69.6, 66.5 (C-2, C-3, C-4, C-5, C-8, C-9, C-10), 72.5, 72.3 (CH_2Ph), 67.9, 67.6 (C-11), 54.3, 48.9 (C-7), 35.8, 35.4 (C-6), 27.1, 26.8, 26.6, 26.2, 25.0 (6 × Me); HRMS (FAB): Calcd for $C_{27}H_{42}NO_9$ [M + H]: *m/z* 524.28593. Found: *m/z* 524.28597.

Hydrogenolysis of isoxazoline **10**.—According to the general procedure isoxazoline **10** (168 mg, 0.38 mmol) afforded the following compounds after 5 h in order of elution: methyl 6-deoxy-2,3:8,9:10,11-tri-*O*-isopropylidene-D-*arabino*-α-D-*manno*-undecos-7-ulo-1,4-furanose (**15**) as a clear oil (55 mg, 55%) [ν_{max}/cm^{-1} (neat): 3497 (OH), 1725 (C=O); HRMS (FAB): Calcd for $C_{21}H_{35}O_{10}$ [M + H]: *m/z* 447.22300. Found: *m/z* 447.22301; for NMR data, see Tables 1–3] and an oil, which gave a positive ninhydrin stain on TLC and was identified as an inseparable mixture of γ-aminoalcohols methyl 7-amino-6-deoxy-2,3:8,9:10,11-tri-*O*-isopropylidene-D-*gluco*- and D-*manno*-α-D-*manno*-undecofuranoside (34 mg, 34%) ^{1}H NMR (200 MHz, $CDCl_3$): 4.86, 4.83 (2 × s, 1 H, 1-H), 4.84–4.81 (m, 1 H), 4.53, 4.52 (2 × d, 1 H, $J_{2,3}$ 6.0, $J_{2,3}$ 6.0 Hz, 2-H), 4.28–3.56 (m, 8 H), 3.28 (s, 3 H, OMe), 2.92 (br s, 3 H, OH, NH_2), 2.03–1.75 (m, 2 H, 6-H_2), 1.44, 1.38, 1.37, 1.35, 1.32, 1.30 (s, 18 H, 6 × Me); ^{13}C NMR (50 MHz, $CDCl_3$): 112.4, 112.2, 109.8, 109.6, 109.3, 109.1 (3 × *C*Me$_2$), 107.4, 107.2 (C-1), 84.7, 84.2, 82.6, 81.5, 80.3, 79.9, 79.5, 77.0, 76.9, 70.5, 67.3 (C-2, C-3, C-4, C-5, C-8, C-9, C-10), 67.9, 67.8 (C-11), 52.5, 51.1 (OMe), 52.7, 51.1 (C-7), 37.2, 35.1 (C-6), 27.0, 26.9, 26.6, 26.4, 25.9, 25.2, 25.1, 25.0, 24.6, 24.5, 23.2, 22.9 (6 × Me); HRMS (FAB): Calcd for $C_{21}H_{36}NO_9$ [M + H]: *m/z* 448.25464. Found: *m/z* 448.25467.

Hydrogenolysis of isoxazoline **11**.—According to the general procedure isoxazoline **11** (300 mg, 0.68 mmol) afforded the following compounds after 5.5 h in order of elution: methyl 6-deoxy-2,3:8,9:10,11-tri-*O*-isopropylidene-L-*arabino*-α-D-*manno*-undecos-7-ulo-1,4-furanose (**16**) as a clear oil (156 mg, 52%) [ν_{max}/cm^{-1} (neat): 3498 (OH), 1727 (C=O); HRMS (FAB): Calcd for $C_{21}H_{35}O_{10}$ [M + 2H]: *m/z* 448.23082. Found: *m/z* 448.23083; for NMR data, see Tables 1–3] and an oil, which gave a positive ninhydrin stain on TLC and was identified as an inseparable mixture of γ-aminoalcohols methyl 7-amino-6-deoxy-2,3:8,9:10,11-tri-*O*-isopropylidene-L-*gluco*- and L-*manno*-α-D-*manno*-undecofuranoside (54 mg, 18%). ^{1}H NMR (200 MHz, $CDCl_3$): 4.91–4.71 (m, 2 H, 1-H, 3-H), 4.52, 4.51 (2 × d, 1 H, $J_{2,3}$ 6.0, $J_{2,3}$ 6.0 Hz, 2-H), 4.24–3.62 (m, 8 H), 3.27, 3.26 (2 × s, 3 H, OMe), 2.76 (br s, 3 H, OH, NH_2), 1.85–1.79 (m, 2 H, 6-H_2), 1.44, 1.40, 1.37, 1.35, 1.33, 1.30, 1.28 (s, 18 H, 6 × Me); ^{13}C NMR (50 MHz, $CDCl_3$): 112.3, 109.5, 109.2 (3 × *C*Me$_2$), 107.1 (C-1), 84.7, 84.1, 80.8, 79.8, 78.0, 77.0, 67.3 (C-2, C-3, C-4, C-5, C-8, C-9, C-10), 67.6 (C-11), 54.2, 54.3 (OMe), 49.1 (C-7), 35.9 (C-6), 27.2, 26.9, 26.5, 25.9, 25.1, 24.5 (6 × Me); HRMS (FAB): Calcd for $C_{21}H_{36}NO_9$ [M + H]: *m/z* 448.25464. Found: *m/z* 448.25467.

Reduction of β-hydroxyketones **4**, **13**, **15** *and* **16** *to 1,3-diols* **17–24**.—The reductions were performed using either sodium borohydride (Method A) or L-Selectride (Method B), as described below. All the products were oils and were purified by preparative TLC on silica (70–100% Et_2O in hexane). The isomer ratios (Table 4) were measured by comparison of the integrals for corresponding signals in the ^{1}H NMR spectra of the mixtures. NMR data for the products are given in Tables 1–3.

General procedure using sodium borohydride: Method A.—A solution of sodium borohydride (0.4 M equiv) in water (2 mL per 100 mg of ketone) was added dropwise to an ice-chilled, stirred solution of the β-hydroxyketone (1 equiv) in EtOH and water (3:1, ~4 mL per 100 mg of ketone). The resulting solution was stirred overnight while warming to room temperature (rt). The EtOH was removed in vacuo, acetone (two to three drops) was added to decompose any remaining reagent and the solution extracted with $CHCl_3$. The combined extracts were dried ($MgSO_4$), filtered and evaporated to afford the crude mixture of diastereomeric diols.

General procedure using L-Selectride: Method B.—1 M L-Selectride in THF (1.4 equiv) was added dropwise to a solution of the β-hydroxyketone (1 M equiv) in dry THF (~10 mL per 100 mg of β-hydroxyketone) at −78 °C under nitrogen. The resulting solution was stirred for 30 min at −78 °C and for 45 min at rt. After cooling to 0 °C, the reaction was quenched by the successive slow additions of water (0.3 mL per mL L-Selectride), EtOH (1.3 mL per mL L-Selectride), 3 M NaOH (1.7 mL per mL L-Selectride) and 30% hydrogen peroxide (1.3 mL per mL L-Selectride). The aq layer was satd with K_2CO_3 and extracted with 1:1 Et_2O–THF (3 × 6 mL). The combined organic layers were dried ($MgSO_4$) and concd in vacuo to afford the products.

3-*O*-Benzyl-6-deoxy-1,2:8,9:10,11-tri-*O*-isopropylidene-D-*gluco*-α-D-*gluco*-undecofuranose (**17**); $[\alpha]_D^{26}$ −13.1° (*c* 1.78 in $CHCl_3$); HRMS (FAB): Calcd for $C_{27}H_{40}O_{10}$ [M]: *m/z* 524.26217. Found: *m/z* 524.26213. Yield: Method A, 44%; Method B, 98%.

3-*O*-Benzyl-6-deoxy-1,2:8,9:10,11-tri-*O*-isopropylidene-D-*manno*-α-D-*gluco*-undecofuranose (**18**); $[\alpha]_D^{26}$ −11.0° (*c* 1.11 in $CHCl_3$); HRMS (FAB): Calcd for $C_{27}H_{41}O_{10}$ $[M+H]^+$: *m/z* 525.26995. Found: *m/z* 524.26996. Yield: Method A, 27%.

3-*O*-Benzyl-6-deoxy-1,2:8,9:10,11-tri-*O*-isopropylidene-L-*manno*-α-D-*gluco*-undecofuranose (**19**); $[\alpha]_D^{26}$ −20.3° (*c* 1.56 in $CHCl_3$); HRMS (FAB): Calcd for $C_{27}H_{40}O_{10}$ [M]: *m/z* 524.26217. Found: *m/z* 524.26213. Yield: Method A, 32%; Method B, 8%.

3-*O*-Benzyl-6-deoxy-1,2:8,9:10,11-tri-*O*-isopropylidene-L-*gluco*-α-D-*gluco*-undecofuranose (**20**); $[\alpha]_D^{27}$ −28.8° (*c* 1.33 in $CHCl_3$); HRMS (FAB): Calcd for $C_{27}H_{41}O_{10}$ $[M+H]^+$: *m/z* 525.26995. Found: *m/z* 524.26996. Yield: Method A, 46%; Method B, 59%.

Methyl 6-deoxy-2,3:8,9:10,11-tri-*O*-isopropylidene-D-*gluco*-α-D-*manno*-undecofuranose (**21**) and methyl 6-deoxy-2,3:8,9:10,11-tri-*O*-isopropylidene-D-*manno*-α-D-*manno*-undecofuranose (**22**) as an inseparable mixture; HRMS (FAB): Calcd for $C_{21}H_{37}O_{10}$ $[M+H]^+$: *m/z* 449.23865. Found: *m/z* 449.293868. Combined yield: Method A, 72%; Method B, 94%.

Methyl 6-deoxy-2,3:8,9:10,11-tri-*O*-isopropylidene-L-*gluco*-α-D-*manno*-undecofuranose (**23**) and methyl 6-deoxy-2,3:8,9:10,11-tri-*O*-isopropylidene-L-*manno*-α-D-*manno*-undecofuranose (**24**) as an inseparable mixture; HRMS (FAB): Calcd for $C_{21}H_{37}O_{10}$ $[M+H]^+$: *m/z* 449.23865. Found: *m/z* 449.293862. Combined yield: Method A, 82%; Method B, 76%.

Preparation of 5,7-isoproplidene ketals **25**–**32***: general procedure.*—The 1,3-diol (35–165 mg) was dissolved in 1:1 dry acetone and 2,2-dimethoxypropane (~3 mL per 40 mg of diol), a catalytic amount of *p*-toluenesulfonic acid was added, and the mixture stirred for 16 h at rt. Satd aq $NaHCO_3$ was added and the mixture extracted with CH_2Cl_2. The combined organic layers were dried ($MgSO_4$) and evaporated in vacuo to afford the crude ketal, which was purified by preparative TLC on silica. NMR data for the products are given in Tables 1–3.

3-*O*-Benzyl-6-deoxy-1,2:5,7:8,9:10,11-tetra-*O*-isopropylidene-D-*gluco*-α-D-*gluco*-undecofuranose (**25**) (76%); $[\alpha]_D^{27}$ +3.0° (*c* 2.99 in $CHCl_3$); HRMS (FAB): Calcd for $C_{30}H_{45}O_{10}$ $[M+H]^+$: *m/z* 565.30125. Found: *m/z* 565.30129.

3-*O*-Benzyl-6-deoxy-1,2:5,7:8,9:10,11-tetra-*O*-isopropylidene-D-*manno*-α-D-*gluco*-undecofuranose (**26**) (72%); $[\alpha]_D^{27}$ +12.2° (*c* 1.4 in $CHCl_3$); HRMS (FAB): Calcd for $C_{30}H_{45}O_{10}$ $[M+H]^+$: *m/z* 565.30125. Found: *m/z* 565.30126.

3-*O*-Benzyl-6-deoxy-1,2:5,7:8,9:10,11-tetra-*O*-isopropylidene-L-*manno*-α-D-*gluco*-undeco-

furanose (**27**) (89%); $[\alpha]_D^{27}$ −20.0° (*c* 2.13 in $CHCl_3$); HRMS (FAB): Calcd for $C_{30}H_{45}O_{10}$ $[M+H]^+$: *m/z* 565.30125. Found: *m/z* 565.30129.

3-*O*-Benzyl-6-deoxy-1,2:5,7:8,9:10,11-tetra-*O*-isopropylidene-L-*gluco*-α-D-*gluco*-undecofuranose (**28**) (76%); $[\alpha]_D^{26}$ −11.0° (*c* 2.39 in $CHCl_3$); HRMS (FAB): Calcd for $C_{30}H_{45}O_{10}$ $[M+H]^+$: *m/z* 565.30125. Found: *m/z* 565.30128.

Methyl 6-deoxy-1,2:5,7:8,9:10,11-tetra-*O*-isopropylidene-D-*gluco*-α-D-*manno*-undecofuranose (**29**) and methyl 6-deoxy-1,2:5,7:8,9:10,11-tetra-*O*-isopropylidene-D-*manno*-α-D-*manno*-undecofuranose (**30**) as an inseparable mixture (92%); HRMS (FAB): Calcd for $C_{24}H_{41}O_{10}$ $[M+H]^+$: *m/z* 489.26995. Found: *m/z* 489.26992.

Methyl 6-deoxy-1,2:5,7:8,9:10,11-tetra-*O*-isopropylidene-L-*manno*-α-D-*manno*-undecofuranose (**31**) and methyl 6-deoxy-1,2:5,7:8,9:10,11-tetra-*O*-isopropylidene-L-*gluco*-α-D-*manno*-undecofuranose (**32**) as an inseparable mixture (81%); HRMS (FAB): Calcd for $C_{24}H_{41}O_{10}$ $[M+H]^+$: *m/z* 489.26995. Found: *m/z* 489.26998.

Conversion of diols **17** *and* **20** *to undecopyranose derivatives* **35/36** *and* **37/38**: *general procedure*.—The diol (~ 50 mg) in trifluoroacetic acid (~ 1 mL) and water (0.1 mL) was stirred for 30 min at rt. The mixture was evaporated in vacuo, then water added and evaporated several times. Pyridine (1 mL), Ac_2O (1 mL) and a catalytic amount of 4-dimethylaminopyridine were added and the mixture stirred for ~ 18 h. The resulting solution was poured into water (4 mL) and the product was extracted with CH_2Cl_2 (3 × 4 mL). The combined organic layers were dried ($MgSO_4$), evaporated in vacuo, and the resulting oil purified by preparative TLC on silica (80% Et_2O in hexane, double elution) to afford, in order of elution, the α- and β-octaacetates. NMR data for the products are given in Tables 1 and 2.

3-*O*-Benzyl-6-deoxy-1,2,4,7,8,9,10,11-octa-*O*-acetyl-D-*gluco*-α-D-*gluco*-undecopyranose (**35**) as an oil (20%); $[\alpha]_D^{21}$ +8.0° (*c* 2.8 in $CHCl_3$); ^{13}C NMR (90 MHz, $CDCl_3$): 170.4, 170.3, 169.8, 169.7, 169.6, 169.5, 169.4, 169.0 (8 × CH_3C=O), 137.9 (PhC), 128.3, 127.7, 127.3 (5 × PhCH), 88.3 (C-1), 74.6 (CH_2Ph), 77.0, 72.5, 71.3, 70.1, 69.7, 69.6, 68.3, 68.2 (C-2, C-3, C-4, C-5, C-7, C-8, C-9, C-10), 61.4 (C-11), 31.6 (C-6), 20.7, 20.6, 20.5, 20.3 (8 × CH_3C=O); HRMS (FAB): Calcd for $C_{32}H_{41}O_{16}$ $[M+CH_3CO_2]^+$: *m/z* 681.23943. Found: *m/z* 681.23940.

3-*O*-Benzyl-6-deoxy-1,2,4,7,8,9,10,11-octa-*O*-acetyl-D-*gluco*-β-D-*gluco*-undecopyranose (**36**) as an oil (30%); $[\alpha]_D^{21}$ +5.9° (*c* 1.1 in $CHCl_3$); ν_{max}/cm^{-1} (neat): 1754 (C=O); ^{13}C NMR (90 MHz, $CDCl_3$): 170.4, 169.9, 169.8, 169.64, 169.59, 169.0, 169.8 (8 × CH_3C=O), 137.5 (PhC), 128.3, 127.8, 127.6 (5 × PhCH), 91.7 (C-1), 74.0 (CH_2Ph), 79.2, 72.4, 72.1, 71.6, 71.0, 69.3, 68.5, 68.4 (C-2, C-3, C-4, C-5, C-7, C-8, C-9, C-10), 61.4 (C-11), 31.7 (C-6), 20.67, 20.62, 20.60, 20.54, 20.34 (8 × CH_3C=O); HRMS (FAB): Calcd for $C_{32}H_{41}O_{16}$ $[M+CH_3CO_2]^+$: *m/z* 681.23943. Found: *m/z* 681.23940.

3-*O*-Benzyl-6-deoxy-1,2,4,7,8,9,10,11-octa-*O*-acetyl-L-*gluco*-α-D-*gluco*-undecopyranose (**37**) as an oil (31%); $[\alpha]_D^{21}$ +21.3° (*c* 1.8 in $CHCl_3$); ν_{max}/cm^{-1} (neat): 1745 (C=O); ^{13}C NMR (90 MHz, $CDCl_3$): 170.40, 169.75, 169.64, 169.61, 169.55, 169.52, 169.4, 168.9 (8 × CH_3C=O), 137.9 (PhC), 128.3, 127.6, 127.2 (5 × PhCH), 88.3 (C-1), 74.5 (CH_2Ph), 77.2, 72.5, 71.4, 70.8, 68.3, 68.0, 67.9, 67.6 (C-2, C-3, C-4, C-5, C-7, C-8, C-9, C-10), 61.3 (C-11), 32.7 (C-6), 20.69, 20.62, 20.60, 20.57, 20.51, 20.43, 20.32, 20.28 (8 × CH_3C=O); HRMS (FAB): Calcd for $C_{32}H_{41}O_{16}$ $[M+CH_3CO_2]^+$: *m/z* 681.23943. Found: *m/z* 681.23940.

3-*O*-Benzyl-6-deoxy-1,2,4,7,8,9,10,11-octa-*O*-acetyl-L-*gluco*-β-D-*gluco*-undecopyranose (**38**) as a white solid (48%); mp 104–105 °C (from EtOH); $[\alpha]_D^{21}$ −6.2° (*c* 0.41 in $CHCl_3$); ν_{max}/cm^{-1} (neat): 1754, 1741 (C=O); ^{13}C NMR (90 MHz, $CDCl_3$): 170.39, 169.76, 169.67, 169.53, 169.48, 169.36, 168.90, 168.71 (8 × CH_3C=O), 137.5 (PhC), 128.3, 127.7, 127.6 (5 × PhCH), 91.7 (C-1), 73.8 (CH_2Ph), 79.9, 72.4, 71.5, 71.1, 70.5, 68.8, 68.5, 68.1 (C-2, C-3, C-4, C-5, C-7, C-8, C-9, C-10), 61.4 (C-11), 32.0 (C-6), 20.67, 20.58, 20.56, 20.52, 20.48, 20.34, 20.30 (8 × CH_3C=O); HRMS (FAB): Calcd for $C_{32}H_{41}O_{16}$ $[M+CH_3CO_2]^+$: *m/z* 681.23943. Found: *m/z* 681.23940.

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