THE PREPARATION OF 4,6-O-BENZYLIDENE-D-GLUCAL AND THE REACTION OF METHYLLITHIUM WITH METHYL 2,3-ANHYDRO-4,6-O-BENZYLIDENE-α-D-ALLOPYRANOSIDE

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ABSTRACT

4,6-O-Benzylidene-D-glucal has been prepared by the reaction of benzaldehyde with D-glucal. The reaction of commercial methyllithium with methyl 2,3-anhydro-4,6-O-benzylidene- α -D-allopyranoside produces the C₂-methylated 1,2-unsaturated compound 4,6-O-benzylidene-1,2-didehydro-1,2-dideoxy-2-methyl-D-*ribo*-hexopyranose. Their structures have been proven by first-order analyses of their nuclear magnetic resonance spectra.

INTRODUCTION

4,6-O-Benzylidene-1,2-didehydro-1,2-dideoxy-D-*arabino*-hexopyranose (4,6-O-benzylidene-D-glucal, I) and 4,6-O-benzylidene-1,2-didehydro-1,2-dideoxy-D-*ribo*-hexopyranose (4,6-O-benzylidene-D-allal, II) were required as reference compounds for some work in progress in our laboratories.



Compound II has been prepared recently by the reaction of methyllithium with methyl 2,3-anhydro-4,6-O-benzylidene- α -D-allopyranoside (1). However, to our knowledge, no report exists describing the formation of compound I. This paper shows a successful preparation of I and, as well, our results of a reexamination of the reaction of methyllithium with methyl 2,3-anhydro-4,6-O-benzylidene- α -D-allopyranoside.

RESULTS AND DISCUSSION

4,6-O-Benzylidene-D-glucal(I)

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The reaction of freshly distilled benzaldehyde with D-glucal in the presence of anhydrous zinc chloride and anhydrous sodium sulfate gave I in a 30% yield (Reaction Scheme 1). The following evidence supported the structure assigned.

The infrared spectrum in CHCl₃ showed a rather narrow band at 3 590 cm⁻¹ (OH), and a sharp, intense band at 1 645 cm⁻¹. The latter agrees with the position (\sim 1 650 cm⁻¹) and intensity (strong) of the absorption band that is found generally for glycals and which is

caused by their vinyl ether structural feature, -C - C = C - O - (2). The infrared spec-

trum in Nujol showed two broad overlapping bands with maxima at 3 190 cm⁻¹ and ¹Postdoctorate Fellow.

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Reaction Scheme 1.

3 290 cm⁻¹ (OH), a sharp, intense band at 1 650 cm⁻¹ (-C = C = O), and two sharp

bands at 697 cm⁻¹ and 747 cm⁻¹ characteristic of the 4,6-O-benzylidene aromatic group (3).

Integration of the 60 Mc.p.s. nuclear magnetic resonance (n.m.r.) spectrum in CDCl₃ gave a ratio of aromatic protons to total protons of 5 to 14. The H_1 and H_2 signals appeared as an AB spectrum consisting of a pair of doublets centered at τ 3.67 and τ 5.27 ($J_{1,2} = 6$ c.p.s.) and both split by the allylic H₃ ($J_{1,3} = 1.8$ c.p.s. and $J_{2,3} = 2.0$ c.p.s.). The aromatic protons appeared as a multiplet between τ 2.35 and τ 2.83. The benzylidene proton signal was a sharp singlet at τ 4.43, and the OH proton gave a broad "singlet" at τ 7.32 (half width, 6 c.p.s.). The remaining proton signals appeared as a complicated multiplet between τ 5.4 and τ 6.3. In pyridine, the n.m.r. spectrum at 60 Mc.p.s. (Fig. 1) gave a clearly separated signal for the H_3 proton centered at τ 5.23 (multiplet), and signals for the H_1 and H_2 quartets at τ 3.58 and τ 4.98 (Table I). At 100 Mc.p.s., the H_3 signal was clearly resolved into a pair of triplets each showing additional small splitting caused by long-range coupling.² Double irradiation definitely showed that this proton was coupled to both H_1 and H₂, and thus identified it as H₃. The spectrum (Fig. 1) was amenable to first-order analysis³ and gave the observed chemical shifts and coupling constants shown in Table I. The large values of $J_{3,4}$ (7.5 c.p.s.) and $J_{4,5}$ (~9.0 c.p.s.) support the *trans* diaxial arrangement of the protons on C_3 and C_4 as well as the half-chair H1 structure (4) shown in I.

^{2"} Virtual coupling" (J. I. Musher and E. J. Corey, Tetrahedron, 18, 791 (1962)) with C_5H may be responsible for the multiplicity of the signal for H_3 beyond that of a pair of triplets.

for the multiplicity of the signal for H_3 beyond that of a pair of triplets. ³Although first-order analysis is generally not recommended unless the ratio of the chemical shift difference (δ) to the coupling constant (J) is >6 (E. D. Beker, J. Chem. Educ., 42, 591 (1965)), a number of papers have appeared in which reasonable values of couplings and chemical shifts have been extracted by using first-order analysis even though in some cases $\delta/J < 6$ (D. Horton and W. N. Turner, J. Org. Chem., 30, 3387 (1965); R. J. Abraham, K. A. McLauchlan, L. D. Hall, and L. Hough, Chem. Ind. London, 213 (1962); R. J. Ferrier, W. G. Overend, and G. H. Sankey, J. Chem. Soc., 2830 (1965); L. D. Hall, Advan. Carbohydrate Chem., 19, 58 (1964)). In the present work, the configuration of the molecules is known. The similarities in the structures of all six molecules, and recognition of repetitive patterns of signals for such key positions as H_5 , H_{5e} , and H_{5a} , along with a comparison of the multiplets with those expected, enabled us to pick out a unique arrangement in each case which agreed with the structure. The general agreement in the first-order analysis among the six spectra led us to believe that this approach was reasonably sound.

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FIG. 1. Nuclear magnetic resonance spectrum at 60 Mc.p.s. of 4,6-O-benzylidene-1,2-didehydro-1,2dideoxy-*n*-*arabino*-hexopyranose (1) in pyridine. Inset, 100 Mc.p.s. spectrum in pyridine. F16. 2. Nuclear magnetic resonance spectrum at 60 Mc.p.s. of 3-O-acetyl-4,6-O-benzylidene-1,2-didehydro-1,2-dideoxy-D-arabino-hexopyranose (III) in pyridine. Inset, 100 Mc.p.s. spectrum in pyridine.

Acetylation of I gave III, whose infrared spectrum in Nujol showed no absorption for

OH. Strong bands appeared at 1.652 cm^{-1} (-C-C=C-O-) and 1.742 cm^{-1} (C=O).

The presence of the 4,6-O-benzylidene group was indicated by bands at 698 cm^{-1} and 753cm⁻¹. Double irradiation was used to locate the signals for specific protons in the 100 Mc.p.s. spectrum of III in pyridine (Fig. 2). A first-order analysis was possible and gave the observed coupling constants and chemical shifts shown in Table I. The large values of

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					НО	~	1	7.47 s	
					C ₂ —CH ₃	I	I		ļ.
					Acetyl CH3		8.03 s	i	7.95s
		lexopyranoses		(r)	Benzylidene	4.27 s	4.25s	4.41 s	4.42 s
		aturated h		nethylsilane	H 6a	6.15 t	6.14 t	6.20 t	6.18t
		ul 1,2-uns H	H	ed to tetrai	${ m H}_{66}$	5.60 q	5.61 q	5.57 q	5, 53 q
		for severa		shift*referr	l-í s	5.98 sx	5.94 sx	5.83 sx	5.80 sx
		TABLE ared data C,H ₅ -C		Chemical	١I،	5.85 q	5.75q	6.23q	6.05 q
		and infr	х = Ж		H ₃	5.23 s	4.21s	5.81 q	4.57 q
		ic resonance			H_{2}	4.98 q	5.12 q	5.05 t	5.01 t
		lear magneti			Н	3.58 q	3.50 q	3.62 d	3.54 q
n georgeneter 1997 - Alter Maria		Nuc			Solvent	Pyridine	Pyridine	CDCI3	CDCI3
			-		×	I R'= R''= H R'''= OH	III $\mathbf{R}' = \mathbf{R}'' = \mathbf{H}$ $\mathbf{R}''' = \mathbf{CH}_{J} - \mathbf{C} - \mathbf{O} - \mathbf{C}$	0 II R'=R'''=H R''=OH	$IX R' = R''' = H$ $R'' = CH_{s} - C - O - H$

7.48s

ł

 $\begin{array}{l} 8.30\,q \\ J_1 (CH_3 = 1.5\,c.p.s. \\ J_3 (CH_3 = 0.3\,c.p.s. \\ 8.38\,d \\ J_1 (CH_3 = 1.5\,c.p.s. \end{array}$

7.92

4.48s

6.24t

5.58q

5.98 sx

6.12 q

4.48 d

I

3.75 d $J_{1,CH_3} = 1.5 c.p.s.$

CDC13

V R'=CH₃ R"=OH R"=H VI R'=CH₃ R"=CH₃ C O

4.44s

6.26t

5.59 q

5.94 sx

6.28 q

5.99 d

1

3.82 d

CDC13

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TABLE I (Concluded)

Infrared absorption† (cm⁻¹)

				C	upling con	stants (c.p.	.s.)				Cethec	
х	Solvent	J _{1,2}	J _{1,3}	J2,3	J 3,4	J4,6	J 6, 60	J 5, 6a	J ée, éa	c=c	—0 н	НО
I $R'=R''=H$	Pyridine	6.0	1.8	2.0	7.5	9.0	4.0	9.0	0.6	1650S	697, 747	3 190, 3 290
$\begin{array}{c} \mathbf{K}^{\prime\prime\prime} = \mathbf{OH} \\ \mathbf{III} \ \mathbf{R}^{\prime} = \mathbf{R}^{\prime\prime\prime} = \mathbf{H} \\ \mathbf{R}^{\prime\prime\prime} = \mathbf{CH}_{3} - \mathbf{C}_{-} \mathbf{O}_{-} \end{array}$	Pyridine	6.0	1.8	2.0	7.5	0.6	4.0	0.0	0.0	1 652 S	698, 753	1
 0 II R'=R'''=H	CDC1 ³	6.0	0~	6.0	3.5	9.5	4.5	9.5	10.0	1 640 S	705, 753	3 170
R''=OH IX R'=R'''=H $n''-CU = C O$	CDC13	6.0	0.5	5.7	3.5	9.5	4.4	9.5	9.5	1 638 S	697, 763	
			:									011
V R'=CH ₃ R''=OH	CDCI ²	I	1.5	I	3.5	9.5	4.5	9.5	9.5	1 670 S	098, 753	000 8
R‴=Н VI R'=СН₃ R″=СЫС	CDCI ₁	I	ź	ļ	3.0	9.5	3.0	9.5	9.5	1 668 S	755, 697	Ī
0=0												
R'''=H												
<pre>*s = singlet; d = doublet; t tIn Nujol; calibrated agains</pre>	= triplet; q = quar t polystyrene, 1 601	tet; sx = cm^{-1} ; S	sextet. ≕ strong.									

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 $J_{3,4}$ (7.5 c.p.s.) and $J_{4,5}$ (9.0 c.p.s.) are in agreement with the *trans* diaxial arrangement of the protons attached to C₃, C₄, and C₅. The signal for the proton on C₃, upon acetylation of the C₃—OH group, was shifted markedly downfield (from τ 5.3 (Fig. 1) to τ 4.21 (Fig. 2)), providing proof that the OH group at C₃ was unsubstituted in II and hence that the benzylidene group involved the hydroxyl functions on C₄ and C₆.

The above information leaves no doubt that 4,6-*O*-benzylidene-D-glucal has been formed by the reaction of D-glucal with benzaldehyde under our conditions.

The Reaction of Methyllithium with 2,3-Anhydro-4,6-O-benzylidene- α -D-allopyranoside

The reaction of commercial methyllithium⁴ with methyl 2,3-anhydro-4,6-O-benzylidene- α -D-allopyranoside (IV) according to the directions described in the literature (1), or by adding the methyllithium to an ether solution of IV directly, gave a compound whose analytical data showed it to be 4,6-O-benzylidene-1,2-didehydro-1,2-dideoxy-2-methyl-D*ribo*-hexopyranose (V) rather than II (Reaction Scheme 2).



REACTION SCHEME 2.

The infrared spectrum in Nujol showed a broad band at 3550 cm^{-1} (OH), a sharp, intense band at 1670 cm^{-1} (vinyl ether), and bands at 698 cm^{-1} and 753 cm^{-1} (benzylidene). The n.m.r. spectrum in CDCl₃, with the aid of spin decoupling and resolution of the signals at 100 Mc.p.s., was amenable to complete first-order analysis (Fig. 3). The observed chemical shifts and coupling constants are listed in Table I. The coupling constants $J_{3,4}$ (3.5 c.p.s.) and $J_{4,5}$ (9.5 c.p.s.) are in agreement with the half-chair H1 structure V.

Acetylation of V gave VI, whose infrared spectrum showed no absorption in the OH region; strong absorption occurred at 1.742 cm^{-1} (C=O) and 1.668 cm^{-1} (vinyl ether) as

⁴Obtained from the Lithium Corporation of America via Alfa Inorganics Inc., 8 Congress Street, Beverly, Massachusetts, U.S.A.

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well as at 755 cm⁻¹ and 697 cm⁻¹ (benzylidene). First-order analysis of the n.m.r. spectrum (Fig. 4) in CDCl₃ gave coupling constants and chemical shifts (Table I) in complete agreement with the half-chair H1 structure VI. Acetylation of C₃OH shifted the C₃H signal markedly from τ 5.99 to τ 4.48.



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FIG. 3. Nuclear magnetic resonance spectrum at 60 Mc.p.s. of 4,6-O-benzylidene-1,2-didehydro-1,2-dideoxy-2-methyl-D-*ribo*-hexopyranose (V) in CDCl₃. Inset, 100 Mc.p.s. spectrum in CDCl₃. FIG. 4. Nuclear magnetic resonance spectrum at 60 Mc.p.s. of 3-O-acetyl-4,6-O-benzylidene-1,2-dide-hydro-1,2-dideoxy-2-methyl-D-*ribo*-hexopyranose (VI) in CDCl₃. Inset, 100 Mc.p.s. spectrum in CDCl₃.

1

CH₃

8.0

TMS

The formation of V rather than II and the fate of the rest of IV are under investigation and will be reported upon later.

Compound II could be obtained by the reaction of methyl2,3-anhydro-4,6-O-benzylidene- α -D-allopyranoside (IV) with methyllithium prepared according to the directions of Feast *et al.* (1), or by the reaction of commercial methyllithium with the iodohydrin VII. The iodohydrin could be prepared according to published directions (5) by the reaction of ethylmagnesium iodide with methyl 2,3-anhydro-4,6-O-benzylidene- α -D-allopyranoside (IV), or more conveniently by treatment of an ether solution of IV with lithium iodide in fourfold excess to force the equilibrium towards VII. No doubt, the conversion of VII into II involved lithium-iodine exchange to produce the carbanion VIII, which would eliminate the methoxide anion to form the α , β -unsaturated ether II (Reaction Scheme 3).⁵ The formation of II by the reaction of the 2,3-anhydroallopyranoside IV with methyllithium, as found by Feast *et al.* (1), will be discussed in an early communication by R. U. Lemieux of our department.



First-order analysis of the n.m.r. spectra of II (Fig. 5) and its acetylated derivative IX (Fig. 6) gave the coupling constants and chemical shifts listed in Table I. These, along with the infrared spectra, corroborated the structures II and IX. In both cases, the coupling constants $J_{3,4}$ (3.5 c.p.s. and 3.0 c.p.s.) and $J_{4,5}$ (9.5 c.p.s.) support the "gauche" arrangement of H₃ and H₄ and the *trans* diaxial configuration of H₄ and H₅.

⁵The referee pointed out that IX might be obtained via a concerted reaction such as



rather than by stepwise formation of the carbanion intermediate.

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FIG. 5. Nuclear magnetic resonance spectrum at 60 Mc.p.s. of 4,6-O-benzylidene-1,2-didehydro-1,2-dideoxy-D-ribo-hexopyranose (II) in CDCl₃. Inset, 100 Mc.p.s. spectrum in CDCl₃. FIG. 6. Nuclear magnetic resonance spectrum at 60 Mc.p.s. of 3-O-acetyl-4,6-O-benzylidene-1,2-dide-hydro-1,2-dideoxy-D-ribo-hexopyranose (IX) in CDCl₃. Inset, 100 Mc.p.s. spectrum in CDCl₃.

It is interesting that in compounds I and III, where H_3 and H_4 are *trans* diaxial, the signal for H_4 is downfield from that for H_5 , whereas in compounds II and IX as well as V and VI, where H₃ is "gauche" to H₄, the H₄ signal lies upfield from that for H₅. This observation has been of some utility in locating both the H₄ and H₅ signals in several compounds to be reported upon later.

EXPERIMENTAL

Melting points are uncorrected. Infrared spectra were obtained with a model 421 Perkin-Elmer spectrometer. Nuclear magnetic resonance spectra were obtained with Varian Associates A60 and HR100 spectrometers. Elemental analyses were performed by Miss Darlene Roberts, Department of Chemistry, University of Alberta, Edmonton. Rotations were found with a Perkin-Elmer model 141 polarimeter.

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D-Glucal

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The following modification of the published procedure (6) gave better results.

Pure tri-O-acetyl-D-glucal (5 g) (7) was stirred at room temperature for 18 h with anhydrous sodium carbonate (5 g) in dry methanol (75 ml). The mixture was filtered and the solid residue washed with dry methanol. The combined washings and filtrate were freed from methanol and the residue was extracted with hot ethyl acetate. When this extract was concentrated under reduced pressure and allowed to stand in the refrigerator, 2.0 g (70%) of D-glucal slowly separated as crystals. These were pure enough for the next reaction, m.p. $57-59^{\circ}$ (lit. m.p. $57-59^{\circ}$ (6)). A mixed melting point gave no depression.

4,6-O-Benzylidene-D-glucal (I)

A mixture of pure p-glucal (1 g), benzaldehyde freshly distilled under nitrogen (2 ml), freshly fused zinc chloride (600 mg), and anhydrous sodium sulfate (heated to drive off residual moisture) (500 mg) was stirred for 12 h at room temperature under nitrogen. (The presence of the dry sodium sulfate was thought to be necessary to remove water which might otherwise react with the glucal double bond. Later experiments showed that its absence made little difference in the yield of product.) The solid materials, except sodium sulfate, slowly dissolved, giving a pale-green solution. An aqueous solution of sodium carbonate (10%, 10 ml) was stirred into the mixture, which then stood for 10 min. The white precipitate of zinc hydroxide was removed by filtration, and washed with water and then with ether. The organic layer was separated from the combined ether solutions were washed twice with water and then dried (Na₂SO₄). The ether was removed and the residue was freed from benzaldehyde by passage of the material through a column of neutral alumina (grade II, 15 g) and elution of the column with *n*-hexane until the eluent was free from benzaldehyde. The 4,6-O-benzylidenep-glucal was removed from the column with diethyl ether. Evaporation of the ether gave a colorless solid, m.p. 136–138°, yield 31%. Crystallization from ether-hexane raised the melting point to 142–143°; $[\alpha]_p^{27}$ -20° (c, 1 in CHCl₃).

Anal. Calcd. for C₁₃H₁₄O₄: C, 66.70; H, 6.02. Found: C, 66.72; H, 5.77.

3-O-Acetyl-4,6-O-benzylidene-D-glucal (III)

To 4,6-O-benzylidene-D-glucal (120 mg) in dry pyridine (2 ml) was added acetic anhydride (0.5 ml), and the mixture was allowed to stand at room temperature for 12 h. It was then poured into ice water, from which, after 1 h, was obtained a solid (100 mg, 70%). The solid was separated, washed with water, and crystallized from acetone-hexane, m.p. 136–137°, $[\alpha]_{0}^{27}$ –85° (c, 1 in CHCl₃).

Anal. Calcd. for C15H16O5: C, 65.21; H, 5.84. Found: C, 65.19; H, 5.50.

4,6-O-Benzylidene-1,2-didehydro-1,2-dideoxy-2-methyl-D-ribo-hexopyranose (V)

To a suspension of 2 g of methyl 2,3-anhydro-4,6-O-benzylidene- α -D-allopyranoside (IV) (8) in anhydrous ether (50 ml) was added an ether solution of methyllithium (100 ml of a 4.5% solution, Lithium Corporation of America) at 0 to 5° under a nitrogen atmosphere. Ten minutes later the mixture was refluxed for a period of 8 h, during which time the alloside slowly dissolved. The yellow mixture was poured slowly, with stirring, into ice water (50 ml). The ether layer was separated and the aqueous portion extracted four times with ether. The combined ether layers were washed with water, dried (Na₂SO₄), and freed from solvent. The residual syrup, upon trituration with hexane, gave a crystalline solid, m.p. 120–122° (400 mg, 22%). Crystallization from ether-hexane gave 370 mg (20%) of material melting at 126–127°; $[\alpha]_{\rm p}^{\rm gr}$ +175° (c, 1 in CHCl₃). Anal. Calcd. for C₁₄H₁₆O₄: C, 67.73; H, 6.50. Found: C, 67.52; H, 6.25.

3-O-Acetyl-4,6-O-benzylidene-1,2-didehydro-1,2-dideoxy-2-methyl-D-ribo-hexopyranose (VI)

Acetic anhydride (0.5 ml) was added to a solution of V (120 mg) in dry pyridine (2 ml). The mixture was left overnight at room temperature, and then poured into ice water. After 1 h, the crystalline product was separated by filtration, washed with water, and air-dried (120 mg, 85%), m.p. 70–72°. When crystallized from hexane it melted at 74–75° (100 mg, 76%); $[a]p^{27}$ +185° (c, 1 in CHCl₃).

Anal. Calcd. for C16H18O5: C, 66.20; H, 6.25. Found: C, 66.42; H, 6.16.

Methyl 4,6-O-Benzylidene-2-deoxy-2-iodo-a-D-altropyranoside (VII)

A mixture of methyl 2,3-anhydro-4,6-O-benzylidene- α -D-allopyranoside (IV) (1.32 g) and dry lithium iodide (2.6 g) in anhydrous ether (80 ml) was refluxed for 1 h. The clear solution was cooled, washed with water until neutral to litmus, and then dried (Na₂SO₄). Removal of the ether gave a syrup which crystallized on trituration with hexane (1.5 g, 76%), m.p. 102–104°. Recrystallization from ether-hexane gave a melting point of 104–105° (lit, m.p. 105–106° (5)). A mixed melting point was undepressed.

Attempted Methylation of the 2-Iodoaltroside VII

To a solution of VII (1.96 g) in 1,2-dimethoxyethane (40 ml, distilled from potassium metal) and methyl iodide (5 g) was added sodium hydride (0.5 g, obtained as a 55% dispersion in mineral oil, from which the mineral oil was first removed with dry hexane). A white solid appeared immediately after the addition of the first portion of the sodium hydride. After the addition of the hydride, the mixture was stirred for 2 h at room temperature and filtered; then the residue (1 g) was washed with water. Crystallization from chloroformether gave methyl 2,3-anhydro-4,6-O-benzylidene- α -D-allopyranoside, m.p. 199–200°. A further quantity was

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recovered from the filtrate, total yield 89%. A mixed melting point with an authentic sample (8) was undepressed. No methylated material was obtained.

4,6-O-Benzylidene-1,2-didehydro-1,2-dideoxy-D-ribo-hexopyranose (4,6-O-Benzylidene-D-allal, II)

Method A

To a stirred solution of the 2-iodoaltroside VII (1.95 g) in dry ether (50 ml), cooled in an ice bath, was added moderately slowly and under nitrogen a solution of n-butyllithium (10 ml of a 15% solution). The solution slowly became cloudy. It was refluxed for 2 h, cooled, and poured into ice water. The ether layer was separated and the aqueous portion extracted with ether. The combined ether solutions were washed with water, dried (Na₂SO₄), and freed from ether. The light-yellow syrupy residue crystallized slowly as fine long needles. Recrystallization from ether-hexane gave a melting point of 84-85°; yield 1.1 g (93%). A mixed melting point with an authentic sample (1) was undepressed.

When methyllithium replaced n-butyllithium, similar results were obtained.

Method B

2.

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A mixture of methyl 2,3-anhydro-4,6-O-benzylidene-a-D-allopyranoside (IV) (3.5 g) and dry lithium iodide (6 g) in anhydrous ether (250 ml) was stirred and refluxed under nitrogen for 1 h. The clear, light-yellow solution was cooled in an ice bath; to this was added an ether solution of *n*-butyllithium (40 ml of a 15%) solution) at a moderate rate. After the addition, the cloudy solution was refluxed for 2 h, cooled, and poured into ice water. The ether layer was separated and the aqueous portion extracted with ether. The combined organic layers were washed with water, dried (Na₂SO₄), and freed from solvent. The semisolid residue (3.0 g, 94%) was crystallized from ether-hexane, m.p. 84-85°, yield 2.85 g (89%).

Similar results were obtained when methyllithium was added in place of *n*-butyllithium.

Example of the Method for the First-Order Analysis (with Compound IX)

The signal at low field (τ 3.54) is no doubt caused by H₁. The signal for H₃ was located by its change of position from τ 5.81 (for compound II) to τ 4.57 on acelulation of 11 to produce IX. The signal for H₂ must then be that at $\tau 5.01$.

Irradiation at τ 3.54 (H₁) converted the triplet at τ 5.01 (H₂) into a doublet ($J_{2,3} = 5.7$ c.p.s.). Irradiation at τ 4.57 (H₃) changed the triplet at τ 5.01 (H₂) to a doublet ($J_{1,2} = 6.0$ c.p.s.). Irradiation at τ 4.57 converted the quartet at τ 6.05 into a doublet with a coupling of 9.5 c.p.s. ($J_{4,5}$), eliminating the two small couplings of 3.5 c.p.s. $(J_{3,4})$ and thus indicating that the signal for H₄ was at τ 6.05 and that H₃ and H₄ have an equatorial-axial (gauche) steric relationship. The large coupling of 9.5 c.p.s. is no doubt caused by coupling of H₄ with H₅, thus indicating that these protons are *trans* diaxial.

The quartet at τ 5.53 is most likely that for H_{6c} since it agrees with the expected quartet for H_{6c}, and the triplet at τ 6.18 would be that expected for H_{6a} if this proton were coupled equally to H_{6e} and H₅. On this assumption, H₅ must be centered at τ 5.80 with $J_{4,5} = 9.5$ c.p.s. (as indicated above) and $J_{5,6a} = 9.5$ c.p.s., giving a triplet which, in turn, is split by coupling of H5 with H6e by 4.5 c.p.s. caused by their gauche arrangement.

Irradiation at τ 5.53 (H_{6e}) caused a strong collapse at both the τ 5.80 and τ 6.18 regions.

With the aid of this information, and the use of similar reasoning along with a careful comparison of all of the spectra, the HR100 spectra of the remaining compounds were analyzed to give multiplets which agreed reasonably well with those expected.

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