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Note

Synthesis of 1-*O*-acylaldoses by the reaction of carboxylic acids with 1,2-orthoacetates, or with aldoses in the presence of trifluoroacetic anhydride

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Studies[1] on the chemistry of glycosyl ester conjugates of bilirubin prompted us to examine methods for the synthesis of compounds of this class. Glycosyl esters, or 1-*O*-acylaldoses, may be synthesized by the reaction of a metal salt of a carboxylic acid with a glycosyl halide[2,3] or a 1-thioglycoside[4], or by the reaction[5] between an aldose and an acyl halide. Two alternative procedures are described here. One is based on the solvolysis of a 1,2-orthoester by a carboxylic acid[6], which is analogous to[7,8] the formation of a glycoside by an acid-catalyzed reaction between a 1,2-orthoester and an alcohol. In the second method, trifluoroacetic anhydride is used to promote[9,10] the esterification of a suitably protected aldose with a carboxylic acid.

RESULTS AND DISCUSSION

A. Reactions of carboxylic acids with 1,2-orthoacetates. — Experiments were conducted with 3,4,6-tri-*O*-acetyl-1,2-*O*-(1-ethoxyethylidene)-α-D-glucopyranose (**1**) and 3,4,5-tri-*O*-acetyl-1,2-*O*-(1-methoxyethylidene)-β-D-mannopyranose (**2**). Both of these orthoesters are *exo* diastereomers[11,12], having been prepared from the corresponding tetra-*O*-acetylglycosyl bromides in the presence of *s*-collidine[13]. In a solvolysis reaction using, for example, cyclohexanecarboxylic acid, ring opening of **1** (one mole per 3 moles of the acid) proceeded in dry oxolane at room temperature, affording crystalline 2,3,4,6-tetra-*O*-acetyl-1-*O*-(cyclohexylcarbonyl)-β-D-glucopyranose (**3**) in 66% yield. Orthoester **2**, being less acid-labile[7], required heating under reflux with this acid in dry oxolane, whereupon crystalline 2,3,4,6-tetra-*O*-acetyl-1-*O*-(cyclohexylcarbonyl)-α-D-mannopyranose (**4**) was obtained in a yield of 63%.

Several other 1-*O*-acylaldoses, listed in Table I, were prepared by using a variety of aliphatic and aromatic carboxylic acids. As the latter compounds exhibited wide differences in reactivity at room temperature, a uniform procedure was adopted wherein the solutions were heated for 12 h at 100°. According to chromatographic

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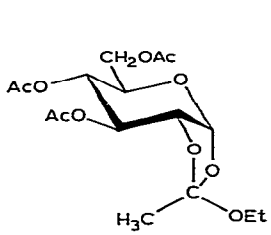

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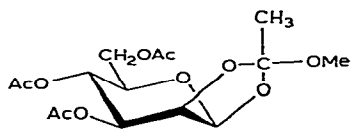

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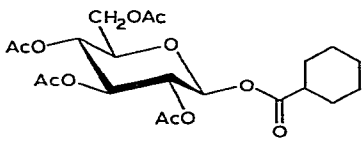

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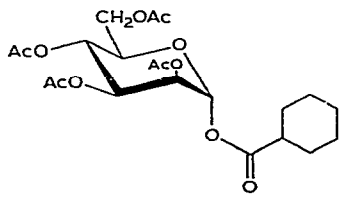

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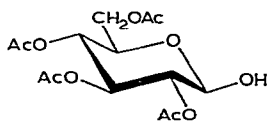

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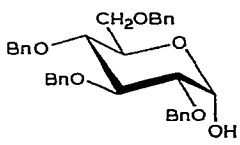

6

Bn = $PhCH_2$

TABLE I

1-*O*-ACYLALDOSES SYNTHESIZED BY REACTIONS BETWEEN CARBOXYLIC ACIDS AND 3,4,6-TRI-*O*-ACETYL-(1,2-ALKOXYETHYLIDENE)-α-D-GLUCOPYRANOSE (**1**) OR -β-D-MANNOPYRANOSE (**2**)

Compound treated	*Carboxylic acid*	*Yield of 1-O-acylaldose (%)*[a]	*M.p. (degrees)*	$[\alpha]_D$[b] *(degrees)*	$J_{1,2}$[c]	δ_{C-1}[c]
1	Cyclohexanecarboxylic	66	114–115	+2	7.5	92.5[d]
	Acetylsalicylic	48	177–178	−43	6.9	92.3
	2,2-Dimethylpropanoic	34	136–137.5	+11	7.4	91.8
	Propanoic	49	98–100	+4	7.4	91.6
	Picolinic	25[e]	133–134	−27	7.7	92.7
	Benzoic	57	141.5–142.5	−20	7.6	92.3
—[f]	2,4,6-Trimethylbenzoic[f]	—	139.5–141	+4	7.7	91.9
2	Cyclohexanecarboxylic	63	126.5–127.5	+60	2.0	90.5

[a]Yield of pure crystalline product recovered. [b]Solvent, $CHCl_3$. [c]Solvent, $CDCl_3$. [d]δ_{C-1} of 1,2,3,4,6-penta-*O*-acetyl-β-D-glucopyranose is 92.5, and of the α anomer is 89.8. [e]Calc. for $C_{20}H_{23}NO_{11}$: C, 53.0; H, 5.1; N, 3.1. Found: C, 53.1; H, 5.5; N, 3.3. [f]Prepared by esterification of 2,3,4,6-tetra-*O*-acetyl-D-glucose.

evidence, all reactions were complete within this period. By analogy with the preparation of **3**, the only product detected in all reactions of **1** was the β-D-glucosyl ester. The configuration of these products was verified by ^{1}H- and ^{13}C-n.m.r. spectroscopy, as well as by optical rotation. The use of n.m.r. spectroscopy for configurational assignments in the *manno* series is less straightforward. Thus, 1,2,3,4,6-penta-*O*-acetyl-α- and -β-D-mannopyranose have almost the same H-1 chemical shifts (δ 6.0–6.1), C-1 chemical shifts (δ 90.5–90.7), and values of $^{3}J_{1,2}$ (1–2 Hz). However, as is characteristic of aldoses[14,15], they differ widely in the coupling between C-1 and H-1, *i.e.*, 177 Hz for the α and 162 Hz for the β anomer. The corresponding value, 178 Hz, for product **4**, and a molecular rotation of +273°, showed that it is an α-D-mannosyl ester*.

The present findings therefore show that the attack of a carboxylic acid at C-1 of an orthoester, either in the *gluco* or *manno* series, results in ring opening and the formation of a 1-*O*-acylaldose of inverted configuration**.

B. Reactions of carboxylic acids and trifluoroacetic anhydride with aldoses. — In this part of the study, 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranose (**5**) and 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranose (**6**) were selected as suitably protected aldoses. A

TABLE II

REACTIONS OF 2,3,4,6-TETRA-*O*-ACETYL-β-D-GLUCOPYRANOSE (**5**) (EXPTS. 1–10) OR 2,3,4,6-TETRA-*O*-BENZYL-α-D-GLUCOPYRANOSE (**6**) (EXPTS. 11, 12) WITH CARBOXYLIC ACIDS AND TRIFLUOROACETIC ANHYDRIDE[a]

	Experiment											
	1	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*	*11*	*12*
Carboxylic acid (meq)	1.0[b]	7.0[b]	1.2[b]	1.0[c]	4.0[c]	8.3[c]	1.0[d]	1.1[d]	10.3[d]	1.0[e]	4.0[e]	4.0[b]
Trifluoroacetic anhydride (meq)	1.8	4.2	5.2	1.3	1.°	3.0	7.2	3.0	6.4	3.0	1.0	1.8
CH_2Cl_2 (2 mL)[f]	+	—	—	+	+	—	—	—	—	—	+	+
	Products (% yield)[g]											
α-Ester	35	20	26	23	40	25	15	18	34	22	46	81
β-Ester	35	80	74	37	60	75	32	18	64	78	49	19
α-Trifluoroacetate	20	0	0	17	0	0	23	35	6	0	<5	0
β-Trifluoroacetate	20	0	0	23	0	0	30	29	6	0	0	0

[a]Most reactions were complete in ~0.5 h (t.l.c. evidence). [b]Cyclohexanecarboxylic. [c]Propanoic. [d]Pivalic. [e]Mesitoic. [f]Per mole of **5** or **6**. [g]By integration of ^{1}H-n.m.r. spectra: the H-1 signals of the α- and β-trifluoroacetates (δ 6.5 and 6.0, respectively) were usually adequately separated from those of the corresponding H-1 signals produced by the other esters in the mixture.

*It is worth noting that, in the 22.6-MHz, ^{13}C-n.m.r. spectra of **3** and **4**, individual signals are observed for all six of the cyclohexyl ring-carbon atoms. Hence, the nonequivalence of C-2′ and -6′, and of C-3′ and -5′, imparted by the relatively remote sugar moiety, is not obscured by time-averaging.

The reaction of **1 with dibenzyl hydrogenphosphate similarly results in formation of the β-anomeric phosphate derivative[16].

number of experiments were conducted to examine such factors as (*a*) the optimum molar ratio of aldose with respect to carboxylic acid and trifluoroacetic anhydride, (*b*) the effect of a diluent, or (*c*) the sequence of addition of reactants. ^{1}H-N.m.r. spectroscopy proved, in most instances, to be satisfactory for analyzing the product composition.

Representative data for reactions of **5** (see Table II) show that a β ester of the acid employed was usually the major product. However, the formation of trifluoroacetates was favored by a diluent (dichloromethane) (Expts. 1 and 4) or a relatively high proportion of trifluoroacetic anhydride, or both (Expts. 7 and 8). Trifluoroacetates were produced in each of several experiments (*e.g.*, Expts. 8 and 9) conducted with 2,2-dimethylpropanoic (pivalic) acid, whereas the rate of esterification of 2,4,6-trimethylbenzoic (mesitoic) acid by **5** (*e.g.*, Expt. 10) was much higher than that of trifluoroacetate. In acid-catalyzed esterification-reactions, both pivalic and mesitoic acid exhibit[17,18] severe steric hindrance. By contrast, steric factors appear to be far less prominent when trifluoroacetic anhydride is employed[19], as both of these acids, and other hindered ones, are readily esterified by alkanols and phenols. Hence, the latter observation has been cited[19] as support for the view[20] that an acylonium ion (**8**), rather than the protonated, mixed anhydride (**7**), is the acylating agent in these reactions.

$$\underset{\mathbf{7}}{RC(=O)-O-C(OH)^+CF_3} \leftrightarrows CF_3CO_2H + \underset{\mathbf{8}}{RC\equiv O^+} \xrightarrow{R'OH} RC(=O)-O-R' + H^+$$

Consequently, the relatively low rate of esterification of pivalic acid by **5** is exceptional, and may imply that the nature of the alcohol influences the relative contributions of intermediates **7** and **8** to the overall outcome of the reaction.

The mixtures of products obtained in these experiments were not readily separable chromatographically, as shown by t.l.c. However, fractional recrystallization afforded pure samples of β-anomeric 1-*O*-acylaldoses (where acyl is cyclohexylcarbonyl, propanoyl, and pivalyl, already prepared *via* the orthoester reaction), as well as 2,3,4,6-tetra-*O*-acetyl-1-*O*-mesitoyl-β-D-glucopyranose (see Table I).

In esterification reactions of 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranose (Expts. 11 and 12, Table II, are representative), dichloromethane was used throughout, in order to solubilize the aldose. Trifluoroacetic anhydride alone gave a 5:1 mixture of the α- and β-trifluoroacetates, whereas (see Table II) the latter products were barely detectable when a carboxylic acid was added. Cyclohexanecarboxylic acid afforded the α- and β-esters in the ratio of 5:1 (Expt. 11), as also did propanoic acid. However, the product ratio obtained with mesitoic acid was 1:1 (Expt. 12); the β-mesitoate was isolated from this mixture by fractional recrystallization. As aldose **6** was introduced into these reactions as its pure α anomer, it is likely that the higher $\alpha:\beta$ ratios observed reflect higher rates of esterification of the α-aldose as compared with its rate of mutarotation.

Overall, the esterification reactions of **5** and **6** exhibit a much lower degree of stereoselectivity than is observed in the orthoester reaction, or by esterification with acyl halides under specially controlled conditions[21]. However, the procedure is simple, rapid, and applicable to a variety of aliphatic and aromatic carboxylic acids, and it gives high yields of (mixed) product.

EXPERIMENTAL

General methods. — Solutions were usually evaporated below 40° under diminished pressure. Optical rotations were determined at room temperature, for solutions in 1-dm tubes, with a Carl Zeiss polarimeter (Model 367732). Microanalyses were performed by C. Daessle, Montreal. Plates of Silica Gel G were used for t.l.c., and the developing solvents were 9 : 1 chloroform–ether and 9 : 1 chloroform–acetone. Proton magnetic resonance spectra were recorded with a Varian HA-100 or a Bruker WH-90 spectrometer. ^{13}C-N.m.r. spectra were recorded at 22.6 MHz with a Bruker WH-90 spectrometer. Chemical shifts (δ) are reported with reference to tetramethylsilane.

*2,3,4,6-Tetra-*O*-acetyl-1-*O*-(cyclohexylcarbonyl)-β-*D*-glucopyranose* (**3**). — A solution of orthoester[12] **1** (3.3 g) and cyclohexanecarboxylic acid (3.9 g) in dry oxolane (10 mL) was stirred for 2 h, and then evaporated. When dissolved in ether, the residue afforded crystalline material (2.9 g, 66%); m.p. 114–115°, $[\alpha]_D$ +2° (*c* 2, chloroform) (lit.[22] m.p. 114.5–115.5°); ^{1}H-n.m.r. data ($CDCl_3$): δ 5.8 (1 H, d, H-1, $J_{1,2}$ 7.5 Hz), 5.4–5.0 (3 H, overlapping m, H-2,3,4), 4.4 (1 H, q, H-6, $J_{5,6}$ 4.4, $J_{6,6'}$ 12.5 Hz) 4.1 (1 H, q, H-6', $J_{5,6'}$ 2.0, $J_{6,6'}$ 12.5 Hz), 4.0 (1 H, m, H-5), 2.0 (12 H, br s, 4 CH_3), and 2.5–1.1 (11 H, m, C_6H_{11}); ^{13}C-n.m.r. data ($CDCl_3$): δ 174.6, 171.3, 170.7, 170.1, 169.0 (5 CO), 93.5 (C-1), 73.7 (C-3,5), 71.4 (C-2), 69.0 (C-4), 62.6 (C-6), 43.6 (C-1'), 29.8, 29.3 (C-2',6'), 26.7, 26.4, 26.0 (C-3',4',5'), and 21.5 (4 CH_3).

Anal. Calc. for $C_{21}H_{30}O_{11}$: C, 55.0; H, 6.5. Found: C, 54.6; H, 6.8.

*2,3,4,6-Tetra-*O*-acetyl-1-*O*-(acetylsalicylyl)-β-*D*-glucopyranose. General procedure.* — A solution of orthoester **1** (0.75 g, 2.0 mmol) and acetylsalicylic acid (0.54 g, 3.0 mmol) in dry oxolane (5 mL) was heated on a steam bath for 12 h, and then cooled. Chloroform was introduced, and the organic layer was successively washed with saturated sodium hydrogencarbonate and water, and evaporated. A solution of the residue in ethanol afforded crystals (0.5 g, 48%); m.p. 177–178°, $[\alpha]_D$ −43° (*c* 2, chloroform); ^{1}H-n.m.r. data ($CDCl_3$): δ 7.9–6.8 (4 H, m, Ar), 6.0 (1 H, d, H-1, $J_{1,2}$ 6.9 Hz), 5.4–5.1 (3 H, overlapping m, H-2,3,4), 4.5–3.9 (3 H, overlapping m, H-5,6,6'), and 2.1 (15 H, br s, 5 CH_3); ^{13}C-n.m.r. data ($CDCl_3$): δ 170.2, 169.8, 169.0, 168.8, 168.0, 162.0 (6 CO), 136.7, 130.2, 119.6, 117.6 (Ar), 92.3 (C-1), 72.9, 72.6 (C-3,5), 70.1 (C-2), 67.9 (C-4), 61.5 (C-6), and 20.5 (5 CH_3).

Anal. Calc. for $C_{23}H_{26}O_{13}$: C, 54.1; H, 5.2. Found: C, 54.5; H, 5.4.

*2,3,4,6-Tetra-*O*-acetyl-1-*O*-(cyclohexylcarbonyl)-α-*D*-mannopyranose* (**4**). — A solution of orthoester[11,13] **2** (0.5 g) and cyclohexanecarboxylic acid (0.6 g) in dry

oxolane (5 mL) was heated on a steam bath for 3 h (there was no reaction in 2 h at room temperature), and then evaporated. The residue was dissolved in ether, and upon addition of petroleum ether, crystals were formed (yield, 0.39 g, 63%); after recrystallization from the same solvent, m.p. 126.5–127.5°, $[\alpha]_D$ +60° (*c* 2, chloroform); ^{1}H-n.m.r. data ($CDCl_3$): δ 6.1 (1 H, d, H-1, $J_{1,2}$ 2.0 Hz), 5.5–5.3 (3 H, overlapping m), 4.2–4.0 (3 H, overlapping m), and 2.4–1.3 (23 H, overlapping, 4 CH_3 and C_6H_{11}); ^{13}C-n.m.r. data ($CDCl_3$): δ 172.8, 170.3, 169.8, 169.6, 169.5 (5 CO), 90.5 (C-1, $^1J_{C\text{-}1,H\text{-}1}$ 178 Hz), 70.8, 69.0, 68.5, 65.7 (C-2 to C-5), and 62.2 (C-6). ^{13}C-N.m.r. data ($CDCl_3$) for 1,2,3,4,6-penta-*O*-acetyl-D-mannopyranoses: (α anomer) δ 90.6 (C-1, $^1J_{C\text{-}1,H\text{-}1}$ 177 Hz), 70.8, 68.9, 68.5, 65.7 (C-2 to C-5), and 62.2 (C-6); (β anomer) δ 90.7 (C-1, $^1J_{C\text{-}1,H\text{-}1}$ 162 Hz), 73.4, 70.8, 68.5, 65.7 (C-2 to C-5), and 62.2 (C-6).

Anal. Calc. for $C_{21}H_{30}O_{11}$: C, 55.0; H, 6.5. Found: C, 54.9; H, 6.6.

2,3,4,6-Tetra-O-*acetyl-1*-O-(*2,4,6-trimethylbenzoyl*)-β-D-*glucopyranose, by esterification of 2,3,4,6-tetra*-O-*acetyl*-β-D-*glucopyranose* (**5**). — This experiment (No. 10, Table II) is representative of those employing trifluoroacetic anhydride. A solution of 2,4,6-trimethylbenzoic acid (0.16 g, 1 mmol) and trifluoroacetic anhydride (0.6 g, 3 mmol) in dichloromethane (2 mL) was prepared, and, after 5 min, compound **5** (0.35 g, 1 mmol) was introduced. When the reaction was complete (~1 h; t.l.c. evidence), the solution was poured into cold, M sodium hydrogencarbonate, the mixture was extracted with chloroform, and the extract was washed with water, dried (anhydrous sodium sulfate), and evaporated. Examination of the residue (0.47 g, 94%) by ^{1}H-n.m.r. spectroscopy showed that it consisted of a 1:4 mixture of α- and β-mesitoates. On addition of petroleum ether to the oily residue, crystals were obtained (0.32 g, 64%); after recrystallization from ethanol, m.p. 139.5–141°, $[\alpha]_D$ +4.0° (*c* 1, chloroform); (lit.[23] m.p. 142–143°, $[\alpha]_D$ +4.3°); ^{1}H-n.m.r. data ($CDCl_3$): δ 6.8 (2 H, s, Ar), 6.0 (1 H, d, H-1, $J_{1,2}$ 7.7 Hz), 5.2–5.1 (3 H, overlapping m, H-2,3,4), 4.4 (1 H, q, H-6, $J_{5,6}$ 4.7 Hz), 4.1 (1 H, q, H-6′, $J_{5,6'}$ 2.2, $J_{6,6'}$ 12.5 Hz), 3.9 (1 H, m, H-5), 2.3 (3 H, s, Ar CH_3), and 2.08, 2.06, 2.03, and 2.02 (12 H, 4 s. 4 $COCH_3$); ^{13}C-n.m.r. data ($CDCl_3$): δ 170.5, 170.1, 169.4, 169.0, 167.9 (5 CO), 140.2 (C-4′), 135.7 (C-2′,6′), 129.2 (C-1′), 91.9 (C-1), 73.2, 72.8 (C-3,5) 70.4 (C-2), 68.2 (C-4), 61.7 (C-6), 20.5 (4 $COCH_3$, CH_3-4′), and 19.7 (CH_3-2′,6′).

2,3,4,6-Tetra-O-*benzyl-1*-O-(*2,4,6-trimethylbenzoyl*)-β-D-*glucopyranose, by esterification of 2,3,4,6-tetra*-O-*benzyl*-D-*glucopyranose* (**6**). — This experiment (No. 12, Table II) is representative of those employing trifluoroacetic anhydride. A solution of 2,4,6-trimethylbenzoic acid (0.64 g, 4 mmol) and trifluoroacetic anhydride (0.3 g, 1.8 mmol) in dichloromethane (2 mL) was prepared, and, after 5 min, compound **6** (0.35 g, 1 mmol) was introduced. After processing of the reaction mixture, and analysis by ^{1}H-n.m.r. spectroscopy, as described in the preceding section, crystalline material (0.16 g, 23%) was obtained; this was recrystallized from ethanol; m.p. 129.5–131.5°, $[\alpha]_D$ +8° (*c* 2.4, chloroform); ^{1}H-n.m.r. data ($CDCl_3$): δ 7.4–7.1, 6.8 (22 H, m,

Ar), 5.9 (1 H, d, H-1, $J_{1,2}$ 7.0 Hz), 4.9–4.5 (8 H, overlapping, 4 CH_2), 4.0–3.8 (6 H, overlapping m, H-2–6'), 2.31 (6 H, s, 2 CH_3), and 2.27 (3 H, s, CH_3).

Anal. Calc. for $C_{44}H_{46}O_7$: C, 76.9; H, 6.8. Found: C, 77.0; H, 6.8.

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REFERENCES

1 E. R. Gordon, C. A. Goresky, T. H. Chan, and A. S. Perlin, *Biochem. J.*, 155 (1976) 477–486.
2 B. Lindberg, *Acta Chem. Scand.*, 3 (1949) 1355–1358.
3 M. L. Wolfrom and W. A. Szarek, in W. Pigman and D. Horton (Eds.), *The Carbohydrates: Chemistry and Biochemistry*, 2nd edn., Vol. 1A, Academic Press, New York, 1972, p. 217.
4 C. Pedersen and H. G. Fletcher, Jr., *J. Am. Chem. Soc.*, 82 (1960) 3215–3217.
5 P. A. Levene and G. M. Meyer, *J. Biol. Chem.*, 76 (1928) 513–519.
6 R. U. Lemieux and J. D. T. Cipera, *Can. J. Chem.*, 34 (1956) 906–910.
7 A. S. Perlin, *Can. J. Chem.*, 41 (1963) 555–561.
8 N. K. Kochetkov and A. F. Bochkov, *Methods Carbohydr. Chem.*, 6 (1972) 480–486.
9 E. J. Bourne, M. Stacey, C. E. M. Tatlow, and J. C. Tatlow, *J. Chem. Soc.*, (1954) 2006–2012.
10 F. Weygand and E. Rauch, *Chem. Ber.*, 87 (1954) 211–214.
11 A. S. Perlin, *Can. J. Chem.*, 41 (1963) 399–406.
12 R. U. Lemieux and A. R. Morgan, *Can. J. Chem.*, 43 (1965) 2199–2204.
13 M. Mazurek and A. S. Perlin, *Can. J. Chem.*, 43 (1965) 1918–1923.
14 A. S. Perlin and B. Casu, *Tetrahedron Lett.*, (1969) 2921–2924.
15 K. Bock and C. Pedersen, *J. Chem. Soc., Perkin Trans. 2*, (1974) 293–297.
16 L. V. Volkova, L. L. Danilov, and R. P. Evstigneeva, *Carbohydr. Res.*, 32 (1974) 165–166.
17 M. S. Newman, *Steric Effects in Organic Chemistry*, Wiley, New York, 1956, p. 204.
18 E. S. Gould, *Mechanism and Structure in Organic Chemistry*, Holt–Dryden, New York, 1959, p. 318.
19 R. C. Parish and L. M. Stock, *J. Org. Chem.*, 30 (1965) 927–929.
20 E. J. Bourne, M. Stacey, J. C. Tatlow, and R. Worrall, *J. Chem. Soc.*, (1958) 3268–3282.
21 P. E. Pfeffer, E. S. Rothman, and G. G. Moore, *J. Org. Chem.*, 41 (1976) 2925–2927.
22 J. G. Severson, B. A. Bohm, and C. E. Seaforth, *Phytochemistry*, 9 (1970) 107–110.
23 H. B. Wood, Jr., and H. G. Fletcher, Jr., *J. Am. Chem. Soc.*, 78 (1956) 207–210.