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Note

A convenient route to 6-functionalized derivatives of D-glucal

DUŠAN MILJKOVIĆ*, NADA VUKOJEVIĆ, DAMIR MEDAKOVIĆ,
Institute of Chemistry, Faculty of Sciences, University of Novi Sad, V. Vlahovića 2, 21000 Novi Sad (Yugoslavia)

AND GYULA BATTA
Department of Organic Chemistry, L. Kossuth University, Debrecen 4010 (Hungary)

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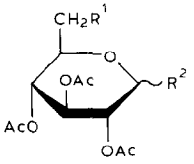
Two syntheses of 3,4-di-*O*-acetyl-1,5-anhydro-2-deoxy-6-*O*-*p*-toluenesulphonyl-D-*arabino*-hex-1-enitol (**9**) have been reported[1,2], starting from D-glucal and 1,2,3,4-tetra-*O*-acetyl-6-*O*-*p*-toluenesulphonyl-α-D-glucopyranose.

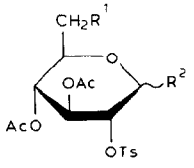
We now report a novel and simple procedure for the synthesis of two 6-functionalized derivatives of D-glucal, namely, 3,4-di-*O*-acetyl-1,5-anhydro-2-deoxy-6-*O*-*p*-toluenesulphonyl- (**9**) and 6-*S*-acetyl-6-thio-D-*arabino*-hex-1-enitol (**10**). The method involves two consecutive one-pot procedures.

The first one-pot procedure involves 6- and 2,6-di-tosylation of D-glucose (with 2 mol of tosyl chloride in dry pyridine at room temperature) followed by acetylation according to modified literature procedures[3–5]. The resulting mixture (1:3) of **1** and **5** was used for the second one-pot procedure, involving conventional conversion into the glucosyl bromides (**2** and **6**) and then treatment with zinc dust in aqueous acetic acid to give **9** (85%) as the sole product. The structure of **9** was confirmed by the ^{1}H- and ^{13}C-n.m.r. data (see Table I).

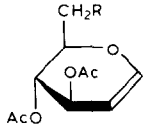
In another reaction sequence, the 1:3 mixture of **1** and **5** was treated with



1 R^1 = OTs, R^2 = OAc
2 R^1 = OTs, R^2 = Br(α)
3 R^1 = SAc, R^2 = OAc
4 R^1 = SAc, R^2 = Br(α)



5 R^1 = OTs, R^2 = OAc
6 R^1 = OTs, R^2 = Br(α)
7 R^1 = SAc, R^2 = OAc
8 R^1 = SAc, R^2 = Br(α)



9 R = OTs
10 R = SAc

*Author for correspondence.

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TABLE I

N.M.R. DATA FOR **9** AND **10**[a]

Compound	*^{1}H-N.m.r. data (δ in p.p.m., J in Hz)*									
	H-1	*H-2*	*H-3*	*H-4*	*H-5*	*H-6*	*H-6'*	*OAc*	*Me(OTs)*	*SAc*
9	6.35 dd $J_{1,2}$ 6 $J_{1,3}$ 1.25	4.82 dddd $J_{2,1}$ ~6 $J_{2,3}$ 3.5 $J_{2,4}$ ~1	5.27 m	5.13 t		←5.13–4.0→		2.05 s	2.47 s	
10	6.44 dd $J_{1,2}$ 6 $J_{1,3}$ 1.1	4.83 dd $J_{2,1}$ 6 $J_{2,3}$ 3.2	5.33 m $J_{3,2}$ 3.2	5.18 t $J_{4,3}$ 5.5 $J_{4,5}$ 7.5	4.18 ddd $J_{5,6}$ 6.5 $J_{5,6'}$ 5.0	3.32 dd	3.22 dd $J_{6,6'}$ 14	2.10 s 2.05 s		2.36
	^{13}C-N.m.r. data (δ in p.p.m.)									
	C-1	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*	*Me(OTs)*	*OAc*	*CO(OAc)*	*CO(SAc)*	*Me(SAc)*
9	145.10	98.91	66.60	67.05	73.24	66.44	21.45	20.71 20.49	169.96 169.18		
10	145.33	98.98	67.33	68.84	74.55	28.90 (SCH_2)		20.74 20.53	170.03 169.40	194.07	30.16

[a]In $CDCl_3$.

potassium thioacetate (*N,N*-dimethylformamide, room temperature, 24 h). The mixture of products (**3** and **7**) was then treated as above for **1** and **5**, to give **10** (87% after chromatography). The structure of **10** was confirmed by the ^{1}H- and ^{13}C-n.m.r. data (Table I).

EXPERIMENTAL

General procedures. — Melting points were not corrected. I.r. spectra were recorded for KBr pellets with a Perkin–Elmer 457 spectrophotometer. ^{1}H-N.m.r. and ^{13}C-n.m.r. spectra were recorded with a Bruker WP-200-SY instrument.

*3,4-Di-*O*-acetyl-1,5-anhydro-2-deoxy-6-*O*-p-toluenesulphonyl-*D*-arabino-hex-1-enitol* (**9**). — To a solution of D-glucose (10 g, 55 mmol) in dry pyridine (150 mL) at 0° was added tosyl chloride (21 g, 110 mmol). The mixture was left at 0° for 30 min, then at room temperature for 5 h. Acetic anhydride (50 mL) was added, and the mixture was left for 24 h at room temperature, then acidified with dilute HCl (300 mL, pH 2) at 0°. The products were extracted with chloroform, the extract was concentrated to an oil which was crystallized from ethanol to afford a 1:3 mixture (23.7 g, 76%) of **1** and **5**, m.p. 160–165°, $[\alpha]_D$ +101° (*c* 0.7, chloroform); ν_{max}^{KBr} 1760–1750, 1600, 1370, 1340, 1210, 1190, 1175, 1050–1000 cm^{-1}.

The mixture (10 g) of **1** and **5** was stirred with a solution of hydrogen bromide in acetic acid[6] (240 mL) for 24 h at room temperature and then poured onto crushed ice (1000 g). The mixture was neutralized with sodium hydrogencarbonate (at 0°), the crude glucosyl bromides were extracted quickly with dichloromethane (3 × 100 mL), and the combined extracts were washed with cold water, dried (Na_2SO_4), and concentrated to a syrupy mixture (8.5 g, 82%) of **2** and **6**; ν_{max}^{KBr} 1750, 1600, 1370, 1340, 1230, 1210, 1170, 1090–1000 cm^{-1}. Since **2** and **6** are unstable, they were used immediately.

To a solution of sodium acetate (40 g) in water (54 mL) and glacial acetic acid (40 mL) at −5° was added powdered Zn (20 g) with stirring followed by a solution of $CuSO_4 \cdot 5H_2O$ (2.2 g) in water (8 mL). The mixture was stirred until the blue colour disappeared (~30 min)[6].

A solution of the mixture (1.5 g) of **2** and **6** in glacial acetic acid (30 mL) was added to the above Zn–Cu suspension (at −5°), and the mixture was stirred for 3 h (at 0°), then filtered, and poured onto ice (150 g). The mixture was neutralized with sodium hydrogencarbonate and extracted with chloroform (3 × 30 mL), the combined extracts were dried (Na_2SO_4) and concentrated *in vacuo*, and the residue was crystallized from ether to afford **9** (0.86 g, 85%), m.p. 103–105°, $[\alpha]_D$ +14° (*c* 1, chloroform); lit.[2] m.p. 106–107°.

*3,4-Di-*O*-acetyl-6-*S*-acetyl-1,5-anhydro-2-deoxy-6-thio-*D*-arabino-hex-1-enitol* (**10**). — To a solution of the 1:3 mixture (2.22 g) of **1** and **5** in *N,N*-dimethylformamide (28 mL) was added potassium thioacetate (2.2 g, 10 mmol) with stirring. The resulting solution was left at room temperature for 24 h and then poured onto ice (100 g). Sodium chloride was added and the products were extracted with benzene–

light petroleum (1:1, 3 × 40 mL). The combined extracts were dried (Na_2SO_4) and concentrated. The residue (1.85 g) was crystallized from ethanol to give a mixture (1.3 g, 70.65%) of **3** and **7**, m.p. 105–106°; ν_{max}^{KBr} 1760–1750, 1695, 1600, 1670, 1230, 1190–1180, 1050–1000 cm^{-1}.

The 1:3 mixture (1 g) of **3** and **7** was converted into **10** via a mixture of **4** and **8** as described for preparation of **9**. Column chromatography on silica gel (4:1 benzene–ethyl acetate) of the product gave **10** (0.55 g, 87%), $[\alpha]_D$ +59° (*c* 1, chloroform); ν_{max}^{Nujol} 1740, 1690, 1650, 1370, 1240–1220 cm^{-1}.

Anal. Calc. for $C_{12}H_{16}O_6S$: C, 50.00; H, 5.50; S, 11.11. Found: C, 50.23; H, 5.39; S, 11.45.

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