Carbohydrate Research, 68 (1979) 33–41

SYNTHESIS OF ALKYL 4,6-DI-*O*-ACETYL-2,3-DIDEOXY-α-D-*threo*-HEX-2-ENOPYRANOSIDES FROM 3,4,6-TRI-*O*-ACETYL-1,5-ANHYDRO-2-DEOXY-D-*lyxo*-HEX-1-ENITOL (3,4,6-TRI-*O*-ACETYL-D-GALACTAL)

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(Received November 21st, 1977; accepted for publication, December 29th, 1977)

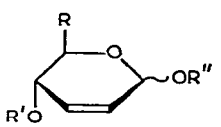
ABSTRACT

3,4,6-Tri-*O*-acetyl-D-galactal, on treatment in 1,2-dichloroethane with alcohols and stannic chloride as catalyst, readily undergoes allylic rearrangement–substitution, forming alkyl 4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*threo*-hex-2-enopyranosides in yields of 43–92%. Alkyl 3,4,6-tri-*O*-acetyl-2-deoxy-αβ-D-*lyxo*-hexopyranosides are formed as side-products in yields of 2–14%. Stannic chloride-catalysis is also useful in allylic rearrangement of 3,4,6-tri-*O*-acetyl-1,5-anhydro-2-deoxy-D-*arabino*-hex-1-enitol (3,4,6-tri-*O*-acetyl-D-glucal) which, with methanol or ethanol, affords the corresponding alkyl 4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranosides in yields of 83 and 94%.

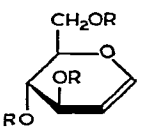
INTRODUCTION

Glycosides of 2,3-dideoxy-2,3-unsaturated aldoses (alkyl 2,3-dideoxyglyc-2-enopyranosides (**1**) can be obtained from saturated precursors by simultaneous elimination of substituents at C-2 and C-3[1] or, more conveniently, by allylic rearrangement of glycals in the presence of alcohols. This last process, extensively studied by Ferrier and his colleagues[2], has found wide application for the preparation of alkyl 2,3-dideoxy-D-*erythro*-hex-2-enopyranosides (**3**).

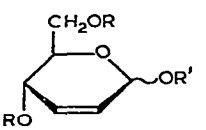
Two routes to **3** were devised: (*1*) treatment of 3,4,6-tri-*O*-acetyl-1,5-anhydro-2-deoxy-D-*arabino*-hex-1-enitol (**2**) with alcohols at elevated temperatures and pressures[3], and (*2*) boron trifluoride-catalysed isomerization of **2** in the presence of



1 R = H or CH_2OAc
R' = Ac or Bz
R'' = alkyl



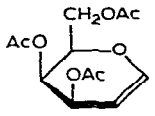
2 R = Ac
4 R = $PhCH_2$



3 R = Ac, R' = alkyl
5 R = $PhCH_2$, R' = alkyl

alcohols[4,5]. Route (*2*) led to higher yields and purer products, but mixtures of both anomers of **3** were formed with the α isomer preponderating.

Application of both methods to 3,4,6-tri-*O*-acetyl-1,5-anhydro-2-deoxy-D-*lyxo*-hex-1-enitol (**6**) gave less satisfactory results. With methanol at 130°, **6** gave a mixture of methyl 4,6-di-*O*-acetyl-2,3-dideoxy-D-*threo*-hex-2-enopyranoside (**7**, isolated in ~9% yield[6]) and unreacted **6** (35%). Boron trifluoride-catalysed reaction was more convenient from the preparative point of view, but the yield of **7** was not improved significantly[7].



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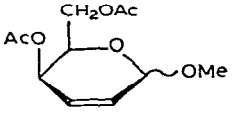

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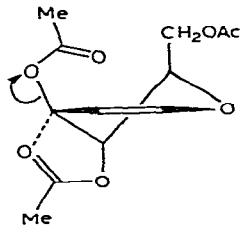
In order to explain the difference in reactivity of **2** and **6** in the rearrangement, Ferrier[5,8] assumed that AcO-4 anchimerically assisted the leaving group at C-3; both groups should therefore be *trans* (**8**).



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Anchimeric assistance may not always be indispensable. Thus, Descotes and Martin[9] showed that 1,5-anhydro-3,4,6-tri-*O*-benzyl-2-deoxy-D-*arabino*-hex-1-enitol (**4**) isomerised readily in the presence of BF_3 to give benzyl 4,6-di-*O*-benzyl-2,3-dideoxy-αβ-D-*erythro*-hex-2-enopyranoside. In the presence of methanol or ethanol, the corresponding methyl or ethyl glycosides (**5**) were formed.

We now report that **6** can be easily isomerised in the presence of alcohols to give alkyl 4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*threo*-hex-2-enopyranosides in high yield. The reactions are catalysed by stannic chloride.

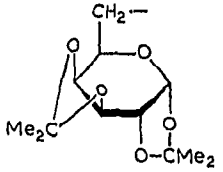
RESULTS AND DISCUSSION

The reaction of 3,4,6-tri-*O*-acetyl-1,5-anhydro-2-deoxy-D-*lyxo*-hex-1-enitol (**6**) in 1,2-dichloroethane with alcohols, catalysed by stannic chloride, proceeded at room temperature in 1–2 h. Two types of products were usually formed, namely, alkyl 4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*threo*-hex-2-enopyranosides (major, 43–92%) and alkyl 3,4,6-tri-*O*-acetyl-2-deoxy-αβ-D-*lyxo*-hexopyranosides (minor, 2–14%). The presence of dimeric compounds[13] could usually also be detected by t.l.c.

The summary of the reactions performed and the properties of products are

TABLE I

DATA FOR ALKYL 4,6-DI-*O*-ACETYL-2,3-DIDEOXY-α-D-*threo*- AND -*erythro*-HEX-2-ENOPYRANOSIDES

	R	*Compound*	*Yield (%)*	*M.p. or b.p./Torr (degrees)*	$[\alpha]_D^{20}$ [a] (degrees)	$[\alpha]_{578}^{20}$ [a] (degrees)	*Analysis*				
							Formula	*Calc.*		*Found*	
								C	*H*	*C*	*H*
1	Me	9[b]	80	59	−174	−184	$C_{11}H_{16}O_6$	54.1	6.6	—	—
2	Et	10[c]	92	19.5–20.5	−171	−180	$C_{12}H_{18}O_6$	55.8	7.0	55.6	7.2
3	$PhCH_2$	11	82	140/0.6 180/0.7	−156	−169	$C_{17}H_{20}O_6$	63.7	6.3	63.7	6.4
4	Me_2CH	12	58	110/0.4	−167	−179.5	$C_{13}H_{20}O_6$	57.3	7.4	57.0	7.6
5	C_6H_{11}	13	66	170/0.8	−118	−135.5	$C_{16}H_{24}O_6$	61.5	7.8	61.5	7.9
6	Me_3C	14	60	160/0.6	−209	−220	$C_{14}H_{22}O_6$	58.7	7.8	58.7	7.8
7	Ph	15	43	160/0.4	−66	−72	$C_{16}H_{18}O_6$	62.7	5.9	62.7	6.1
8	*p*-Br—C_6H_4	16	57	84–85	−33	−35	$C_{16}H_{17}BrO_6$	49.9	4.4	49.8	4.5
9		17	56	98–99	−152.5	−161.5	$C_{22}H_{32}O_{11}$	55.9	6.8	55.6	7.0
10		3(R′ = Me)[d]	83	110/0.2	+172	+181	$C_{11}H_{16}O_6$	54.1	6.6	54.0	6.8
11		3(R′ = Et)[e]	94	79	+133	+139	$C_{12}H_{18}O_6$	55.8	7.0	—	—

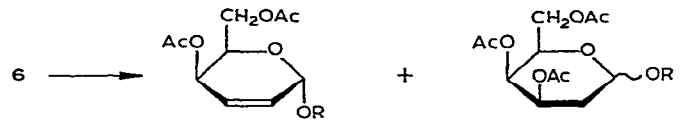
[a] In CH_2Cl_2 (*c* 1). [b] M.p. 60.5–61.5°, $[\alpha]_D$ −174° ($CHCl_3$)[6], m.p. 59–60°, $[\alpha]_D$ −172° ($CHCl_3$)[7]. [c] B.p. 94–96°/10^{-4}, $[\alpha]_D$ −86° ($CHCl_3$)[6]. [d] B.p. 122–124°/0.2, $[\alpha]_D$ +126° ($CHCl_3$)[3]. [e] M.p. 78–79°, $[\alpha]_D$ +107° (C_6H_6)[3].

TABLE II

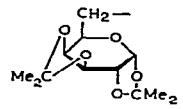
DATA FOR ALKYL 3,4,6-TRI-*O*-ACETYL-2-DEOXY-D-*lyxo*-HEXOPYRANOSIDES

	R	*Anomer*	*Compound*	*Yield (%)*	*M.p. or b.p./Torr (degrees)*	$[\alpha]_D^{20}$ [a]	$[\alpha]_{578}^{20}$ [a] *(degrees)*	*Analysis*				
								Formula	*Calc.*		*Found*	
									C	*H*	*C*	*H*
1	Me	α	18[b]	5	130/0.6	+132	+138	$C_{13}H_{20}O_8$	51.3	6.6	51.0	6.7
2	Me	β	19	8	80 140/0.3	−9	−9				51.2	6.7
3	Et	α	20	1	58–59	+137	+142.5	$C_{14}H_{22}O_8$	52.8	7.0	52.9	7.1
4	Et	β	21	1	45–47	−7.5	−8				52.8	7.1
5	$PhCH_2$	α	22	6	185/0.8	+121	+126	$C_{19}H_{24}O_8$	60.0	6.4	60.3	6.4
6	Me_2CH	α	23	14	140/0.6	+111	+116	$C_{15}H_{24}O_8$	54.2	7.3	54.0	7.3
7	C_6H_{11}	α	24	12	135/0.4	+67	+70	$C_{18}H_{28}O_8$	58.1	7.6	58.0	7.8
8	Me_3C	α	25	9	140/0.2	+32	+33	$C_{16}H_{26}O_8$	55.5	7.6	—	—

[a] In CH_2Cl_2 (*c* 1). [b] B.p. 125–131°/0.03 Torr, $[\alpha]_D^{20}$ +159° (*c* 1, C_6H_6)[15]; syrup, $[\alpha]_D^{21}$ +143° (*c* 1, $CHCl_3$)[16].



9–17 18–25

R	Products α-anomer	β-anomer		R	Product
Me	9	18	19	Ph	15
Et	10	20	21	p-BrC$_6$H$_4$	16
PhCH$_2$	11	22	–		17
Me$_2$CH	12	23	–		
C$_6$H$_{11}$	13	24	–		
Me$_3$C	14	25			

collected in Tables I (entries 1–9) and II. Some of the products obtained were described earlier; the structure of others could be easily deduced from the ^{1}H-n.m.r. spectra (see Experimental).

Unsaturated alkyl glycosides from primary alcohols (Table I, entries 1–3) were formed in very high yields. For comparison purposes, allylic rearrangement of **6** with ethanol was performed in the presence of boron trifluoride. Ethyl glycoside **10** was obtained (~35%), and **20** (9.4%) and **21** (7.5%) were also isolated.

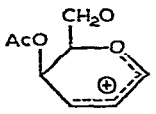
From phenols, and secondary and tertiary alcohols, the yields of unsaturated glycosides were in the range 40–60% (Table I, entries 4–8). Stannic chloride was also suitable as catalyst for the formation of an unsaturated disaccharide (Table I, entry 9).

The presence of any β anomers of 2,3-unsaturated alkyl hexosides was not detected. There are suggestions in the literature[10–12] that, under equilibration conditions, α anomers of alkyl hex-2-enopyranosides are more strongly favoured than β. In the *threo* series, the αβ equilibrium is almost totally shifted towards the α form, provided that anomerisation is faster than allylic rearrangement.

Stannic chloride can be applied for the preparation of 2,3-unsaturated alkyl hexosides of the *erythro* series. Allylic rearrangement of 3,4,6-tri-*O*-acetyl-1,5-anhydro-2-deoxy-D-*arabino*-hex-1-enitol (**2**) in the presence of methanol or ethanol readily afforded the corresponding glycosides **3** (R^1 = Me or Et) in yields of 83 and 94%, respectively (Table I, entries 10 and 11). It is emphasised that catalysis by $SnCl_4$ is particularly suitable for the preparation of the latter of these glycosides, which is widely used in carbohydrate synthesis[1, 13]; **3** (R^1 = Et) is obtained by our procedure in a state of high purity. Simple crystallisation is sufficient for the isolation of the product.

Thus, it is evident that Ferrier's hypothesis[4, 7] invoking anchimeric assistance in the allylic rearrangement of glycals does not apply for reactions catalysed by Lewis acids. The first step in these reactions involves[14] the formation of a complex between AcO-3 and a molecule of the catalyst; elimination of a complex anion gives

allylic carbonium ion **26** which reacts further with an alcohol molecule. Presumably, stannic chloride forms a better leaving group than does boron trifluoride.



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The synthetic utility of 2,3-unsaturated alkyl hexosides of the *threo* series has been much less studied than for the *erythro* series. The ready access to the *threo* compounds will allow exploration of their usefulness in synthesis in carbohydrate chemistry.

EXPERIMENTAL

General methods. — Melting points were determined with a Kofler micro-stage apparatus. Boiling points refer to air-bath temperatures. T.l.c. was performed on silica gel (Merck) with light petroleum–ethyl acetate (2:1). Column chromatography was performed on Macherey–Nagel (100–200 mesh) or Merck (230–400 mesh) silica gels. ^{1}H-N.m.r. spectra (100 MHz) were recorded with a Jeol JNM-4H-100 spectrometer for solutions in $CDCl_3$ and C_6D_6 with internal Me_4Si. I.r. spectra were recorded with a Beckman IR 4240 spectrophotometer.

Compounds **9–25** exhibited i.r. spectra compatible with their structures, *i.e.*, the spectra contained bands at 1735–1750 and 1230–1240 cm^{-1} (AcO), and 3–4 bands between 1000 and 1120 cm^{-1} (acetal); compounds **9–17** showed weak bands at 1655–1660 cm^{-1} (C=C).

Optical rotations were determined with a Perkin-Elmer 141 automatic polarimeter for 1% solutions in dichloromethane at 20°. A solution of stannic chloride (~75 mg) in 1,2-dichloroethane (1 ml) was used as catalyst.

*Ethyl 4,6-di-*O*-acetyl-2,3-dideoxy-α-*D*-threo-hex-2-enopyranoside* (**10**). — A solution of 3,4,6-tri-*O*-acetyl-1,5-anhydro-2-deoxy-D-*lyxo*-hex-1-enitol (**6**; 272 mg, 1.0 mmol) and ethanol (92 mg, 2 mmol) in dry 1,2-dichloroethane (10 ml) was treated with catalyst solution (1 ml). After 1 h at room temperature, the mixture became yellowish-brown; t.l.c. showed the disappearance of **6** and the formation of a single product. The mixture was quenched with triethylamine or aqueous sodium hydrogen carbonate, diluted with chloroform (50 ml), washed twice with water, dried ($MgSO_4$), and concentrated. The oily residue was eluted from silica gel (10 g), to give **10** (237 mg, 92%), b.p. 140°/0.6 Torr, m.p. 19.5–20.5°. For other data, see Table I.

The presence of **20** and **21** was detected by g.l.c. (3% of JXR on Gas Chrom Q, 100–120 mesh, 200°).

TABLE III

^{1}H-N.M.R. DATA FOR ALKYL 4,6-DI-*O*-ACETYL-2,3-DIDEOXY-α-D-*threo*-HEX-2-ENOPYRANOSIDES (9–17)[a]

Compound	*Solvent*	*H-1*	*H-2*	*H-3*	*H-4*	*H-5*	*H-6,6'*	*OAc*	$J_{1,2}$	$J_{2,3}$	$J_{2,4}$	$J_{3,4}$	$J_{4,5}$
9	C_6D_6	4.75	5.80	5.99	4.95	4.26[b]		1.75 1.81	2.3	10.0		5.3	1.3
10	C_6D_6	4.85	5.77	5.98	4.95	4.30[b]		1.70 1.80	2.7	10.0	0.9	5.4	
11	$CDCl_3$	5.13	5.89–6.20		5.01	4.40	4.20	2.05	2.1			4.5	2.4
12	C_6D_6	4.99	5.75	6.01	4.96	4.35[b]		1.67 1.76	2.5	10.2		5.2	1.7
13	$CDCl_3$	5.19	5.99	6.11	5.00	4.41	4.20	2.07	2.0	10.0		4.2	2.4
14	$CDCl_3$	5.47	5.95	6.10	5.01	4.46	4.22	2.06 2.10	2.8	10.0	0.9	5.2	2.5
15	C_6D_6	5.48	5.76	6.03	4.94	4.10–4.46		1.60 1.66	2.7	10.1		5.3	2.0
16	$CDCl_3$	5.70	6.16	6.28	5.10	4.45	4.23	1.91 2.21	2.5	10.0	0.5	4.5	2.4
17	$CDCl_3$	5.11	6.01	6.12	5.00	4.28[b]		2.20	2.0	10.0		4.5	2.5

[a]First order. Signals of aglycon protons are omitted. Other coupling constants (*e.g.*, $J_{1,3}$ and $J_{5,6}$) were not determined. [b]Center of a multiplet.

TABLE IV

^{1}H-N.M R. DATA FOR ALKYL 3,4,6-TRI-*O*-ACETYL-2-DEOXY-α- AND -β-D-*lyxo*-HEXOPYRANOSIDES (**18–24**)

18 (CDCl$_3$)	5.34 (m, 2H, H-3,4), 4.90 (m, 1 H, H-1), 4.28 (m, 1 H, H-5), 4.13 (m, 2 H, H-6,6'), 3.38 (s, 3 H, OMe), 1.98, 2.06, and 2 14 (3s, 9 H, 3 OAc), and 2.10 (m, 2 H, H-2,2').
19 (C$_6$D$_6$)	5.31 (bd, 1 H, H-4), 4.89 (o, 1 H, $J_{2e,3}$ 5.5, $J_{2a,3}$ 12, $J_{3,4}$ 3.3 Hz, H-3), 3.96–4 25 (m, 3 H, H-1,6,6'), 3.45 (m, 1 H, H-5), 3 29 (s, 3H, OMe), 1.75 (s, 9 H, 3 OAc), and 1.70–2.15 (m, 2 H, H-2,2').
20 (C$_6$D$_6$)	5 35–5 56 (m, 2 H, H-3,4), 4.77 (m, 1 H, H-1), 3.95–4 22 (m, 3 H, H-5,6,6'), 3.20 and 3.56 (4 q, 2 H, AB system of C*H*$_2$CH$_3$), 1 70–2.08 (m, 2 H, H-2,2'), 1.70, 1.74, and 1.78 (3s, 9 H, 3 OAc), and 1.06 (t, 3 H, Me).
21 (C$_6$D$_6$)	5.34 (bd, 1 H, H-4), 4 95 (o, 1 H, $J_{2e,3}$ 5 7, $J_{2a,3}$ 11.7, $J_{3,4}$ 3.0 Hz, H-3), 4.13–4.34 (m, 3 H, H-1,6,6'), 3.52 (m, 1 H, H-5), 3 35 and 3 85 (4 q, 2 H, AB system of C*H*$_2$CH$_3$), 1.80–2 24 (m, 2 H, H-2,2'), 1 80 (s, 9 H, 3 OAc), and 1.14 (t, 3 H, Me).
22 (CDCl$_3$)	5.19–5 40 (m, 2 H, H-3,4), 5 06 (m, 1 H, H-1), 4.46 and 4 66 (2 d, 2 H, AB system of C*H*$_2$Ph), 4 01–4 25 (m, 3 H, H-5,6,6'), 1 94, 2 03, and 2.10 (3 s, 9 H, 3 OAc), and 1.81–2 30 (m, 2 H, H-2,2').
23 (C$_6$D$_6$)	5 34–5 55 (m, 2 H, H-3,4), 4 91 (m, 1 H, H-1), 4 14–4 31 (m, 3 H, H-5,6,6'), 3.70 (quin, 1 H, C*H*Me$_2$), 1 64–2 21 (m, 2 H, H-2,2'), 1 69, 1.74, and 1.77 (3 s, 9 H, 3 OAc), 1 09 and 0.97 (2 d, 6 H, CH*Me*$_2$).
24[a] (CDCl$_3$)	4 95–5 41 (m, 3 H, H-1,3,4), 4 02–4.41 (m, 3 H, H-5,6,6'), 3.58 (m, 1 H, CH-O of aglycon), 1.98, 2.05, and 2.14 (3 s, 9 H, 3 OAc), and 1.11–2 19 [m, 12 H, H-2,2', (CH$_2$)$_5$ of aglycon].

[a]Sample contained some β anomer.

Reactions of **6** with other alcohols in the presence of $SnCl_4$ followed the above description. Chromatography of the products afforded the corresponding alkyl 4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*threo*-hex-2-enopyranoside and alkyl 3,4,6-tri-*O*-acetyl-2-deoxy-D-*lyxo*-hexopyranoside. The results are collected in Tables I and II. ^{1}H-N.m.r. data for **9–24** are given in Tables III and IV.

The reaction of **6** with *tert*-butyl alcohol gave the 2,3-unsaturated compound **14**, together with a product that was assigned the structure *tert*-butyl 3,4,6-tri-*O*-acetyl-2-deoxy-α-D-*lyxo*-hexopyranoside (**25**); ν_{max} 1743, 1370, 1230, 1184, 1042, 1020, 925, 900, 867, 840, and 750 cm^{-1}.

The reaction of **6** (2.72 g) with ethanol (0.92 g) in 1,2-dichloromethane (100 ml) in the presence of boron trifluoride etherate (0.5 ml) was performed according to the method described above. Chromatography of the product mixture gave **10** (0.9 g, 35%), **20** (0.3 g, 9.4%), **21** (0.24 g, 7.5%), and ethyl 4,6-di-*O*-acetyl-2-deoxy-3-*O*-ethyl-D-hexopyranoside (80 mg), b.p. 150°/0.6 Torr, $[\alpha]_D$ +4.5°, $[\alpha]_{578}$ +5°. ^{1}H-N.m.r. data: δ 4.74–4.90 (m, 2 H, H-1,4), 4.24 (m, 3 H, H-5,6,6'), 4.00 (m, 1 H, H-5?), 3.64 (m, 4 H, 2 C*H*$_2$CH$_3$), 2.10 (s, 6 H, 2 OAc), 1.80–2.28 (m, 2 H, H-2,2'), and 1.40 (2 t, 6 H, 2 CH$_2$C*H*$_3$).

Anal. Calc. for $C_{14}H_{24}O_7$: C, 55.2; H, 8.0. Found: C, 55.4; H, 7.8.

*Ethyl 4,6-di-*O*-acetyl-2,3-dideoxy-α-D-erythro-hex-2-enopyranoside* (**3**, R^1 = Et). — From 3,4,6-tri-*O*-acetyl-1,5-anhydro-2-deoxy-D-*arabino*-hex-1-enitol (**2**, 272 mg), ethanol (92 mg), 1,2-dichloroethane (10 ml), and stannic chloride (50 mg),

following the method described for **10**, crystalline **3** (R^1 = Et) was obtained (242.5 mg, 94%) without chromatographic purification.

REFERENCES

1 R. J. FERRIER, *Adv. Carbohydr. Chem*, 20 (1965) 67–137; 24 (1969) 199–266.
2 R. J. FERRIER, W. G. OVEREND, AND E. A RYAN, *J. Chem Soc*, (1962) 3667–3670, and subsequent papers in the same series.
3 R. J. FERRIER, *J. Chem. Soc.*, (1964) 5443–5449.
4 R. J. FERRIER AND N. PRASAD, *J. Chem. Soc., C*, (1969) 570–575.
5 R. J. FERRIER AND N. PRASAD, *J. Chem. Soc., C*, (1969) 581–586.
6 D. M. CIMENT AND R J. FERRIER, *J. Chem. Soc*, *C*, (1966) 441–445.
7 R. J. FERRIER AND N. PRASAD, *J. Chem. Soc., C*, (1969) 575–580.
8 R. J. FERRIER, N. PRASAD, AND G. H. SANKEY, *J. Chem Soc., C*, (1968) 974–977.
9 G. DESCOTES AND J.-C. MARTIN, *Carbohydr. Res.*, 56 (1977) 168–172.
10 R. J. FERRIER AND G. H. SANKEY, *J. Chem. Soc., C*, (1966) 2339–2345, 2345–2349.
11 R. U. LEMIEUX AND R. J. BOSE, *Can. J. Chem.*, 44 (1966) 1855–1862.
12 A. ZAMOJSKI, A. KONOWAL, AND J. JURCZAK, *Rocz. Chem*, 44 (1970) 1981–1986.
13 B. FRASER-REID, *Acc. Chem. Res.*, 8 (1975) 192–201.
14 K. HEYNS AND J. I. PARK, *Chem. Ber.*, 109 (1976) 3262–3281.
15 A. B. FOSTER, W G. OVEREND, AND M STACEY, *J. Chem Soc.*, (1951) 974–979.
16 K. TAKIURA AND S. HONDA, *Carbohydr. Res*, 21 (1972) 379–391.