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Note

A novel route to 2-deoxy-2-iodo-D-mannopyranose derivatives

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1,5-Anhydro-2-deoxy-D-hex-1-enitols are versatile synthons[1,2]. Various functional groups, such as chloro[3], fluoro[4–7], bromo[8], or iodo[9–11], may be introduced at position 2 by either direct or indirect addition of suitable agents across the double bond.

Iodination of D-glucal triacetate, using iodine and silver benzoate in dry benzene[9,10], iodine and silver acetate in methanol[8], *N*-iodosuccinimide in dry methanol[11], or iodonium bis(2,4,6-trimethylpyridine)perchlorate[12], have been described, corresponding to the formal addition of alkyl or acyl hypoiodite across the double bond. However, the formation of free 2-deoxy-2-iodo sugars has not been described hitherto.

We now report a formal electrophilic addition of "hypoiodous acid" to 3,4,6-tri-*O*-acetyl-D-glucal[13] (**1**) and 3,4-di-*O*-acetyl-6-*O*-tosyl-D-glucal[14] (**2**). Depending on the buffer system used and the pH, a mixture of the 2-deoxy-2-iodo esters **3** of **5** together with the corresponding 2-deoxy-2-iodo sugars **4** or **6**, or only **4** or **6**, were obtained. The compounds obtained could be used for the preparation of 2-deoxy sugars or Brigl's anhydrides.

Thus, treatment of **1** or **2** with iodine in *tert*-butyl alcohol in the presence of acetate buffer (pH 5, room temperature, 3 h) gave a mixture of the 2-deoxy-2-iodo-*manno*-esters **3** or **5** together with the corresponding 2-deoxy-2-iodo-α-D-mannopyranose derivatives **4** or **6**, in the ratio 3:1. However, when this reaction was carried out in the presence of a phosphate or carbonate buffer (pH 6–7, room temperature, 3 h), the 2-deoxy-2-iodo-α-D-mannopyranose derivatives **4** or **6** were the only isolable products (50–60%). The structures of **3–6** were confirmed by the NMR data (Table I) and $[\alpha]_D$ values.

The above procedure for the preparation of the 2-deoxy-2-iodo-α-D-manno-

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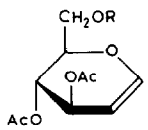
TABLE I

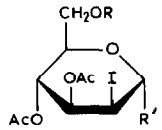
NMR data for **3–6**

Compound	^{1}H (δ in ppm, J in Hz)								
	H-1	H-2	H-3	H-4	H-5	H-6a	H-6b	Ac	Me(OTs)
3	6.39 d $J_{1,2}$1.5	4.53 dd $J_{2,3}$ 4.3	4.58 dd $J_{3,4}$ 9.2	5.44 t	4.20m	4.13–4.18m		2.07 s 2.11 s 2.12 s 2.17 s	
4	5.60 d $J_{1,2}$ 1.3	4.57 dd $J_{2,3}$ 4.3	4.73 dd $J_{3,4}$ 9.5	5.40 t	4.28 m $J_{4,5}$ 9.5	4.20 m		2.07 s 2.10 s 2.13 s	
5	6.28 d $J_{1,2}$ 1.5	4.47 dd $J_{2,3}$ 4.3	4.56 dd $J_{3,4}$ 9.0	5.29 t $J_{4,5}$ 9.0	4.16 m	4.11 m		2.06 s 2.09 s 2.15 s	2.45 s
6	5.51 d $J_{1,2}$ 1.4	4.51 dd $J_{2,3}$ 4.3 $J_{2,4}$ 9.5	4.69 dd	5.17 t $J_{3,4}$ 9.5	4.33 m	4.01–4.09m		2.01 s 2.07 s	2.44 s
	^{13}C (δ in ppm)								
	C-1	C-2	C-3	C-4	C-5	C-6	Me(OTs)	CH_3CO	CH_3CO
4	95.71	30.28	68.76	67.63	69.09	62.24		20.65 20.78 20.93	169.64 170.04 171.05
5	94.36 $J_{C\text{-}1,H\text{-}1}$ 184	26.82 $J_{C\text{-}2,H\text{-}2}$ 158	68.48	67.44	71.21	67.88	21.68	20.59 20.83 20.89	168.08 169.42 169.84
6	95.72 $J_{C\text{-}2,H\text{-}2}$ 159	30.00	68.57	67.89	68.90	68.36	21.61	20.56 20.88	169.72 169.87

pyranose derivatives **4** and **6** gives satisfactory yields and involves inexpensive reagents.



1 R = Ac
2 R = Ts



3 R = Ac, R′ = OAc
4 R = Ac, R′ = OH
5 R = Ts, R′ = OAc
6 R = Ts, R′ = OH

EXPERIMENTAL

General methods.—Melting points (uncorrected) were determined with a Büchi SMP-20 apparatus. The ^{1}H and ^{13}C NMR spectra were recorded with a Bruker AC 250 E instrument on solutions in $CDCl_3$ (internal Me_4Si).

1,3,4,6-*Tetra*-O-*acetyl*-2-*deoxy*-2-*iodo*-α-D-*mannopyranose* (**3**) *and* 3,4,6-*tri*-O-*acetyl*-2-*deoxy*-2-*iodo*-α-D-*mannopyranose* (**4**).—(*a*) To a solution of **1** (1.39 g, 5.1 mmol) in 8:1 *tert*-butyl alcohol–water (45 mL) at room temperature was added a solution of iodine (4.06 g, 16 mmol) in 2:1 *tert*-butyl alcohol–water (45 mL) and acetate buffer [27.73 g (0.34 mol) of NaOAc and 41.45 mL (0.72 mol) of HOAc] at pH 5. The mixture was stirred in the dark for 3 h (room temperature), then poured into water (150 mL), neutralised with $NaHCO_3$, and extracted with ether. The extracts were combined, washed with 0.1 M sodium thiosulfate (50 mL), dried (Na_2SO_4), and concentrated. Column chromatography (silica gel; benzene–EtOAc, 19:1) of the syrupy residue (1.95 g, 87.3%) gave **3** (1.14 g, 48.7%), $[\alpha]_D$ +13° (*c* 0.5, $CHCl_3$), and **4** (0.293 g, 13.8%), $[\alpha]_D$ −20° (*c* 0.2, $CHCl_3$), isolated as colorless oils.

(*b*) To a solution of **1** (0.455 g, 1.67 mmol) in 8:1 *tert*-butyl alcohol–water (20 mL) at room temperature was added a solution of iodine (1.05 g, 4.14 mmol) in 2:1 *tert*-butyl alcohol–water (20 mL) at pH 6–7 (phosphate buffer; Na_2HPO_4 and NaH_2PO_4, 40 mL, 0.2 M). The mixture was stirred in the dark for 24 h (room temperature), then poured into water (100 mL), and extracted with $CHCl_3$. The extracts were combined, washed with 0.1 M sodium thiosulfate (25 mL), dried (Na_2SO_4), and concentrated. Column chromatography (benzene–EtOAc, 19:1) of the syrupy residue (0.558 g, 80.2%) gave **4** (0.435 g, 62.5%), isolated as an oil.

1,3,4-*Tri*-O-*acetyl*-2-*deoxy*-2-*iodo*-6-O-p-*toluenesulphonyl*-α-D-*mannopyranose* (**5**) *and* 3,4-*di*-O-*acetyl*-2-*deoxy*-2-*iodo*-6-O-p-*toluenesulphonyl*-α-D-*mannopyranose* (**6**). —(*a*) Treatment of **2** (1.96 g, 5.1 mmol), as described in (*a*) for **1**, gave **5** as a syrup (1.55 g, 53.3%), $[\alpha]_D$ +27.5° (*c* 0.54, $CHCl_3$), and **6** (0.35 g, 13.0%), mp 123–124° (dec) (from CH_2Cl_2–hexane), $[\alpha]_D$ +10° (*c* 0.5, $CHCl_3$).

(*b*) Treatment of **2** (0.295 g, 0.768 mmol), as described in (*b*) for **1**, with iodine (0.591 g, 2.32 mmol) for 3 h [the pH was adjusted with 0.54 M $NaHCO_3$ (3.6 mL)] gave, after column chromatography, **6** (0.214 g, 52.8%), which crystallised from CH_2Cl_2–hexane and had mp 123–124° (dec), $[\alpha]_D$ +10° (*c* 0.5, $CHCl_3$).

Anal. Calcd for $C_{17}H_{21}IO_9S$: C, 38.67; H, 3.97. Found: C, 39.07, H, 4.28.

REFERENCES

1 R.J. Ferrier, *Adv. Carbohydr. Chem.*, 20 (1967) 67–137.
2 R.J. Ferrier, *Adv. Carbohydr. Chem. Biochem.*, 24 (1969) 199–266.
3 K. Igarashi, T. Honma, and T. Imagawa, *J. Org. Chem.*, 35 (1969) 610–616.
4 J. Adamson and D.M. Marcus, *Carbohydr. Res.*, 22 (1972) 257–264.
5 J. Adamson, A.B. Foster, L.D. Hall, R.N. Johnson, and R.H. Hesse, *Carbohydr. Res.*, 15 (1970) 351–359.
6 E.L. Albano, R.L. Tolman, and R.K. Robins, *Carbohydr. Res.*, 19 (1971) 63–70.
7 C.G. Butchard and P.W. Kent, *Tetrahedron*, 27 (1971) 3457–3463.
8 R.U. Lemieux and B. Fraser-Reid, *Can. J. Chem.*, 42 (1964) 535–538.
9 J. Stanek and V. Schwarz, *Collect. Czech. Chem. Commun.*, 20 (1955) 42.
10 R.U. Lemieux and S. Levine, *Can. J. Chem.*, 10 (1962) 1926–1932.
11 D. Horton, W. Priebe, and M. Sznaidman, *Carbohydr. Res.*, 205 (1990) 71–86.
12 P.J. Garegg and B. Samuelsson, *Carbohydr. Res.*, 84 (1980) c1–c4.
13 W. Roth and W. Pigman, *Methods Carbohydr. Chem.*, 2 (1963) 405–406.
14 D. Miljković, N. Vukojević, and D. Medaković, *Carbohydr. Res.*, 193 (1989) 275–278.