Carbohydrate Research, 58 (1977) 109–124

PHOTOCHEMICAL CONVERSION OF SUGAR DIMETHYLTHIOCARBAMATES INTO DEOXY SUGARS*†

R. HAYS BELL, DEREK HORTON**, DIANA M. WILLIAMS‡, AND EVA WINTER-MIHALY
Department of Chemistry, The Ohio State University, Columbus, Ohio 43210 (U. S. A.)
(Received December 11th, 1976; accepted for publication, January 11th, 1977)

ABSTRACT

Protected sugar derivatives having one free hydroxyl group may be deoxygenated at the alcoholic position by ultraviolet irradiation of the corresponding dimethylthiocarbamic esters; a concomitant process leads also to the original alcohol. Thus, on photolysis, the 6-dimethylthiocarbamate (**1**) of 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (**3**) gives 6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (**2**) together with **3**. Likewise, the 4-dimethylthiocarbamate (**6**) of 1,6-anhydro-2,3-*O*-isopropylidene-β-D-mannopyranose (**8**) gives a mixture of the 4-deoxy derivative **7** and the alcohol **8**. 3-Deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofuranose (**10**) was obtained by irradiation of 3-*O*-(dimethylthiocarbamoyl)-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**9**), and was accompanied by 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**11**). The 3-deoxy-3-iodo analog (**14**) of **11** underwent conversion into **10** by photolysis, and the deoxy sugar **10** was also prepared from 3,3′-dithiobis(1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose) (**12**) by the action of Raney nickel. Photolysis of the 2-dimethylthiocarbamate (**16**) of methyl 3,4-*O*-isopropylidene-β-L-arabinopyranoside (**18**) gave the 2-deoxy derivative (**17**), together with the parent alcohol **18**, and the same pair of products was obtained by the action of tributylstannane on the 2-(methylthio)thiocarbonyl derivative (**19**) of **18**, although the dimethylthiocarbamate **16** was unreactive toward tributylstannane.

INTRODUCTION

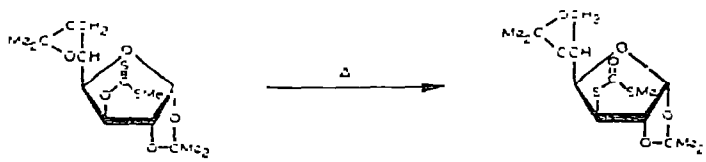
The specific deoxygenation of sugars is an important objective in the preparation of many biologically important sugars from readily available sugar precursors[2,3], and

*Supported, in part, by the Agricultural Research Service, U. S. Department of Agriculture, Grant No. 12-14-9201(71) (O.S.U. Research Foundation Project 2573) administered by the Northern Regional Research Laboratory, Peoria, Illinois, and by the National Institute of General Medical Sciences, U. S. Public Health Service, Bethesda, Maryland, Grant No. GM-11976 (O.S.U. Research Foundation Project 1820).
†For a preliminary report, see ref. 1.
**To whom inquiries should be addressed.
‡National Science Foundation summer research participant.

the application of deoxygenation reactions to such complex carbohydrates as nucleosides[4], carbohydrate antibiotics[5], and polysaccharides[6] offers a wealth of potential applications. Most of the established routes[2] for achieving such deoxygenation involve several steps and may be applicable only in specialized situations.

In principle, the use of thio sugar derivatives[7] provides a general route to deoxy sugars, either by desulfurization with Raney nickel[8] or by photolytic cleavage of the carbon–sulfur bond[9]; an application of this type of approach has been illustrated[10] in a synthesis of 2′-deoxynucleosides. However, preparation of the requisite thio sugar precursors may be difficult, especially when reaction at a secondary alcoholic position is desired[7].

The rearrangement described by Freudenberg and Wolf[11], involving pyrolytic conversion of 1,2:5,6-di-*O*-isopropylidene-3-*O*-(methylthio)thiocarbonyl-α-D-glucofuranose into 1,2:5,6-di-*O*-isopropylidene-3-*S*-(methylthio)carbonyl-3-thio-α-D-glucofuranose, replaces O-3 by a sulfur atom, and subsequent desulfurization[12] yields the 3-deoxy derivative.



This reaction proceeds with retention of configuration[13], probably by an SNi type of process[7]; presumably, the more-conventional Chugaev type of elimination to generate an alkene is inhibited by the electron-withdrawing substituents at the positions vicinal to the xanthate group.

A major drawback of the Freudenberg reaction is the extreme severity of the reaction conditions[11,14], leading to low yields of rearranged product, even with the robust ring-system of the particular xanthic ester studied.

As aryl dimethylthiocarbamates quite readily undergo a related rearrangement[15] to give dimethylcarbamates of arenethiols, it was considered that dimethylthiocarbamates of sugars[13] would probably be susceptible to a similar rearrangement, to give thio sugar derivatives[16]. The reaction might also be feasible by photochemical rather than thermal excitation, as the dithiocarbamate group absorbs[13] u.v. radiation at wavelengths longer[13] than those for other groups in these sugar derivatives. Furthermore, the known lability of the C–S bond to photolytic cleavage[9] offered the possibility for a succeeding, homolytic, C–S bond-cleavage with accompanying capture of a hydrogen atom at this carbon atom and consequent generation of a deoxy sugar. A net deoxygenation reaction thus achieved, proceeding under free-radical conditions, would not be subject to the multitude of alternative reaction-pathways that may complicate deoxygenation reactions conducted under ionic conditions.

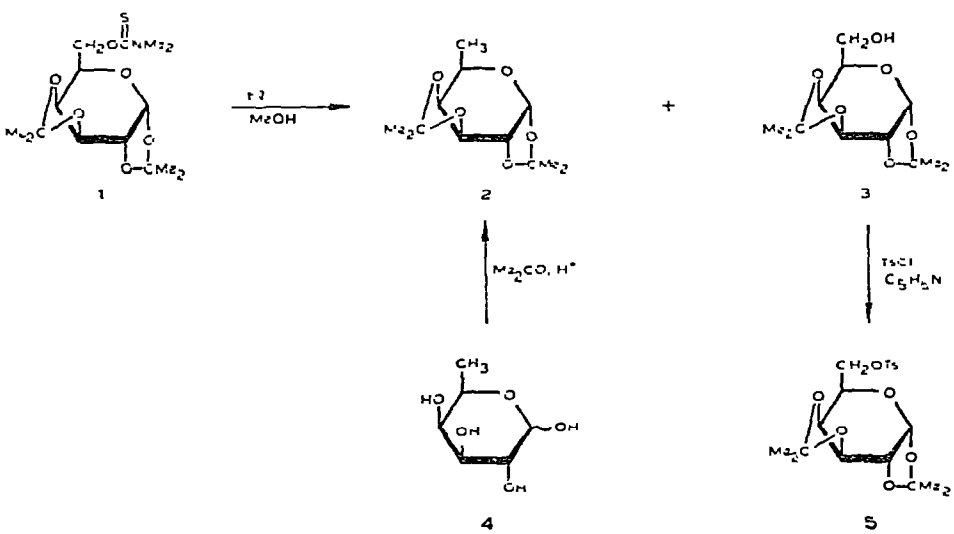
The feasibility of this reaction was established and described in the 1968 preliminary report[1], with examples of 2-, 3-, 4-, and 6-esters[13] of suitable sugar

derivatives. The present article provides full details of these conversions. It is shown that, in each instance, photolysis of the esters affords a mixture of two products, the deoxy derivative and the parent alcohol from which the dimethylthiocarbamate[13] had been prepared. The reaction is compared with other methods for deoxygenation under free-radical conditions at secondary positions, in particular with photolysis of an iodo sugar derivative[17] and with a recently described procedure[18] for conversion of dithiocarbonates of sugars into deoxy derivatives by the action of tributylstannane.

DISCUSSION

Methanolic solutions of each of the four dimethylthiocarbamates studied were subjected to irradiation for extended periods of time at room temperature with unfiltered light from a mercury-arc lamp. The solutions progressively deposited a brown precipitate of material that was apparently a polymeric side-product, and this was removed at intervals by filtration. Irradiation was continued until t.l.c. indicated that no starting material remained, at which point the solutions contained two principal products, which were separated by column chromatography on silica gel. In each instance, the less-polar product was found to be the deoxy sugar formed by net loss of the dimethylthiocarbamate group, and the more-polar product was the corresponding alcohol arising by simple cleavage of the *O*-(dimethylthiocarbamoyl) group.

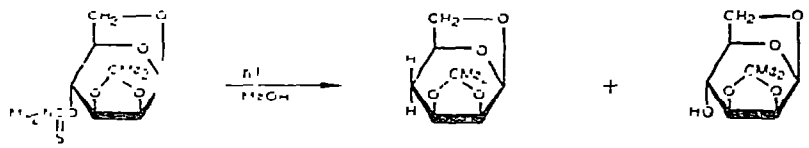
By this procedure, 6-*O*-(dimethylthiocarbamoyl)-1,2:4,3-di-*O*-isopropylidene-α-D-galactopyranose[13] (**1**) gave 6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (**2**) in 15% yield, accompanied by 35.5% of 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (**3**). Crystalline compound **2** was identical with an authentic sample prepared[19] by acetonation of D-fucose (**4**), and its n.m.r. spectrum was



identical with that recorded by Cone and Hough[20]. The syrupy compound **3** was purified by distillation, and identified by comparison of its specific rotation[21,22] and n.m.r. spectrum[20] with literature data, as well as by conversion into its known[22], crystalline *p*-toluenesulfonate **5**.

In this instance, although the yield of **2** may be augmented by reconverting the alcohol **3** into the dimethylthiocarbamate **1** and resubjecting the latter to photolysis, the reaction is not of significant preparative value for the deoxy derivative **2**, as more-effective, alternative methods for deoxygenation at a primary alcoholic position are available.

Photolysis of a methanolic solution of 1,6-anhydro-4-*O*-(dimethylthiocarbamoyl)-2,3-*O*-isopropylidene-β-D-mannopyranose[13] (**6**) gave a 19% yield of a crystalline product formulated as 1,6-anhydro-4-deoxy-2,3-*O*-isopropylidene-β-D-*lyxo*-hexopyranose (**7**) and 17% of 1,6-anhydro-2,3-*O*-isopropylidene-β-D-mannopyranose (**8**). Repetition of the reaction gave **7** and **8** in 26 and 29% yields, respectively. Formulation of **7** as the 4-deoxy sugar was based on elemental analysis and n.m.r.-spectral data (see Tables I and II), and by analogy with the products from the other photolysis reactions reported here (see also Experimental section). The alcohol **8** was identical with an authentic sample[23,24], and it could be used to augment the net yield of deoxy derivative **7** by photolysis of its dimethylthiocarbamate[13] **6**.



6 **7** **8**

Irradiation of 3-*O*-(dimethylthiocarbonyl)-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose[13] (**9**) gave a 17–23% yield of 3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofuranose (**10**) together with 26–32% of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**11**). Compound **11** was identical with an authentic sample by m.p.[25], n.m.r. spectrum[13], and X-ray powder diffraction data. The 3-deoxy derivative **10** was purified by distillation; its specific rotation[12,26] and n.m.r. spectrum[17] were in accord with reported data, and partial hydrolysis afforded the known[26], crystalline 3-deoxy-1,2-*O*-isopropylidene-α-D-*ribo*-hexofuranose (**15**).

Reference samples of **10** and **15** were prepared by independent methods. Desulfurization of 3,3'-dithiobis(1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose)[11] (**12**) with Raney nickel gave **10** in 33% yield, and the crystalline monoacetal **15** was then obtained by partial hydrolysis of **10** with acid. In an alternative route, the procedure of Brown and Jones[17] was used to convert 3-deoxy-3-hydrazino-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose[27,28] (**13**) into the 3-deoxy-3-iodo analog **14**, and the latter was then reduced with Raney nickel to give **10**, further transformed by partial hydrolysis into crystalline **15**. The iodo derivative **14** showed n.m.r.-spectral

TABLE I

CHEMICAL-SHIFT DATA[a] FOR COMPOUNDS 2, 7, 14, 15, AND 17

Compound	*Solvent*	*Chemical shifts (δ) and signal multiplicities*[b]						
		H-1	*H-2* *H-2a* *H-2b*	*H-3* *H-3a* *H-3b*	*H-4* *H-4a* *H-4b*	*H-5* *H-5a* *H-5b*	*H-6* *H-6a* *H-6b*	*CMe₂ protons*
2	$CDCl_3$[c]	5.56d	4.32q	4.63q	4.10q	3.95o	1.26d	1.53, 1.47, 1.36, 1.34s
	$(CD_3)_2CO$	5.50d	4.32q	4.64q	4.12q	3.93o	1.16d	1.47, 1.39, 1.32s
7	$CDCl_3$[c]	5.34d	3.96q	4.59–4.28m	2.3m 2.08m	3.75m	4.59–4.06q 4.28m	1.59, 1.35s
	$(CD_3)_2CO$	5.22d	3.89q	4.59–4.30m	2.25q [d]	3.64m	4.59–3.99q 4.30m	1.48, 1.27s
10	$CDCl_3$[c]	5.84d	4.78t	2.36–1.92m 2.07–1.39m	4.3 –3.97m	3.95–3.71m	4.3 –3.97m	1.51, 1.42, 1.36, 1.32s
	C_6D_6	5.68d	4.38t	2.18q 1.61[e]	4.31–4.1m	4.02–3.77m	4.02–3.77m	1.44, 1.36, 1.28, 1.18s
	$(CD_3)_2CO$	5.81d	4.81t	2.12q 1.75–1.45m	4.25–3.7m	4.25–3.7m	4.25–3.7m	1.43, 1.35, 1.29, 1.27s
14	$CDCl_3$[c]	5.92d	5.01d	4.42d	3.37–3.11m	4.17–3.92m	4.17–3.92m	1.46, 1.38, 1.31, 1.28s
15	$CDCl_3$	5.86d	4.80t	2.1q 1.83o	4.38–4.14m	4.01–3.61m	4.01–3.58q 3.61m	1.53, 1.34s, 2.68s (OH)
17	$CDCl_3$	4.73q	2.13sx 1.75o	4.42sx	4.09sx	3.84q 3.65q		1.47, 1.30s, 3.35s (OMe)

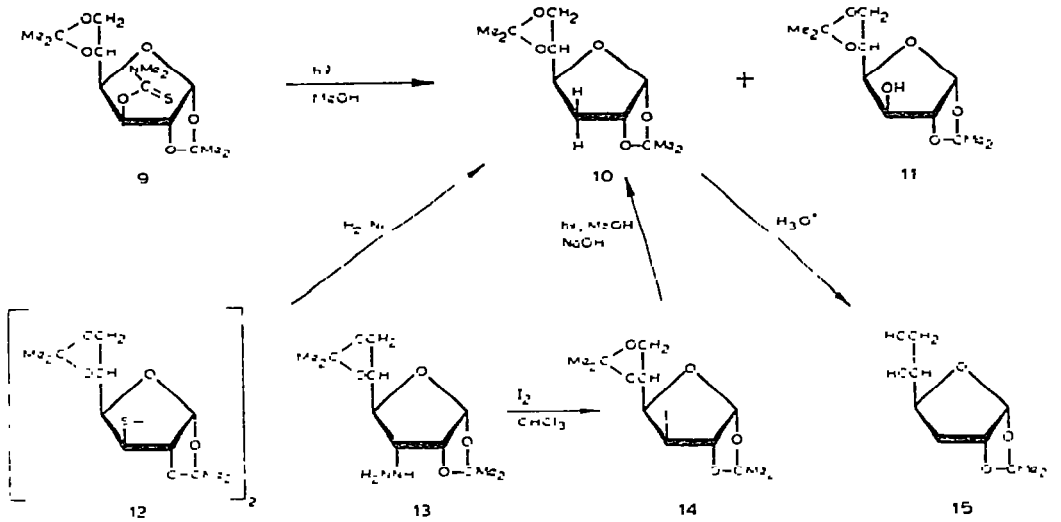
[a]Data from 100-MHz spectra. [b]Signal multiplicity is given as d, doublet; m, multiplet; o, octet; q, quartet; s, singlet; sx, sextet; and t, triplet. [c]Assignments verified by spin decoupling. [d]Obscured by solvent. [e]Under another signal.

TABLE II

FIRST-ORDER COUPLING-CONSTANTS[a] FOR COMPOUNDS **2**, **7**, **10**, **14**, **15**, AND **17**

Compound	*Solvent*	*Coupling constants (Hz)*[b]										
		$J_{1,2}$	$J_{2,3}$		$J_{3,4}$		$J_{3a,3b}$	$J_{3,4a}$	$J_{3,4b}$	$J_{4a,4b}$	$J_{4,5}$	$J_{5,6}$		$J_{6a,6b}$
			$J_{2,3a}$	$J_{2,3b}$	$J_{3a,4}$	$J_{3b,4}$						$J_{5,6a}$	$J_{5,6b}$	
2	$CDCl_3$	5.1	2.3		7.8						1.9	6.6		
	$(CD_3)_2CO$	5.2	2.3		7.8						1.9	6.6		
7	$CDCl_3$	3.0	5.9					5.0[c]	2.8[c]	15.0[c]	[d]	[d]	0	6.4
	$(CD_3)_2CO$	3.0	5.9					4.9	[d]	16.0	[d]	[d]	1.0	6.4
10	$CDCl_3$	4.0	0	4.3	4.1	[d]	14.0				[d]	[d]		[d]
	C_6D_6	4.0	0	4.3	4.3	[d]	13.9				[d]	[d]		[d]
	$(CD_3)_2CO$	4.0	0	4.4	3.7	[d]	[d]				[d]	[d]		[d]
14	$CDCl_3$	3.6	0		3.1						[d]	[d]		[d]
15	$CDCl_3$	3.8	0	4.6	4.9	10.8	13.2				[d]	[d]	6.0	11.6
17	$CDCl_3$	[e]	[e]		6.5						[e]	[e]		

[a]Data from 100-MHz spectra. [b]a = low-field proton; b = high-field proton. [c]Obtained from spin-decoupling data. [d]Not measured because of second-order effects. [e]$J_{1,2a}$ 4.5, $J_{1,2b}$ 6.0, $J_{2a,3}$ 5.0, $J_{2b,3}$ 5.0, $J_{2a,2b}$ 12.5, $J_{4,5a}$ 3.0, $J_{4,5b}$ 3.0, and $J_{5a,5b}$ 12.5 Hz.



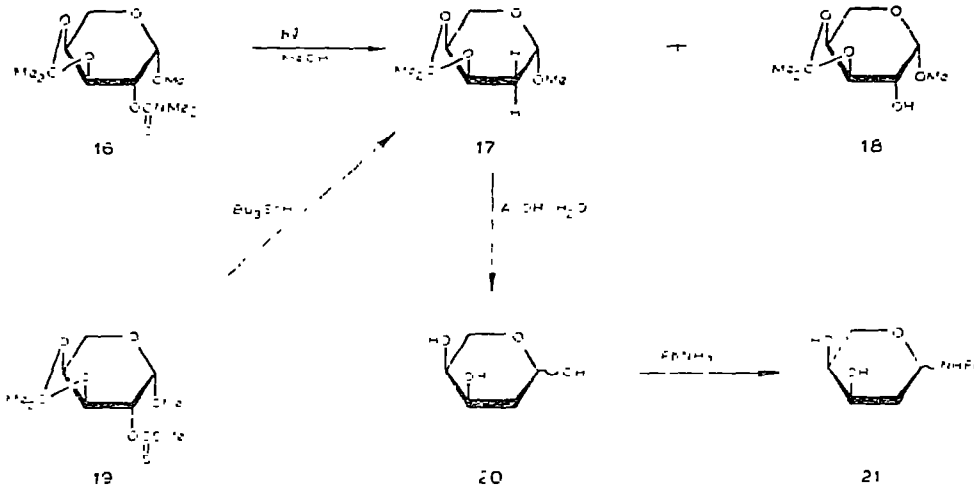
signals for H-1, H-2, and H-3 essentially in accord with those reported in the literature[17], but spin-decoupling experiments showed that a high-field signal originally assigned[17] to H-5 was actually that of H-4 (see Tables I and II for details). However, the other assignments and the spin-coupling data upheld the earlier attribution[17] of the D-*gluco* stereochemistry to this product.

Photolysis of a sugar iodo-substituted at the primary carbon atom, in methanolic solution, has been shown[29] to give the corresponding deoxy sugar in high yield. It was thus of interest to examine the photolysis of the secondary-iodo sugar **14**. The reaction proceeded rapidly to completion (4 h), and a mixture of three compounds was obtained. The major one of these, isolated pure in 32% yield, proved to be the deoxy sugar derivative **10**, and this syrupy product was further characterized as the crystalline monoacetal **15**. Presumably, the conversion of **14** into **10** involves homolysis of the relatively weak C–I bond, followed by abstraction of a hydrogen atom from the solvent by the intermediate, C-3 radical; this reaction is probably very similar to the photochemical conversion[30] of mercurial sugar derivatives into deoxy derivatives, but the yields are higher with the mercury derivatives.

The monoacetal **15** prepared by each of these four methods had $[\alpha]_D^{23}$ −13° in ethanol and −19° in chloroform; the value of $[\alpha]_D^{18}$ −37.8° in ethanol recorded for **15** in the literature[12] appears incorrect.

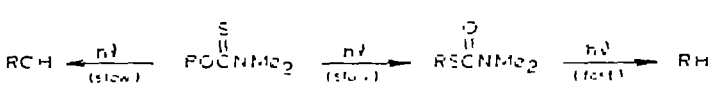
In the final example studied, methyl 2-*O*-(dimethylthiocarbamoyl)-3,4-*O*-isopropylidene-β-L-arabinopyranoside[13] (**16**) was photolyzed in methanolic solution. The reaction afforded an 11% yield of syrupy methyl 2-deoxy-3,4-*O*-isopropylidene-β-L-*erythro*-pentopyranoside (**17**), together with 36% of crystalline methyl 3,4-*O*-isopropylidene-β-L-arabinopyranoside (**18**). Compound **17** was characterized by n.m.r.-spectral data (see Tables I and II), and by hydrolysis with aqueous acetic acid to give 2-deoxy-L-*erythro*-pentose (**20**) as a syrup that was converted by the action of

aniline into the aniline derivative **21**, identical with the known D enantiomer[14,31] except for its sign of optical rotation.



The deoxypentose derivative **17** was prepared independently from methyl 3,4-*O*-isopropylidene-2-*O*-(methylthio)thiocarbonyl-β-L-arabinopyranoside[14] **(19)** by treatment with tributylstannane in boiling toluene according to the general procedure of Barton and McCombie[18]. A mixture of products was obtained that contained the deoxy derivative **17**, isolated in 40% yield, accompanied by the alcohol **18**, obtained in 17% yield. Attempts to convert the dimethylthiocarbamate **16** into the deoxy derivative **17** by the action of tributylstannane were unsuccessful, and the starting material was recovered under a variety of experimental conditions, even when a radical initiator was present.

The foregoing results thus indicate that "isolated" alcohol groups in sugar derivatives may be converted into the corresponding deoxy derivatives by extended photolysis of the corresponding dimethylthiocarbamates. The concurrent production of the original alcohol suggests that two reactions are operating simultaneously, one involving simple cleavage of the ester group, and the other proceeding *via* a Freudenberg type of rearrangement followed by more-rapid, C–S bond homolysis and subsequent abstraction of hydrogen from the methyl group of the solvent to give the deoxy sugar.



R = sugar residue

Although the yields of deoxy sugar are modest, they may be raised by recycling, by way of its dimethylthiocarbamate, the alcohol produced in the reaction; yields then compare favorably with those feasible by conventional, multi-step routes. Comparative evaluation in preparation of the deoxy derivative **17** from the alcohol **18** indicates that the action of tributylstannane on the *S*-methylxanthate **19** gives a yield of **17** superior to that achieved by photolysis of the dimethylthiocarbamate **16**.

EXPERIMENTAL

General methods. — Evaporations were performed under diminished pressure (~10 torr). Specific rotations were measured in either a 1-dm tube (Perkin–Elmer 141 photoelectric polarimeter) or a 2-dm tube (Rudolph manual polarimeter). Melting points were determined with a Thomas–Hoover "Unimelt" apparatus. N.m.r. spectra were recorded at 60 or 100 MHz with Varian A-60 or HA-100 n.m.r. spectrometers. Chemical shifts (see Table I) refer to an internal standard of tetramethylsilane ($\delta = 0.00$). Spin-decoupling experiments were performed with the HA-100 instrument operating in the frequency-sweep mode. First-order couplings are given in Table II. Microanalyses were determined by W. N. Rond. X-ray powder diffraction data give interplanar spacings, Å, for CuKα radiation. The camera diameter was 114.59 mm. Relative intensities were estimated visually: m, moderate; s, strong; v, very; w, weak. The strongest lines are numbered (1, strongest); double numbers indicate approximately equal intensities. T.l.c. was performed with Silica Gel G (E. Merck, Darmstadt, Germany), activated at 120°, as the adsorbent, 3:1 dichloromethane–ether as the developer (unless specified otherwise), and sulfuric acid as the indicator. Column chromatography was performed with silica gel No. 7734 (0.05–0.2 mm; from E. Merck AG, Darmstadt, Germany), with 1 g of the mixture to be separated per 30 g of adsorbent. Columns were packed by allowing a slurry of the adsorbent in the eluant to settle under gravity. The eluant was 3:1 dichloromethane–ether (solvent *A*) or 9:1 dichloromethane–ether (solvent *B*); solvent *A* was used where a specific eluant is not indicated. The petroleum ether used in recrystallizations was a fraction having a boiling range of 60–110°.

Photolysis procedure[9]. — A mercury-arc lamp (Hanovia Type L, Model 697A, Hanovia Lamp Division, Engelhard Hanovia Inc., Newark, N.J.) fitted in a water-cooled, quartz immersion-well (Hanovia Model 19431) was used, and the assembly was mounted in a Pyrex reaction-vessel. Photolysis was effected at ~30° with unfiltered light, and the magnetically stirred, methanolic solutions were continually flushed with nitrogen. The methanol used was Spectro grade (Eastman Organic Chemicals). The dimethylthiocarbamates[13] were subjected to column chromatography to ensure purity before photolysis.

Photolysis of 6-O-(dimethylthiocarbamoyl)-1,2:3,4-di-O-isopropylidene-α-D-galactopyranose[13] (**1**) — A solution of **1** (4.82 g, 13.9 mmol) in methanol (150 ml) was photolyzed for 113 h, and then evaporated to a brown syrup. The latter was triturated in ether (50 ml), and the mixture was filtered to give 553 mg of brown solid.

The solid did not migrate in t.l.c. The filtrate was decolorized with charcoal, and evaporated to a light-yellow syrup that was dissolved in methanol (150 ml), and photolyzed for an additional 48 h. The foregoing isolation-procedure was repeated, to give an additional 410 mg of brown residue and 2.93 g of a yellow syrup. The n.m.r. spectrum of the crude syrup showed no signals[13] for the $-NMe_2$ protons of **1**. T.l.c. (solvent *A*) revealed four components, having R_F 0.98, 0.93 (yellow-brown, major), 0.78, and 0.56 (black). T.l.c. (solvent *B*) revealed nine components, R_F 0.93 (very weak), 0.86 (very weak), 0.80 (very weak), 0.74 (very weak), 0.70 (major, yellow-brown), 0.54 (weak), 0.41 (very weak), 0.38 (very weak), and 0.32 (major, brown-black).

The syrup was resolved by column chromatography on silica gel with solvent *B* as the eluant. Fractions (10 ml) were collected, and monitored by t.l.c. Fractions containing the major component (R_F 0.70) were combined and evaporated, to yield **2** as a light-yellow syrup, yield 505 mg (15%). The syrup was kept for 18 h at −15°, whereupon a solid mass of crystals formed. The compound was distilled at a bath temperature of 100–110°/0.2 torr to give colorless, solid *6-deoxy-1,2:3,4-di-O-isopropylidene-α-D-galactopyranose* (**2**), which had m.p. 33–35°, $[\alpha]_D^{19}$ −53.6° (*c* 1.2, chloroform). For this compound, Freudenberg and Raschig[19] reported m.p. 37°, $[\alpha]_D^{19}$ −52.4°, and Cone and Hough[20] reported m.p. 30–35° after distillation of the product. The 60-MHz n.m.r. spectrum in acetone-d_6 was identical to that described by Cone and Hough[20]; 100-MHz data in chloroform-*d* and acetone-d_6 are given in Tables I and II; X-ray powder diffraction data: 11.86 m, 9.11 s (2,2), 6.57 s (2,2), 6.24 s (3,3), 5.58 s (3,3), 5.22 s (1,1), 4.88 s (1,1), and 4.56 s (1,1).

To obtain an authentic sample of **2**, D-fucose (1.0 g, 6.1 mmol) was acetonated by the procedure of Freudenberg and Raschig[19]. Distillation of the syrupy product at 0.2–0.3 torr (bath temperature 100–116°) gave a colorless syrup, yield 1.15 g (77%), which gave white crystals, m.p. 35–36°, after refrigeration overnight. By comparison of n.m.r.-spectral data and X-ray powder diffraction data, this compound was identical with **2** prepared by photolysis of **1**.

The fractions containing the major component, R_F 0.32, were combined and evaporated, to give *1,2:3,4-di-O-isopropylidene-α-D-galactopyranose* (**3**); yield 1.29 g (35.5%). The light-yellow syrup was distilled (bath temperature 150–165°/0.2–0.3 torr): $[\alpha]_D^{19}$ −53° (*c* 6.2, chloroform) {lit. $[\alpha]_D$ −55° (chloroform)[21] and $[\alpha]_D^{20}$ −59° (*c* 1.4, chloroform)[22]}. The n.m.r. spectrum for a solution of **3** in chloroform-*d* was comparable with that described by Cone and Hough[20].

Compound **3** (311 mg, 1.2 mmol) obtained from the photolysis experiment was treated with *p*-toluenesulfonyl chloride in pyridine as described in the literature[20], to give *1,2:3,4-di-O-isopropylidene-6-O-p-tolylsulfonyl-α-D-galactopyranose* (**5**) as white platelets, obtained in two crops from ethanol, yield 280 mg (58%), m.p. 100–101° (lit.[22] m.p. 99–100°). The X-ray powder diffraction pattern and n.m.r. spectrum were identical with those previously reported[22].

Photolysis of 1,6-*anhydro*-4-O-(*dimethylthiocarbamoyl*)-2,3-O-*isopropylidene*-β-D-*mannopyranose*[13] (**6**). — A solution of **6** (1.838 g, 6.4 mmol) in methanol was

photolyzed for 69 h, and the brown solution was treated by the procedure used for the preparation of **2** from **1**. The brown residue amounted to 52 mg. The decolorized, ethereal solution was evaporated to give a yellow syrup. The n.m.r. spectrum of the crude syrup in chloroform-*d* indicated absence of the NMe_2 group of compound **6**. The syrup crystallized spontaneously, to give white needles (806 mg). The brown residue remained at the point of application in t.l.c. (solvent *A*). The white needles were dissolved in chloroform. T.l.c. of the solution (solvent *A*) revealed seven components, having R_F 0.98 (minor), 0.96 (minor), 0.91 (minor), 0.88 (minor), 0.80 (major), 0.73 (very minor), and 0.45 (major). T.l.c. of the solution (solvent *B*) showed nine components, R_F 0.93 (very minor), 0.86 (minor), 0.78 (minor), 0.70 (minor), 0.63 (minor), 0.57 (major), 0.46 (minor), 0.33 (minor), and 0.28 (major). The chloroform solution was evaporated to give white crystals of crude product. The product was subjected to column chromatography with solvent *A* as the eluant, and 10-ml fractions were collected, and monitored by t.l.c.

Fractions containing the major component (R_F 0.80) were combined and evaporated, to yield crystalline *1,6-anhydro-4-deoxy-2,3-O-isopropylidene-β-*D*-lyxo-hexopyranose* (**7**), yield 228 mg (19%), m.p. 119–120°. Recrystallization from ethanol gave white needles, m.p. 120–121°, $[\alpha]_D^{19}$ −16.7° (*c* 1, chloroform). After three recrystallizations from ethanol, the product had m.p. 125–126°, $[\alpha]_D^{23}$ −21.9° (*c* 0.8, chloroform); for n.m.r. data in chloroform-*d* and acetone-d_6, see Tables I and II; X-ray powder diffraction data: 7.42 s (3), 6.14 m, 5.73 s (3), 5.50 s (1), 5.13 m, 4.82 s (2,2), 4.40 vvw, 4.20 s (2,2), 3.96 w, 3.85 vvw, 3.71 w, 3.53 w, 3.09 w, and 3.02 w.

Anal. Calc. for $C_9H_{14}O_4$: C, 58.49; H, 7.57. Found: C, 58.52; H, 7.61.

The constants for this compound[1] are in good agreement with those recorded[31] for **7** prepared by an alternative route.

Fractions containing the component of R_F 0.28 were pooled and evaporated, to yield *1,6-anhydro-2,3-O-isopropylidene-β-*D*-mannopyranose* (**8**), yield 220 mg (17%), m.p. 157–159°. Recrystallization from butyl alcohol gave pure **8**, m.p. 160–161° (lit.[23] m.p. 161–162°), identical with an authentic sample[24] by n.m.r. spectrum in chloroform-*d* and by X-ray powder diffraction pattern.

The photolysis of **6** was repeated, yielding 26% of **7** and 29% of **8**.

*Photolysis of 3-O-(dimethylthiocarbamoyl)-1,2:5,6-di-O-isopropylidene-α-*D*-glucofuranose*[13] (**9**). — A solution of **9** (5.049 g, 14.5 mmol) in methanol (150 ml) was photolyzed for 37 h, and the resultant, brown solution was treated by the procedure used for the preparation of **2** from **1**. The amount of brown residue formed was 393 mg. The yellow syrup obtained after decolorization of the filtrate was dissolved in methanol (150 ml), and the solution was photolyzed for an additional 31 h. Processing of the product as before gave 262 mg of brown residue. An ethereal solution of the syrup was decolorized and evaporated, to yield a yellow syrup that was dissolved in methanol (150 ml) and photolyzed for 65 h. Isolation as previously described gave 324 mg of brown residue and 2.746 g of a yellow syrup whose n.m.r. spectrum indicated the absence of signals for the $-NMe_2$ protons of **9**. The brown residue

remained at the origin in t.l.c. (solvent *A*). T.l.c. of the syrup in the same solvent system revealed five components, having R_F 0.97, 0.93, 0.85 (major), 0.62 (very minor), and 0.57 (major). T.l.c. of the syrup (solvent *B*) gave eight components, R_F 0.75 (very minor), 0.71 (very minor), 0.66 (very minor), 0.64 (very minor), 0.60 (major), 0.49 (very minor), and 0.36 (major).

The syrup was subjected to column chromatography on silica gel, with solvent *A* as the eluant. Fractions (10 ml) were collected, and monitored by t.l.c. The fractions containing the component having R_F 0.85 were combined and evaporated, to give *3-deoxy-1,2:5,6-di-O-isopropylidene-α-D-ribo-hexofuranose* (**10**) as a light-yellow syrup, yield 610 mg (17%). The syrup was distilled at 0.4 torr (bath temperature 115–125°) to give a colorless syrup having $[\alpha]_D^{21}$ −6.3° (*c* 1.9, chloroform). Černý and Pacák[12] reported $[\alpha]_D^{19}$ −8.6° (*c* 3.7, ethanol), and Overend and co-workers[26] gave $[\alpha]_D^{15}$ −5.78° (*c* 4.2, ethanol) for this compound. The 60-MHz, n.m.r. data for a solution of **10** in carbon tetrachloride were in agreement with those reported by Brown and Jones[17]. N.m.r. data (100 MHz) for solutions of **10** in chloroform-*d*, benzene-d_6, and acetone-d_6 are given in Tables I and II.

A characterizing derivative, *3-deoxy-1,2-O-isopropylidene-α-D-ribo-hexofuranose* (**15**) was prepared from **10** (44 mg, 0.18 mmol) by partial hydrolysis with acid[26]. Syrupy **15** was obtained: yield 32 mg (89%). It was crystallized from chloroform–petroleum ether to give 17 mg (44%) of **15** as white needles, m.p. 82–83° (lit.[26] m.p. 84°). The compound was identical by X-ray powder diffraction data with an authentic sample.

The fractions containing the component having R_F 0.57 were pooled and evaporated, to give *1,2:5,6-di-O-isopropylidene-α-D-glucofuranose* (**11**) as a syrup that crystallized: yield 967 mg, 3.71 mmoles (26%). Recrystallization from cyclohexane gave white needles, m.p. 106° (lit.[25] m.p. 105–109°). The n.m.r. spectrum of **11** in chloroform-*d* was comparable to that previously reported[13], and the X-ray powder diffraction pattern was identical with that of an authentic sample: X-ray powder diffraction data: 11.62 m, 9.73 s (3), 8.07 w, 6.05 w, 5.80 vw, 5.33 s (1), 4.96 s (2,2), 4.67 w, 4.16 s (2,2), 3.89 w, and 3.72 w.

In a duplicate experiment, the yield of **10** was 22.5%, and that of **11**, 32%.

Preparation of 3-deoxy-3-iodo-1,2:5,6-di-O-isopropylidene-α-D-glucofuranose (**14**). — The procedure of Brown and Jones[17] was followed, with minor modifications: triethylamine was used as the base, instead of *N*-methylmorpholine, and the product was isolated by column chromatography instead of by distillation. To 3-deoxy-3-hydrazino-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose **13** (15.0 g, 5.5 mmol) in chloroform (100 ml) containing triethylamine (0.77 ml, 560 mg, 5.5 mmol) was added iodine (870 mg, 11.0 mmol) in chloroform (200 ml). The solution was kept until t.l.c. showed that **13** had reacted completely, and was then washed with aqueous sodium hydrogensulfite (iodine color disappeared), and dried (magnesium sulfate). Evaporation gave crude **14** as a light-yellow syrup, yield 11.0 g (55%). T.l.c. revealed a principal component (R_F 0.91) and four very minor components, R_F 0.80, 0.49, 0.33, and 0.21. The product having R_F 0.91 was isolated by column chromatography

(solvent *A*), and obtained as a light-yellow syrup that was dissolved in ether (200 ml). The solution was decolorized and evaporated, to give **14** as a colorless syrup, yield 8.4 g (42%), that solidified spontaneously, and that could be crystallized from a small volume of dichloromethane to give colorless platelets, m.p. 38–41°, $[\alpha]_D^{21}$ −15.1° (*c* 3.0, chloroform). The platelets reverted to a syrup on storage in air for a short time at room temperature. The n.m.r. spectrum of **14** in carbon tetrachloride was the same as that reported previously[17], but the proton assignments required revision (see Tables I and II).

*Preparation of 3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-*D*-ribo-hexofuranose* (**10**) *from* **14**. — A reference sample of **10** was prepared from **14** essentially according to the method of Brown and Jones[17]. Compound **14** (1.964 g, 5.3 mmol) in ethanol (50 ml) containing sodium acetate (0.5 g) was shaken with 4 g of Raney nickel No. 28 (W. R. Grace and Co., So. Pittsburg, Tenn.) under hydrogen at 20 lb.in^{-2} until uptake of hydrogen ceased. The mixture was filtered, and the filtrate evaporated to a syrup. A solution of the syrup in dichloromethane (50 ml) was washed twice with water, dried (magnesium sulfate), and evaporated to a syrup that was distilled (bath temperature 115–130°/0.1 torr) to give 1.173 g (91%) of a colorless syrup. T.l.c. revealed the presence of two components, R_F 0.87 (minor) and 0.74 (major). The syrup was resolved by column chromatography with solvent *A* as the eluant. Fractions containing the component having R_F 0.74 were pooled and evaporated, to give 642 mg (49%) of **10** as a colorless syrup, $[\alpha]_D^{20}$ −6.0 (*c* 5.5, chloroform) {lit.[12] $[\alpha]_D^{18}$ −8.6° (*c* 3.7, ethanol) and lit.[20] $[\alpha]^{18}$ −5.78° (*c* 4.2, ethanol)}. The n.m.r. data were in agreement with those described previously[17]; detailed assignments made at 100 MHz for solutions in chloroform-*d*, benzene-d_6, and acetone-d_6 are given in Tables I and II.

*Preparation of 3-deoxy-1,2-*O*-isopropylidene-α-*D*-ribo-hexofuranose* (**15**). — A slight modification of the procedure of Overend *et al.*[20] was used. A solution of compound **10** (266 mg, 1.1 mmol) in ethanol (10 ml) containing 0.01M hydrochloric acid (400 ml) was kept for 5 h at ~25°, made neutral with sodium hydrogencarbonate, and evaporated to dryness, and the residue was extracted with three 30-ml portions of chloroform. The extracts were combined and evaporated, to give a colorless syrup, yield 0.177 g (79%). T.l.c. of the syrup revealed two very minor components, R_F 0.79 and 0.75, and a major component at the origin. The syrup was crystallized from chloroform–petroleum ether, to yield **15** as white needles (109 mg, 48%): m.p. 82° (lit.[12] m.p. 84°), $[\alpha]_D^{23}$ −12.6° (*c* 1.1, ethanol), $[\alpha]_D^{21}$ −19.0° (*c* 1.69, chloroform); X-ray powder diffraction data: 9.89 vw, 8.71 vw, 7.51 s (2), 5.42 m, 4.87 s (1,1), 4.35 m, 3.90 w, 3.62 m, 3.45 vw, and 3.20 vw; for n.m.r. data in chloroform-*d*, see Tables I and II.

Concordant $[\alpha]_D$ values in ethanol were recorded for four independent preparations; the literature value[12] of $[\alpha]_D$ −37.8° in ethanol was not confirmed.

*Photolysis of 3-deoxy-3-iodo-1,2:5,6-di-*O*-isopropylidene-α-*D*-glucofuranose* (**14**). — A solution of compound **14** (1.16 g, 3.1 mmol) in methanol (150 ml) containing sodium hydroxide (163 mg, 4.08 mmol, 1.3 equiv.) was photolyzed for 4 h and then

evaporated to a syrup. The latter was swirled with ether (50 ml), and a yellowish-white, insoluble residue (574 mg, presumably inorganic material) was filtered off. T.l.c. of the ethereal solution revealed a major component (R_F 0.85), a minor one (R_F 0.55), and a substantial component having R_F 0.47. Streaking was observed on the t.l.c. plate, from the zone of the component having R_F 0.47 to the point of application. The solution was evaporated to a syrup, which was dissolved in dichloromethane (50 ml). The solution was washed with water (50 ml), dried (magnesium sulfate), and evaporated to a syrup; yield 440 mg. The product was subjected to column chromatography with solvent *A* as the eluant. Fractions containing the component having R_F 0.85 gave **10** as a colorless syrup, yield 248 mg (32%). The syrup was distilled (bath temperature 100–110°/0.2 torr); $[\alpha]_D^{21}$ −7.1° (*c* 1.6, chloroform). The product was identical with **10** prepared by the other routes.

The product **10** (45 mg, 0.2 mmol) was converted into compound **15** by the method already described, yield 26 mg (65%). Crystallization from chloroform–petroleum ether gave **15** as white needles, m.p. 80–81°. The product was identical with authentic **15** by comparison of n.m.r. spectra and X-ray powder diffraction patterns.

Desulfurization of 3,3'-dithiobis(1,2:5,6-di-O-isopropylidene-α-D-glucofuranose)[11] (**12**). — The title compound (328 mg, 0.6 mmol) was dissolved in abs. ethanol (40 ml), and an excess of Raney nickel No. 28 (W. R. Grace and Company, So. Pittsburg, Tenn.) (~ 10 g) was added. The mixture was refluxed for 5 h, and the catalyst was filtered off. The Raney nickel was refluxed with two additional 30-ml portions of ethanol, and the mixture filtered. The combined ethanol filtrates were evaporated to a syrup. T.l.c. of the syrup revealed four components, R_F 0.85 (major), 0.53 (very minor), and 0.36 (minor), and a substantial component that remained at the origin. Column chromatography with solvent *A* as the eluant gave the major component **10** as a colorless syrup; yield 102 mg (33%); $[\alpha]_D^{21}$ −6.3° (*c* 1.9, chloroform), identical with that of an authentic sample.

Partial hydrolysis of the product as already described gave compound **15** as white needles from chloroform–petroleum ether, yield 41 mg (57%), m.p. 81–82°, identical with an authentic sample.

Photolysis of methyl 2-O-(dimethylthiocarbamoyl)-3,4-O-isopropylidene-β-L-arabinopyranoside[13] (**16**). — A solution of **16** (1 g, 3.4 mmol) in methanol was photolyzed for 75 h, and the yellow solution was treated by the procedure used for the preparation of **2** from **1**. The decolorized, ethereal solution was evaporated to a yellow syrup (420 mg). T.l.c. (solvent *A*) revealed two components, R_F 0.69 (major) and 0.44 (major). The syrup was resolved by column chromatography on silica gel with solvent *A* as the eluant. Fractions containing the component having R_F 0.69 were evaporated, to give *methyl 2-deoxy-3,4-O-isopropylidene-β-L-erythro-pentofuranoside* (**17**) as a colorless syrup; yield 69 mg (11%); for n.m.r.-spectral data in chloroform-*d*, see Tables I and II.

Fractions containing the other major component (R_F 0.44) gave *methyl 3,4-O-isopropylidene-β-L-arabinopyranoside* (**18**); yield 247 mg (36%). The n.m.r. spectrum of this product in chloroform-*d* was identical to that recorded earlier[13].

Reaction of methyl 3,4-O-isopropylidene-2-O-(methylthio)thiocarbonyl-β-L-arabinopyranoside[14] **(19)** *with tributylstannane.* — Following the general procedure of Barton and McCombie[18], a solution of compound **19** (1 g, 3.3 mmol) in toluene (40 ml) was added during 3 h to a solution of tributylstannane (4.95 g, 17 mmol) in boiling toluene (30 ml) that was maintained under argon and under reflux. Refluxing was continued for 18 h, and the solvent was then removed at 50°/15 torr. The product was chromatographed on a column of silica gel by eluting with a petroleum ether–diethyl ether gradient. After initial elution of tin derivatives, followed by a carbohydrate byproduct also containing a tributyltin residue, the deoxy derivative **17** was eluted; evaporation of this eluate gave a colorless syrup; yield 248 mg (40%). Further elution then gave the parent alcohol **18**; yield 116 mg (17%). The deoxy derivative **17** was characterized by its n.m.r. spectrum and by conversion into the crystalline derivative **21**; these criteria established that the product was identical to that obtained by photolysis of the dimethylthiocarbamate **16**.

Under the same reaction conditions, methyl 2-*O*-(dimethylthiocarbamoyl)-3,4-*O*-isopropylidene-β-L-arabinopyranoside[13] **(16)** did not react with tributylstannane. Prolongation of the reaction time or the addition of azobis(isobutanonitrile) did not promote reaction, nor did irradiation with light of wavelength 254 nm. In all of these experiments, essentially all of the starting material **16** was recovered.

Conversion of **17** *into 2-deoxy*-L-erythro-*pentose* **(20)** *and its aniline derivative* **21**. — A solution of **17** (283 mg) in 40% aqueous acetic acid (7 ml) was boiled for 0.5 h under reflux, and the solution was evaporated to give compound **20** as a colorless syrup; yield 150 mg (72%). A solution of **20** (100 mg) in ethanol (5 ml) containing freshly distilled aniline (100 mg) was boiled for 2 h under reflux. The solution was cooled, whereupon the aniline derivative **21** crystallized slowly. The crude material was recrystallized from ethanol: yield 64 mg (41%), m.p. 161–163°, $[\alpha]_D^{20}$ −20 (*c* 0.35, ethanol; unchanged during 24 h); X-ray powder diffraction data: 10.61 vs (1), 5.24 s (2), 4.72 s, 4.39 s (3), 3.87 m, and 3.25 w.

For the D enantiomer of compound **21**, the following constants have been recorded: m.p.[14] 163–164° and $[\alpha]_D^{20}$ +19.5° (*c* 0.21, ethanol)[32]. The particular tautomeric form adopted by **21** was not established in this work. A product having m.p. 172–173° and showing upward mutarotation to −6.6° in methanol was prepared by Stacey *et al.*[33] from 2-deoxy-L-*erythro*-pentose and aniline.

REFERENCES

1 R. H. Bell, D. Horton, and D. M. Williams, *Chem. Commun.*, (1968) 323–324.
2 S. Hanessian, *Adv. Carbohydr. Chem.*, 21 (1966) 143–207.
3 D. Horton and W. Weckerle, *Carbohydr. Res.*, 44 (1975) 227–240.
4 D. Horton, *Pure Appl. Chem.*, 12 (1975) 301–325.
5 S. Umezawa, *Adv. Carbohydr. Chem. Biochem.*, 30 (1974) 111–182; S. Hanessian and T. H. Haskell, in W. Pigman and D. Horton (Eds.), *The Carbohydrates, Chemistry and Biochemistry*, Vol. IIA, Academic Press, New York, 1970, Chap. 31.
6 D. Horton and M. H. Meshreki, *Carbohydr. Res.*, 40 (1975) 345–352.
7 D. Horton and D. H. Hutson, *Adv. Carbohydr. Chem.*, 18 (1963) 123–199; J. D. Wander and D. Horton, *Adv. Carbohydr. Chem. Biochem.*, 32 (1976) 16–123.

8 H. G. FLETCHER, JR., AND N. K. RICHTMYER, *Adv. Carbohydr. Chem.*, 5 (1950) 1–28.
9 D. HORTON AND J. S. JEWELL, *J. Org. Chem.*, 31 (1966) 509–513.
10 D. HORTON AND M. SAKATA, *Carbohydr. Res.*, 48 (1976) 41–63.
11 K. FREUDENBERG AND A. WOLF, *Ber.*, 60 (1927) 232–238.
12 M. ČERNY AND J. PACÁK, *Collect. Czech. Chem. Commun.*, 21 (1956) 1003–1006.
13 D. HORTON AND H. S. PRIHAR, *Carbohydr. Res.*, 4 (1967) 115–125.
14 M. L. WOLFROM AND A. B. FOSTER, *J. Am. Chem. Soc.*, 78 (1956) 1399–1403.
15 M. S. NEWMAN AND H. A. KARNES, *J. Org. Chem.*, 31 (1966) 3980–3984.
16 H. S. PRIHAR, M. S. THESIS (D. HORTON, preceptor), The Ohio State University, 1967.
17 D. M. BROWN AND G. H. JONES, *J. Chem. Soc., C*, (1967) 252–256.
18 D. H. R. BARTON AND S. W. MCCOMBIE, *J. Chem. Soc. Perkin Trans. 1*, (1975) 1574–1585.
19 K. FREUDENBERG AND K. RASCHIG, *Ber.*, 60 (1927) 1633–1636.
20 C. CONE AND L. HOUGH, *Carbohydr. Res.*, 1 (1965) 1–9.
21 O. T. SCHMIDT, *Methods Carbohydr. Chem.*, 2 (1963) 324–325.
22 D. HORTON, M. NAKADATE, AND J. M. J. TRONCHET, *Carbohydr. Res.*, 7 (1968) 56–65.
23 A. E. KNAUF, R. M. HANN, AND C. S. HUDSON, *J. Am. Chem. Soc.*, 63 (1941) 1447–1451.
24 D. HORTON AND J. S. JEWELL, *Carbohydr. Res.*, 2 (1966) 251–260.
25 W. L. GLEN, G. S. MYERS, AND G. A. GRANT, *J. Chem. Soc.*, (1951) 2568–2572.
26 E. J. HEDGLEY, W. G. OVEREND, AND R. A. C. RENNIE, *J. Chem. Soc.*, (1963) 4701–4711.
27 M. L. WOLFROM, J. BERNSMANN, AND D. HORTON, *J. Org. Chem.*, 27 (1962) 4505–4509.
28 B. COXON AND L. HOUGH, *J. Chem. Soc.*, (1961) 1643–1549.
29 W. W. BINKLEY AND R. W. BINKLEY, *Carbohydr. Res.*, 11 (1969) 1–8.
30 D. HORTON, J. M. TARELLI, AND J. D. WANDER, *Carbohydr. Res.*, 23 (1972) 440–446.
31 P. KOLL, R.-W. RENNECKE, AND K. HEYNS, *Chem. Ber.*, 109 (1976) 2537–2541.
32 R. E. DERIAZ, W. G. OVEREND, M. STACEY, E. G. TEECE, AND L. F. WIGGINS, *J. Chem. Soc.*, (1949) 1879–1883.
33 K. BUTLER, S. LALAND, W. G. OVEREND, AND M. STACEY, *J. Chem. Soc.*, (1950) 1433–1439.