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Note

New observations on the Garegg–Samuelsson olefination reaction*

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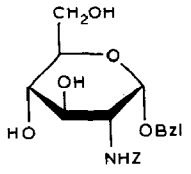
Vicinal *trans*-diol groups, present in the pyranose ring, can be converted readily into a double bond by the triphenylphosphine–iodine–imidazole reagent in toluene–acetonitrile solution[1,2]. Application of this reaction to benzyl 2-benzyloxycarbonylamino-2-deoxy-α-D-glucopyranoside (**1**) led[3] to benzyl 2-benzyloxycarbonylamino-2,3,4,6-tetradeoxy-6-iodo-α-D-*erythro*-hex-3-enopyranoside (**2**) in a high yield and to an unsaturated di-iodo analogue **3** that contained the iodine atoms at C-3 or C-4 and at C-6.



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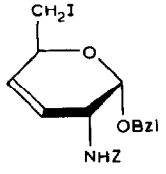

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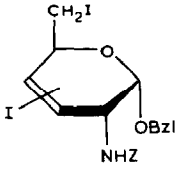

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We wanted to exploit **2** for the synthesis of a diaminohexose needed in another project[4], but repetition of the olefination reaction on **1** (1-mmol scale, 50°, 1.5 h) did not yield any products. Under more vigorous conditions (80°, 3 h), a mixture of products was obtained, chromatography of which gave four components. Two of these, namely, **4** (39%) and **5** (24%), were identified on the basis of analytical and ^{1}H-n.m.r. data as benzyl 2-benzyloxycarbonylamino-2,3,6-trideoxy-3,6-di-iodo-α-D-allopyranoside and benzyl 2-benzyloxycarbonylamino-2,4,6-trideoxy-4,6-di-iodo-α-D-galactopyranoside, respectively. These compounds were not obtained previously[3]. According to the analytical and n.m.r. data, the remaining two compounds corresponded to **2** (13.5%) and **3** (10%).

Although all coupling constants could be found from the 500-MHz ^{1}H-n.m.r. spectrum of **3**, the location of the olefinic proton (at C-3 or C-4) remained uncertain. The physical constants of **2** {m.p. 129–130°, $[\alpha]_D$ +22° (chloroform)} differed markedly

* Dedicated to Professor Leslie Hough in the year of his 65th birthday.
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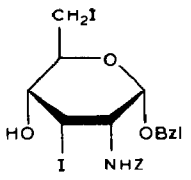

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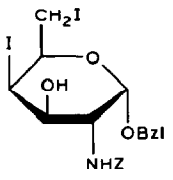

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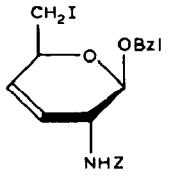

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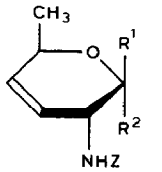
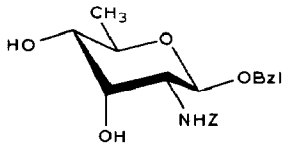
from those reported[3] {m.p. 139–140°, $[\alpha]_D$ −151° (chloroform)} as did those for **3** {m.p. 119–121°, $[\alpha]_D$ +133° (chloroform); *cf.* m.p. 165–167°, $[\alpha]_D$ −102° (chloroform)}.

When the olefination reaction was repeated on a 10-mmolar scale (80°, 3 h), column chromatography of the products gave **2** (56%), **3** (17%), and **6** (7% yield). Compound **6** had physical constants {m.p. 138–140°, $[\alpha]_D^{20}$ −151° (chloroform)} similar to those reported[3] for **2** (see above). Comparison of $[\alpha]_D$ values and ^{13}C-n.m.r. data (see Experimental) of **2** and **6** pointed to a difference in anomeric configuration. In order to substantiate this conclusion, **6** was reduced with tributyltin hydride and the product (**7**) was *cis*-hydroxylated with osmium tetraoxide. The ^{1}H-n.m.r. data ($J_{1,2}$ 8, $J_{4,5}$ 8.2 Hz) of the product **8** were compatible with the structure of benzyl 2-benzyloxycarbonylamino-2,6-dideoxy-β-D-allopyranoside. Further support was provided by the Sinclair–Sleeter rule[5], namely that, in the ^{1}H-n.m.r. spectra of anomeric 6-deoxyhexopyranosides, the signal for H-6,6,6 appears at higher field for the α anomers. To this end, **2** was reduced with tributyltin hydride to give **9**. Comparison of the signals H-6,6,6 for **9** (δ 1.05) and **7** (δ 1.12) confirmed the anomeric assignment.



7 R^1 = OBzl, R^2 = H
9 R^1 = H, R^2 = OBzl



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It is concluded that benzyl 2-benzyloxycarbonylamino-2-deoxy-β-D-glucopyranoside was employed in the original olefination reaction[3]. Furthermore, it seems that benzyl 2-amino-2-deoxy-α-D-glucopyranoside, obtained using the method of Heyns and Paulsen[6], may contain a few percent of the β anomer.

EXPERIMENTAL

Optical rotations were measured with a Jasco DIP 360 automatic polarimeter. N.m.r. spectra were recorded with a Bruker AM 500 spectrometer. T.l.c. was performed on Silica Gel HF-254 and column chromatography on Silica Gel 230–400 mesh (Merck).

Benzyl 2-benzyloxycarbonylamino-2-deoxy-α-D-glucopyranoside (**1**). — Compound **1**, obtained according to ref. 6, had m.p. 174° (after two crystallizations from ethanol), $[\alpha]_D^{26}$ +140° (*c* 1, pyridine); lit.[6]: m.p. 174°, $[\alpha]_D^{20}$ +145° (pyridine).

Reaction of **1** *with triphenylphosphine–iodine–imidazole.* — (*a*) *1-Mmol scale.* A solution of triphenylphosphine (1.57 g, 6 mmol) and iodine (1.52 g, 6 mmol) in toluene (20 mL) was stirred at room temperature for 30 min. A solution of imidazole (0.41 g, 6 mmol) in acetonitrile (10 mL) was added, the mixture was stirred for 10 min at 50°, **1** (0.4 g, 1 mmol) was added, and stirring was continued for 3 h at 80°. The mixture was cooled to room temperature, filtered through Celite, and concentrated to dryness. Column chromatography (toluene–ethyl acetate, 95:5) of the residue gave **3** (60 mg, 10%), **2** (64.7 mg, 13.5%), **4** (243 mg, 39%), and **5** (150 mg, 24%).

Benzyl 2-benzyloxycarbonylamino-2,3,4,6-tetradeoxy-3(4),6-di-iodo-α-D-*erythro*-hex-3-enopyranoside (**3**) had m.p. 119–121°, $[\alpha]_D^{23}$ +133° (*c* 1, chloroform). N.m.r. data: ^{1}H (C_6D_6), *inter alia*, δ 5.96 (t, 1 H, $J_{4,5(3,2)} = J_{4,2(3,5)} = 2.0$ Hz, H-4 or H-3), 5.08 (d, 1 H, $J_{NH,2}$ 9.0 Hz, NH), 4.78 (m, 1 H, $J_{2,5}$ 3.2 Hz, H-2), 4.75 (d, 1 H, $J_{1,2}$ 4.2 Hz, H-1), 3.72 (m, 1 H, $J_{5,6}$ 4.4, $J_{5,6'}$ 6.3 Hz, H-5), 2.56 (q, 1 H, $J_{6,6'}$ 10.4 Hz, H-6), 2.52 (q, 1 H, H-6'); ^{13}C ($CDCl_3$), *inter alia*, δ 99.53 (C-3 or C-4), 95.63 (C-1), 67.13 (C-5), 52.77 (C-2), 6.88 (C-6).

Anal. Calc. for $C_{21}H_{21}I_2NO_4$: C, 41.68; H, 3.50; N, 2.31; I, 41.93. Found: C, 41.71; H, 3.28; N, 2.54; I, 41.44.

Benzyl 2-benzyloxycarbonylamino-2,3,4,6-tetradeoxy-6-iodo-α-D-*erythro*-hex-3-enopyranoside (**2**) had m.p. 129–130°, $[\alpha]_D^{23}$ +22° (*c* 0.8, chloroform). N.m.r. data: ^{1}H (C_6D_6), *inter alia*, δ 5.45, 5.19 (2 bd, 2 H, $J_{3,4}$ 10 Hz, H-3,4), 4.93 (d, 1 H, $J_{NH,2}$ 10 Hz, NH), 4.84 (d, 1 H, $J_{1,2}$ 3.2 Hz, H-1), 4.64 (m, 1 H, H-2), 3.80 (m, 1 H, H-5), 2.76 (q, 1 H, $J_{5,6}$ 4.4, $J_{6,6'}$ 10 Hz, H-6), 2.70 (q, 1 H, $J_{5,6'}$ 6.2 Hz, H-6'); ^{13}C ($CDCl_3$), δ 8.61 (C-6), 47.14 (C-2), 66.81 (Ph*C*H$_2$), 67.18 (C-5), 69.84 (Ph*C*H$_2$), 95.41 (C-1), 126.62 (C-3).

Anal. Calc. for $C_{21}H_{22}INO_4$: C, 52.62; H, 4.63; N, 2.92; I, 26.47. Found: C, 52.35; H, 4.50; N, 2.94; I, 26.96.

Benzyl 2-benzyloxycarbonylamino-2,3,6-trideoxy-3,6-di-iodo-α-D-allopyranoside (**4**) had m.p. 84–86°. ^{1}H-N.m.r. data (C_6D_6): *inter alia*, δ 5.39 (d, 1 H, NH), 4.64 (m, 3 H, H-1,3, PhHC*H*), 3.75 (dt, 1 H, $J_{2,1} = J_{2,3} = 4.0$, $J_{2,NH}$ 9.8 Hz, H-2), 3.50 (bt, 1 H, H-5), 3.19 (q, 1 H, $J_{5,6}$ 2.3, $J_{6,6'}$ 10.5 Hz, H-6), 3.04 (q, 1 H, $J_{5,6'}$ 7.1 Hz, H-6'), 2.25 (m, 1 H, $J_{4,5}$ 8.5, $J_{4,3}$ 3.8 Hz, H-4).

Anal. Calc. for $C_{21}H_{23}I_2NO_5$: C, 40.47; H, 3.72; N, 2.25; I, 40.72. Found: C, 40.43; H, 3.80; N, 2.39; I, 40.55.

Benzyl 2-benzyloxycarbonylamino-2,4,6-trideoxy-4,6-di-iodo-α-D-galactopyranoside (**5**) had m.p. 136–137°, $[\alpha]_D^{20}$ +101° (*c* 1, chloroform). ^{1}H-N.m.r. data ($CDCl_3$), *inter alia*, δ 5.13 (d, 1 H, $J_{NH,2}$ 8.6 Hz, NH), 4.91 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-1), 4.76 (d, 1 H, $J_{4,3}$ 2.7 Hz, H-4), 4.09 (dt, 1 H, $J_{2,3}$ 9.7 Hz, H-2), 3.30 (m, 2 H, H-5,6), 3.12 (q, 1 H, $J_{5,6'}$ 9.9 Hz, H-6').

Anal. Found: C, 40.29; H, 3.67; N, 2.24; I, 40.70.

(*b*) *10-Mmol scale.* The reagent was prepared[3] from triphenylphosphine (15.72 g, 59.9 mmol), iodine (15.2 g, 59.9 mmol), and imidazole (4.5 g, 66.1 mmol) in toluene (100 mL) and acetonitrile (50 mL). Glycoside **1** (4.04 g, 10 mmol) was added and the mixture

was stirred for 3 h at 80°. After work-up as in (*a*), the filtrate was concentrated to dryness, the residue was extracted twice with toluene, and the combined extracts were concentrated. Column chromatography (toluene–ethyl acetate, 95:5) of the residue gave **3** (1.02 g, 17%), **2** (2.68 g, 56%), and **6** (330 mg, 7%).

Benzyl 2-benzyloxycarbonylamino-2,3,4,6-tetradeoxy-6-iodo-β-D-*erythro*-hex-3-enopyranoside (**6**) had m.p. 138–140°, $[\alpha]_D^{20} - 151°$ (*c* 2, chloroform). N.m.r. data: ^1H (C_6D_6), *inter alia*, δ 5.41, 5.36 (2 m, 2 H, $J_{3,4}$ 10 Hz, H-3,4), 4.64 (m, 1 H, H-1), 4.36 (d, 1 H, $J_{NH,2}$ 8.7 Hz, NH), 4.26 (m, 1 H, H-2), 3.93 (m, 1 H, H-5), 2.94 (m, 1 H, $J_{6,6'}$ 10 Hz, H-6), 2.79 (q, 1 H, $J_{6',5}$ 5.9 Hz, H-6'); ^{13}C ($CDCl_3$), δ 8.35 (C-6), 48.16 (C-2), 66.94 and 70.14 (2 Ph*C*H_2), 72.65 (C-5), 99.14 (C-1), 125.49 (C-3), 129.02 (C-4).

Anal. Calc. for $C_{21}H_{22}INO_4$: C, 52.62; H, 4.63; N, 2.92; I, 26.47. Found: C, 52.59; H, 4.36; N, 2.90; I, 26.76.

*Benzyl 2-benzyloxycarbonylamino-2,3,4,6-tetradeoxy-α-D-*erythro*-hex-3-enopyranoside* (**9**). — To a solution of **2** (5.0 g, 10.4 mmol) in benzene (50 mL) was added tributyltin hydride (3.3 g, 11.4 mmol) followed by α-azoisobutyronitrile (10 mg). The mixture was boiled under reflux for 1 h and then concentrated to dryness. Column chromatography (toluene–ethyl acetate, 9:1) of the residue yielded **9** (3.02 g, 82%), m.p. 106–107°, $[\alpha]_D^{26} + 37°$ (*c* 1.2, chloroform). ^1H-N.m.r. data (C_6D_6): *inter alia*, δ 5.45, 5.34 (2 bd, 2 H, $J_{3,4}$ 10.2 Hz, H-3,4), 4.91 (d, 1 H, $J_{1,2}$ 4.2 Hz, H-1), 4.75 (m, 1 H, H-2), 4.08 (m, 1 H, H-5), 1.05 (d, 3 H, H-6,6,6).

Anal. Calc. for $C_{21}H_{23}NO_4$: C, 71.37; H, 6.56; N, 3.96. Found: C, 71.40; H, 6.57; N, 3.50.

Benzyl 2-benzyloxycarbonylamino-2,3,4,6-tetradeoxy-β-D-*erythro*-hex-3-enopyranoside (**7**; 132 mg, 89%) was prepared from **6** (200 mg) by the above method. ^1H-N.m.r. data (C_6D_6): *inter alia*, δ 5.42, 5.29 (2 bd, 2 H, $J_{3,4}$ 10 Hz, H-3,4), 4.55 (m, 1 H, H-2), 4.33 (bd, 1 H, $J_{1,2}$ 6.5 Hz, H-1), 4.00 (m, 1 H, H-5), 1.12 (d, 3 H, H-6,6,6).

Benzyl 2-benzyloxycarbonylamino-2,6-dideoxy-β-D-allopyranoside (**8**). — To a solution of **7** (50 mg) in pyridine (2 mL) was added a solution of osmium tetraoxide (42 mg) in pyridine (1 mL). The mixture was stirred at room temperature for 22 h and then diluted with water (15 mL), and saturated aqueous sodium hydrogensulphite (2 mL) was added. The mixture was stirred for 4 h, diluted with water, and extracted with dichloromethane, and the extract was dried and concentrated. Preparative t.l.c. (benzene–2-propanol, 4:1) of the residue gave **8** (5 mg). ^1H-N.m.r. data ($CDCl_3$): *inter alia*, δ 5.23 (d, 1 H, $J_{NH,2}$ 8 Hz, NH), 4.63 (d, 1 H, $J_{1,2}$ 8 Hz, H-1), 4.20 (m, 1 H, H-3), 3.65–3.73 (m, 2 H, H-2,5), 3.35 (bd, 1 H, $J_{4,5}$ 8.2 Hz, H-4), 1.33 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6,6,6).

ACKNOWLEDGMENTS

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