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Preliminary communication

A new method for *N*-alkyl and *N,N*-dialkyl-D-glucosamines *

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As a result of our work on oxazolidines derived from sugars, we now describe an easy and high-yielding two-step method for synthesising *N*-alkyl and *N,N*-dialkyl-D-glucosamine derivatives from the readily available benzyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranoside (**1**)[2].

Reaction of **1** with dibromomethane under phase-transfer conditions[3] gave, after crystallisation from ethanol, 3-acetyl-(benzyl 4,6-*O*-benzylidene-2,3-dideoxy-α-D-glucopyranosido)[2,3-*d*]oxazolidine (**2**, 89%); mp 167–168°; ν_{max} 3064, 3034 (Ar), and 1664 cm^{-1} (CO, amide). ^1H NMR data (200 MHz, $CDCl_3$, 20°); δ 7.35 (m, 10 H, 2 Ph), 5.90 (d, 1 H, $J_{1,2}$ 2.8 Hz, H-1), 5.61 (s, 1 H, PhC*H*), 5.04 and 4.93 (2 d, 2 H, J_{gem} 3.5 Hz, OCH_2N), 4.69 (AB q, 2 H, ^2J 11.5 Hz, $PhCH_2$), 3.33 (dd, 1 H, $J_{1,2}$ 2.8, $J_{2,3}$ 10.1 Hz, H-2), and 2.00 (s, 3 H, Ac). Mass spectrum (CI): *m/z* 412 (100%) $[M + H]^+$.

Anal. Calcd for $C_{23}H_{25}NO_6$: C, 67.14; H, 6.12; N, 3.40. Found: C, 66.97; H, 6.41; N, 3.27.

It is known that linear or cyclic 1,1-amino ethers, including oxazolidines, are cleaved by nucleophiles at the carbon–oxygen bond[4]. In this way, the reaction of **2** (1 equiv) with lithium aluminium hydride (4 equiv) in anhydrous tetrahydrofuran at room temperature for 30 min yielded, after column chromatography, benzyl 4,6-*O*-benzylidene-2-deoxy-2-ethylmethylamino-α-D-glucopyranoside (**3**, 70%); mp 96–98°; ν_{max} 3413 (OH), 3065, and 3034 cm^{-1} (Ar). ^1H NMR data (200 MHz, $CDCl_3$, 20°): δ 7.36 (m, 10 H, 2 Ph), 5.57 (s, 1 H, PhC*H*), 5.04 (d, 1 H, $J_{1,2}$ 3.2 Hz, H-1), 4.61 (AB q, 2 H, ^2J 11.7 Hz, $PhCH_2$), 2.81 (dd, 1 H, $J_{1,2}$ 3.2, $J_{2,3}$ 10.5 Hz, H-2), 2.69 (m, 2 H, NCH_2CH_3), 2.44 (s, 3 H, NMe), and 1.05 (t, 3 H, *J* 7.1 Hz,

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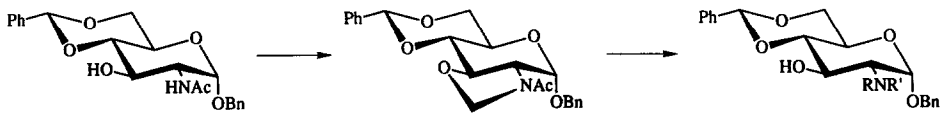
* Oxazolidines from Sugars, Part II. For Part I, see ref. 1.



1 2 3 R=Me, R'=Et 4 R=Me, R'=H 5 R=Pr, R'=H

Scheme 1.

NCH_2CH_3). Mass spectrum (EI): *m/z* 399 (2.5%) $[M]^+$. High-resolution EI: 399.2035; calcd for $C_{23}H_{29}NO_5$: 399.2046.

Anal. Calcd for $C_{23}H_{29}NO_5$: C, 69.15; H, 7.32; N, 3.50. Found: C, 69.17; H, 7.25; N, 3.46.

Moreover, reduction of tertiary amides with lithium triethylborohydride proceeds[5] with carbon–nitrogen bond fission. In this way, the reaction of **2** (1 equiv) with lithium triethylborohydride (Superhydride®) (4 equiv) in anhydrous tetrahydrofuran at room temperature for 30 min gave, after the usual work-up, benzyl 4,6-*O*-benzylidene-2-deoxy-2-methylamino-α-D-glucopyranoside (**4**, 92%); mp 153–155°; ν_{max} 3452 (OH), 3200 (NH), 3063, and 3032 cm^{-1} (Ar). ^1H NMR data (200 MHz, $CDCl_3$, 20°): δ 7.38 (m, 10 H, 2 Ph), 5.55 (s, 1 H, PhC*H*), 5.02 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1), 4.63 (AB q, 2 H, ^2J 11.9 Hz, $PhCH_2$), 2.53 (dd, 1 H, $J_{1,2}$ 3.6, $J_{2,3}$ 9.9 Hz, H-2), and 2.32 (s, 3 H, Me). Mass spectrum (EI): *m/z* 371 (0.6%) $[M]^+$. High-resolution EI: 371.1718; calcd for $C_{21}H_{25}NO_5$: 371.1733.

Anal. Calcd for $C_{21}H_{25}NO_5$: C, 67.91; H, 6.78; N, 3.77. Found: C, 67.99; H, 6.81; N, 3.78.

Furthermore, the reaction of **2** (1 equiv) with ethylmagnesium chloride (3 equiv) in dry toluene at room temperature overnight yielded, after column chromatography, benzyl 4,6-*O*-benzylidene-2-deoxy-2-propylamino-α-D-glucopyranoside (**5**, 91%); mp 96–97°; ν_{max} 3485 (OH), 3210 (NH), 3065, and 3037 cm^{-1} (Ar). ^1H NMR data (200 MHz, $CDCl_3$, 20°): δ 7.34 (m, 10 H, 2 Ph), 5.55 (s, 1 H, PhC*H*), 4.99 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1), 4.62 (AB q, 2 H, ^2J 11.9 Hz, $PhCH_2$), 2.61 (dd, 1 H, $J_{1,2}$ 3.6, $J_{2,3}$ 9.8 Hz, H-2), 2.41 (m, 2 H, $NCH_2CH_2CH_3$), 1.39 (m, 2 H, $NCH_2CH_2CH_3$), and 0.82 (t, 3 H, *J* 7.2 Hz, $NCH_2CH_2CH_3$). Mass spectrum (EI): *m/z* 399 (0.2%) $[M]^+$. High-resolution EI: 399.2056; calcd for $C_{23}H_{29}NO_5$: 399.2046.

Anal. Calcd for $C_{23}H_{29}NO_5$: C, 69.15; H, 7.32; N, 3.50. Found: C, 69.28; H, 7.51; N, 3.51.

The application of these reactions to other oxazolidines derived from sugars and with other Grignard reagents is now being investigated.

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