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Note

Acetal migration during Koenigs-Knorr reactions: isolation of 3-*O*- and 6-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl) derivatives of 1,2:5,6- and 1,2:3,5-di-*O*-isopropylidene-α-D-glucofuranose

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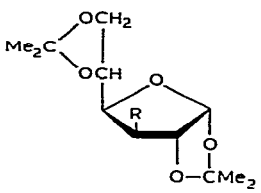
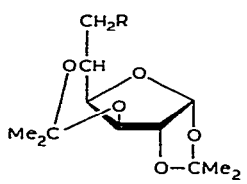
Of the several syntheses[1–11] of laminaribiose (3-*O*-β-D-glucopyranosyl-D-glucose), most used 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**1**) as the aglycon. Low yields were a common feature of these reactions, probably because of acetal migration, which can take place under the conditions of the Koenigs–Knorr reaction[3,5,8,12]. The structure of the product of acetal migration was postulated[5,8] as

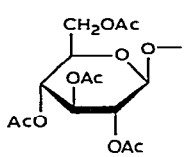


1 R = OH
2 R = R′
4 R = OTs



3 R = R′
5 R = OH
6 R = OTs
7 R = OAc
8 R = H

R′ =



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1,2:3,5-di-*O*-isopropylidene-6-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-α-D-glucofuranose (**3**), for which some data were given recently[11]. Acetal migrations have been observed in other cases of oligosaccharide synthesis[12–13], but no intermediates were isolated.

Condensation of tetra-*O*-acetyl-α-D-glucopyranosyl bromide (1.2 mol) and **1** (1 mol) in benzene–nitromethane (1:1) in the presence of $Hg(CN)_2$ (1.2 mol) at 45° was complete after 4 h, and a mixture of the disaccharide derivatives **2** and **3** was obtained which was fractionated by short-column chromatography. The ratio of **2** and **3** depended upon the reaction temperature and was 1:1 at 45° and 2:3 at 65°. The combined yield of **2** and **3** was 60–65%.

Compound **2** was 1,2:5,6-di-*O*-isopropylidene-3-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-α-D-glucofuranose previously obtained[5,6] by the orthoester method. The ^{13}C-n.m.r. spectrum of **2** accorded well with that[14] of **1**. Glucosylation at position 3 of **1** leads to a shift of 8.2 p.p.m. for the signal for C-3. The structure of **2** was verified by its conversion into laminaribiose. The ^{13}C-n.m.r. spectrum of the 3-*O*-tosyl derivative (**4**) of **1** was also obtained for purposes of comparison.

The ^{1}H- and ^{13}C-n.m.r. spectra of **3** revealed two isopropylidene groups, but the ^{13}C chemical shifts of the glucofuranosyl moiety did not agree with those of **1**. For the analysis of the spectrum of **3**, n.m.r. data for 1,2:3,5-di-*O*-isopropylidene-α-D-glucofuranose[15] (**5**), and the 6-*O*-tosyl[15] (**6**), 6-*O*-acetyl[15] (**7**), and 6-deoxy derivatives[16] (**8**) were used. The assignment of the ^{13}C-spectra of **7** and **8** was based on $J_{C,H}$ values derived from high digital resolution (32 K) proton-coupled spectra.

For each compound, the signal for C-2 was a doublet of doublets (**8**; 6.31 and 3.59 Hz, $J_{C\text{-}2,H\text{-}2}$ 159.4 Hz) and that for C-3 was slightly broad, but without fine structure (**8**; $J_{C\text{-}3,H\text{-}3}$ 154.4 Hz). The absence of the additional splitting of the signals for C-4 and C-5 in the spectrum of **7** in comparison with the corresponding signals in **8** due to the protons of Me-5 proved their assignment (**8**; $J_{C\text{-}5,H\text{-}5}$ 145.4 Hz).

These data indicate **3** to be 1,2:3,5-di-*O*-isopropylidene-6-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-α-D-glucofuranose. Glucosylation at position 6 of **5** resulted in a shift of 6.6 p.p.m. for the C-6 signal. Saponification of **3** followed by mild hydrolysis with acid gave gentiobiose.

Dioxolane and dioxane types of isopropylidene rings are easily recognisable on the basis of the chemical shifts of the quaternary carbons (dioxolanes, 112.0–112.4 p.p.m.; dioxanes, 100.6–101.1 p.p.m.). Furthermore, the chemical shift of C-4 of **8** is high (85.0 p.p.m.), which may be explained by the γ-effect.

The acetal migration may be explained by the presence of $HgBr_2$ formed during the Koenigs–Knorr reaction. The equilibrium of **1** and **5** is shifted in favour of the latter, and HO-6 in **5** reacts more readily than does HO-3 in **1**.

During the reaction of **1** and PCl_5, acetal migration also occurs, and 6-chloro-6-deoxy-1,2:3,5-di-*O*-isopropylidene-α-D-glucofuranose is formed[17].

EXPERIMENTAL

Melting points (uncorrected) were determined with a Kofler apparatus. T.l.c. and column chromatography were performed on Kieselgel G; detection was effected in t.l.c. by charring with 50% sulphuric acid. G.l.c. was performed with a Hewlett–Packard 5830A instrument. Optical rotations were measured with a Perkin–Elmer 241 automatic polarimeter. ^{1}H- and ^{13}C-n.m.r. spectra were recorded with a Varian XL-100-15 F.T. spectrometer (25.16 MHz) under the MOS-E Disk Operation System.

*1,2:5,6-Di-*O*-isopropylidene-3-*O*-(2,3,4,6-tetra-*O*-acetyl-β-*D*-glucopyranosyl)-α-*D*-glucofuranose* (**2**) *and 1,2:3,5-di-*O*-isopropylidene-6-*O*-(2,3,4,6-tetra-*O*-acetyl-β-*D*-glucopyranosyl)-α-*D*-glucofuranose* (**3**). — A solution of **1** (6 g) in benzene (150 ml) and nitromethane (150 ml) was concentrated at atmospheric pressure to half volume, cooled to 45°, and stirred with $Hg(CN)_2$ (6.95 g) and tetra-*O*-acetyl-α-D-glucopyrano-

TABLE I

CHEMICAL SHIFTS (δ) FOR DI-*O*-ISOPROPYLIDENE-α-D-GLUCOFURANOSE DERIVATIVES IN $CDCl_3$

Carbon	*Compound*							
	1	**4**	**2**	**3**	**6**	**7**	**5**	**8**
C-1	104.5	105.2	105.1	106.5	106.5	106.6	106.5	106.4
$J_{C-1,H-1}$						(182.9)		(182)
C-2	85.0	83.5	83.0	84.2	84.1	84.2	84.3	84.4
C-3	73.1	82.2	81.3	75.2	75.1	75.2	75.3	75.0
C-4	80.9	80.0	80.6	79.2	78.8	79.6	79.2	85.0
C-5	72.2	72.0	72.3	71.6	70.3	70.3	72.8	68.0
C-6	66.0	67.1	66.3	70.2	69.9	64.6	63.6	19.6
C-7[a]	110.5	112.5	112.0	112.3	112.4	112.3	112.3	112.0
C-8[b]	107.8	109.1	108.6	101.0	101.1	101.1	101.0	100.6
$C(CH_3)_2$	26.0	26.7	26.9	27.3	27.2	27.3	27.2	27.3
	26.0	26.6	26.7	26.6	26.6	26.6	26.6	26.7
	25.2	25.0	25.4	24.2	23.8	24.0	24.2	24.2
	26.5	26.3	26.4	24.2	23.8	24.0	24.2	24.2
C-1′			99.4	101.3				
C-2′			72.9	72.1				
C-3′			73.1	73.1				
C-4′			68.6	68.9				
C-5′			71.6	71.8				
C-6′			62.0	62.2				
Ph		133.3			133.5			
		128.4			128.1			
		129.8			129.8			
		145.0			144.7			
Ac-Me			20.5	20.6		20.7		
			20.4					
Ph-Me		21.5			21.5			

[a]C-7 is the quaternary carbon atom of the 1,2-*O*-isopropylidene group. [b]C-8 is the quaternary carbon atom of the 5,6-*O*- and 3,5-*O*-isopropylidene groups, respectively.

syl bromide (11.34 g) for 4 h under anhydrous conditions. The mixture was filtered and concentrated, and a solution of the residue in dichloromethane (300 ml) was filtered, washed with 5% aqueous KI (3 × 50 ml) and water (3 × 50 ml), dried (Na_2SO_4), and concentrated. G.l.c. (10% UCW-982, 4-ft column, 275°) of the syrupy residue revealed two components [T 3.86 (**2**) and 5.04 min (**3**)]. The mixture of **2** and **3** was eluted from a column of Kieselgel G (450 g) with dichloromethane–ethyl acetate (4:1) to give, first, **3** (4.14 g, 30.5%), m.p. 104–105° (from ether–hexane), $[\alpha]_D$ +3° (c 1.58, chloroform); R_F 0.57 (dichloromethane–ethyl acetate, 4:1); lit.[11] $[\alpha]_D$ +4°.

Eluted second was **2** (3.50 g, 25.8%), m.p. 132–133°, $[\alpha]_D$ −20° (c 1.55, chloroform), R_F 0.45 (dichloromethane–ethyl acetate, 4:1); lit.[6] m.p. 132–134°, $[\alpha]_D$ −21° (c 2.5, chloroform).

The ^{13}C-n.m.r. data for **2** and **3** are given in Table I.

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