180. Deoxy-nitrosugars

8th Communication[1])

Convenient Preparation of 1-*C*-Nitroglycosyl Chlorides. Halonitro Ethers from Hydroxy Oximes

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Summary

Partially protected 4- or 5-hydroxy-sugar oximes were transformed into 5- or 6-membered 1-*C*-nitroglycosyl chlorides, respectively, by reaction with NaOCl under phase-transfer conditions. With the exception of the oxidation of the *gluco*-derivative **1** giving the anomers **6** and **7**, the reactions were completely diastereoselective.

The 1-*C*-nitroglycosyl bromides are new carbohydrate derivatives [2]. Apart from their transformation into 1-deoxy-1-nitroaldoses [2], virtually nothing is known about their chemical behaviour. The 1-*C*-nitroglycosyl bromides have been prepared from partially protected sugar oximes *via* the corresponding lactone oximes [3] and halonitroso compounds in a high-yielding three-step sequence [2].

We report a convenient preparation of protected 1-*C*-nitroglycosyl chlorides directly from the corresponding sugar oximes which should facilitate investigations of the reactivity of halonitro ethers. The oxidation of 4- or 5-hydroxy-sugar oximes to lactone oximes very probably occurs *via* the tautomeric cyclic hydroxylamines. It should proceed easily also with NaOCl as oxidant. Since *Corey & Estreicher* [4] have described a two-step one-pot transformation of oximes into chloronitro compounds by oxidation first with HOCl in a biphasic system at pH 5.5 and then with NaOCl in a biphasic system at pH 10 in the presence of a phase-transfer catalyst, a direct oxidation of appropriate hydroxy oximes to chloronitro ethers appeared feasible. In the event, treatment of the D-*gluco*- and D-*manno*-configurated 5-hydroxy oximes **1** and **2**, respectively, with NaOCl in a biphasic system at pH 11–12 in the presence of a phase-transfer catalyst gave the corresponding chloronitro ethers **6–8** in a good yield *(Scheme)*. The 4-hydroxy oximes **3** and **4** were transformed by a similar treatment first at a pH of *ca.* 7 and then at pH 11–12 into the chloronitro ethers **9** and **10**, respectively, while the dihydroxy oxime **5** gave the novel nitroacetal **11** by double neighbouring-group participation. With the exception of the oxidation of the D-*gluco* oxime **1** giving a 1:1 mixture of **6** and **7**, the reactions were completely diastereoselective. The anomeric configura-

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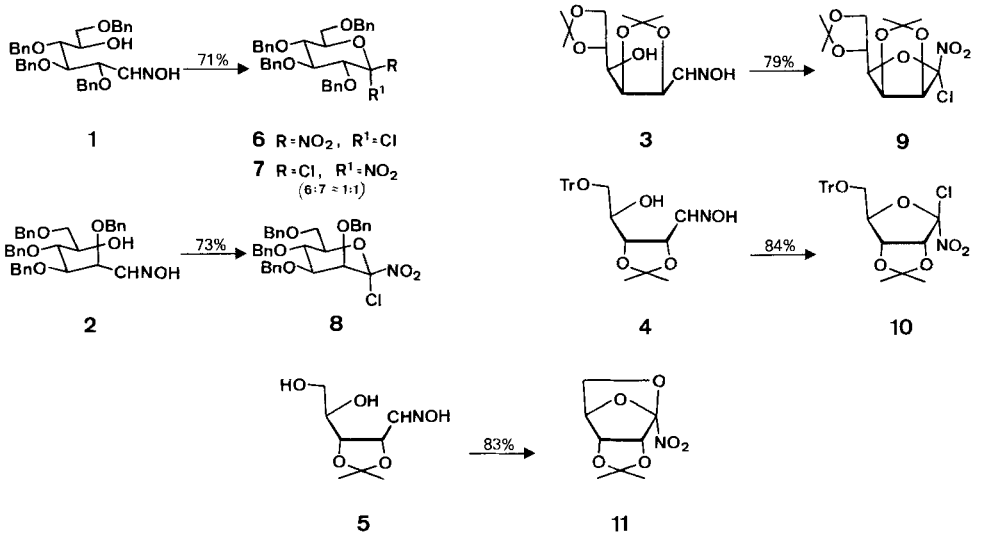
Scheme



tion of the chloronitro ethers **8–10** was deduced from a comparison with the analogous bromonitro ethers [2] and corresponds to an axial (**8**), respectively *exo*-attack (**9,10**) of the chlorinating agent.

The more delicate assignment of the anomeric configuration to the isomeric chloronitro ethers **6** and **7** is mainly based on the IR and ^{13}C-NMR spectra. Thus, the IR spectrum of **6** and **7** shows NO_2-bands (ν_{asym}) at 1580 and 1570 cm^{-1}, respectively. It has been found that 1-deoxy-1-nitroaldoses with an axial NO_2-group give rise to a NO_2-band at lower wave numbers [2], in accordance with the anomeric effect of the NO_2-group [5]. The relative position of this band should not be inverted by the presence of a C(1)–Cl substituent. In the ^{13}C-NMR spectra the signal of C(1) appears at δ = 124.0 ppm for **6** and at 120.4 ppm for **7**. By comparison, C(1) of the 2,3,4,6-tetra-*O*-acetyl-D-glucopyranosyl chlorides appears at 89.5 ppm for the α-D-anomer and at 87.1 ppm for the β-D-anomer [6]. The C(1) signal of the 2,3,4,6-tetra-*O*-benzyl-1-deoxy-1-nitro-D-glucopyranoses appears at 104.2 ppm for the α-D-anomer and at 105.2 ppm for the β-D-anomer [2], the $\Delta\delta$ values sum up to a value of 3.4 ppm, not far from the $\Delta\delta$-value of 3.6 ppm found if **6** and **7** are assigned the indicated configurations. The $[M]_D$ values of these anomers, however, although qualitatively in agreement with the assignment, differ only slightly from each other. This may be correlated with a $J_{2,3}$ value of 6.6 Hz in the ^{1}H-NMR spectrum of **7** and a $J_{2,3}$ value of 9.0 Hz for **6** indicating that these two compounds may have a different conformation.

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Experimental Part

General. See [3]. HPLC was performed on a *Kontron* apparatus (LC pump *410*), prep. HPLC on a *Du Pont 8800* with a UV detector set at 255 nm. Unless otherwise stated, ^{1}H-NMR were recorded at 200 MHz.

*2,3,4,6-Tetra-*O*-benzyl-1-nitro-*D*-glucopyranosyl Chlorides* (**6** *and* **7**). To a mixture of 10 ml of *ca.* 14% aq. NaOCl and 200 mg (0.59 mmol) of Bu_4NHSO_4 was added during 30 min a solution of 1 g (1.8 mmol) of the oxime **1** in 15 ml of AcOEt. The biphasic mixture was stirred at r.t. for 15 min. The blue org. layer was separated and again stirred at r.t. with a mixture of 10 ml of *ca.* 14% aq. NaOCl and 200 mg (0.59 mmol) of Bu_4NHSO_4 until disappearance of the blue colour (*ca.* 85 min). After an additional 20 min, aq. workup followed by chromatography on silica gel (AcOEt/hexane 1:4) gave 771 mg (71%) of **6/7** as a *ca.* 1:1 mixture. The anomers were separated by HPLC (*Zorbax-Sil*, hexane/EtOH 200:1, k' = 2.75 for **6**, k' = 3.00 for **7**).

Data of **6**. $[M]_D^{25} = +518°$ ($c = 1.11$). IR: 3090*w*, 3065*w*, 3035*w*, 2908*w*, 2870*w*, 1580*s*, 1496*w*, 1452*m*, 1400*w*, 1360*m*, 1349*m*, 1152*s*, 1122*s*, 1080*s*, 1070*s*, 1048*m*, 1027*m*, 1000*m*, 910*w*. ^{1}H-NMR (400 MHz): 7.50–7.10 (*m*, 20 arom. H); 4.87–4.49 (*m*, 4 CH_2Ph); 4.38 (*d*, $J = 9.0$, H–C(2)); 4.06 (*ddd*, $J = 9.5$, 3.3 and 1.8, H–C(5)); 3.98–3.91 (*m*, H–C(3), H–C(4)); 3.83 (*dd*, $J = 11.7$ and 3.3, H–C(6)); 3.71 (*dd*, $J = 11.7$ and 1.8, H–C(6')). ^{13}C-NMR: 138.60 (*s*); 138.02 (*s*); 137.42 (*s*); 129.40 (*d*); 128.96 (*d*); 128.82 (*d*); 128.62 (*d*); 124.00 (*s*); 84.16 (*d*); 82.50 (*d*); 79.24 (*d*); 76.85 (*t*); 76.77 (*d*); 76.26 (2*t*); 74.42 (*t*); 67.92 (*t*). MS: 447 (5), 341 (2), 249 (2), 235 (2), 197 (6), 182 (12), 181 (62), 180 (4), 179 (4), 163 (32), 161 (6), 108 (22), 107 (32), 106 (10), 105 (19), 104 (10), 92 (82), 91 (100). Anal. calc. for $C_{34}H_{34}ClNO_7$ (604.10): C 67.60, H 5.67, Cl 5.86, N 2.32; found: C 67.38, H 5.40, Cl 5.75, N 2.43.

Data of **7**. $[M]_D^{25} = +431°$ ($c = 1.11$). IR: 3090*w*, 3065*w*, 3035*w*, 3005*w*, 2940*w*, 2900*w*, 2870*w*, 1570*s*, 1494*w*, 1452*m*, 1362*m*, 1160*m*, 1108*m*, 1083*m*, 1070*m*, 1040*m*, 1026*m*, 1000*m*, 910*m*. ^{1}H-NMR (400 MHz): 7.50–7.15 (*m*, 20 arom. H); 4.87–4.52 (*m*, 4 CH_2Ph); 4.50 (*ddd*, $J = 10.0$, 3.1 and 2.0, H–C(5)); 4.28 (*d*, $J = 6.6$, H–C(2)); 4.06–4.00 (*m*, H–C(3), H–C(4)); 3.79 (*dd*, $J = 11.6$ and 3.1, H–C(6)); 3.75 (*dd*, $J = 11.6$ and 2.0, H–C(6')). ^{13}C-NMR: 137.69 (*s*); 137.47 (*s*); 136.29 (*s*); 128.34 (*d*); 128.12 (*d*); 127.81 (*d*); 127.69 (*d*); 120.47 (*s*); 82.82 (*d*); 80.84 (*d*); 79.59 (*d*); 75.62 (*t*); 75.41 (*d*); 74.39 (*t*); 74.18 (*t*); 73.35 (*t*); 67.41 (*t*). MS: 448 (2), 447 (7), 355 (3), 341 (4), 267 (3), 253 (3), 249 (5), 235 (3), 233 (3), 197 (11), 182 (20), 181 (86), 163 (62), 108 (19), 107 (40), 91 (100). Anal. calc. for $C_{34}H_{34}ClNO_7$ (604.10): C 67.60, H 5.67, Cl 5.86, N 2.32; found: C 67.46, H 5.68, Cl 5.70, N 2.49.

*2,3,4,6-Tetra-*O*-benzyl-1-nitro-*α*-*D*-mannopyranosyl Chloride* (**8**). In a similar way as described for the preparation of **6** and **7**, 500 mg (0.9 mmol) of **2** gave, after chromatography (50 g SiO_2, AcOEt/hexane 1:4) 396 mg (73%) of **8**, $[M]_D^{25} = +267°$ ($c = 2.24$). IR: 3090*w*, 3070*w*, 3010*w*, 2920*w*, 2870*w*, 1587*s*, 1495*w*, 1455*w*, 1390*w*, 1360*m*, 1350*m*, 1220*w*, 1100*s*, 1070*s*, 1025*s*, 910*w*, 893*w*, 840*w*. ^{1}H-NMR: 7.35–7.20 (*m*, 20 arom. H); 5.00–3.80 (*m*, 14 H). ^{13}C-NMR: 137.73 (*s*); 137.44 (*s*); 137.13 (*s*); 136.70 (*s*); 128.41 (*d*); 128.11 (*d*); 127.70 (*d*); 127.37 (*d*); 115.08 (*s*); 79.31 (2*d*); 78.81 (*d*); 75.80 (*t*); 75.30 (*t*); 73.45 (*t*); 73.06 (*t*); 72.68 (*d*); 67.15 (*t*). MS: 512 (2), 181 (11), 126 (25), 108 (15), 107 (21), 106 (46), 105 (60), 92 (42), 91 (100), 89 (18), 79 (21), 78 (12), 77 (70). Anal. calc. for $C_{34}H_{34}ClNO_7$ (604.10): C 67.60, H 5.67, N 2.32; found: C 67.66, H 5.64, N 2.20.

*2,3:5,6-Di-*O*-isopropylidene-1-nitro-*α*-*D*-mannofuranosyl Chloride* (**9**). A solution of 500 mg (1.8 mmol) of **3** in 35 ml of AcOEt was stirred for 15 min with a mixture of 10 ml of *ca.* 14% aq. NaOCl, 200 mg (0.59 mmol) of Bu_4NHSO_4 and 4 ml of a phosphate buffer (pH 7, 0.25M). The aq. phase was replaced by a mixture of 10 ml of *ca.* 14% aq. NaOCl and 200 mg (0.59 mmol) of Bu_4NHSO_4 and stirring was continued for *ca.* 80 min (disappearance of the blue colour). Processing of the mixture as indicated for **6** and **7** gave, after chromatography (40 g SiO_2, AcOEt/hexane 1:3) 463 mg (79%) of **9** as a colourless solid. Recrystallization from AcOEt/hexane, m.p. 121–122°, $[M]_D^{25} = +410°$ ($c = 1.23$). IR: 3020*w*, 2990*m*, 2960*m*, 2940*m*, 2890*w*, 2870*w*, 1590*s*, 1455*w*, 1385*s*, 1375*s*, 1355*m*, 1320*w*, 1260*m*, 1180*s*, 1150*s*, 1120*s*, 1093*m*, 1070*s*, 1045*m*, 1003*m*, 983*m*, 965*m*, 915*s*, 894*m*, 873*m*, 840*m*. ^{1}H-NMR: 5.17 (*d*, $J = 5.3$, H–C(2)); 5.00 (*dd*, $J = 5.3$ and 3.6, H–C(3)); 4.60 (*ddd*, $J = 8.0$, 5.6 and 4.0, H–C(5)); 4.27 (*dd*, $J = 8.0$ and 3.6, H–C(4)); 4.19 (*dd*, $J = 9.0$ and 5.6, H–C(6)); 4.13 (*dd*, $J = 9.0$ and 4.0, H–C(6')); 1.49 (*s*, CH_3); 1.43 (*s*, CH_3); 1.40 (*s*, CH_3); 1.34 (*s*, CH_3). ^{13}C-NMR: 121.57 (*s*), 115.29 (*s*), 109.76 (*s*), 89.32 (*d*), 83.51 (*d*), 78.29 (*d*), 71.88 (*d*), 66.50 (*t*), 26.85 (*q*), 25.37 (*q*), 25.14 (*q*), 24.77 (*q*). MS: 308 (10), 243 (17), 185 (8), 157 (5), 101 (24), 97 (5), 85 (6), 72 (7), 69 (8), 68 (5), 59 (15), 55 (5), 44 (5), 43 (100), 42 (6), 41 (18). Anal. calc. for $C_{12}H_{18}ClNO_7$ (323.73): C 44.52, H 5.60, Cl 10.95, N 4.32; found: C 44.82, H 5.71, Cl 11.19, N 4.38.

*2,3-*O*-Isopropylidene-1-nitro-5-*O*-trityl-β-*D*-ribofuranosyl Chloride* (**10**). The treatment of 580 mg (1.08 mmol) of **4** as described for the preparation of **9** gave, after chromatography (50 g SiO_2, AcOEt/hexane 1:3) 450 mg (84%) of **10** as a colourless solid. Recrystallization from AcOEt/hexane, m.p. 134.5–135.5°, $[M]_D^{25} = -217°$ ($c = 1.48$). IR: 3090*w*, 3060*w*, 2990*w*, 2940*w*, 2920*w*, 2880*w*, 2850*w*, 1585*s*, 1490*m*, 1385*m*, 1378*m*, 1350*m*, 1335*m*, 1320*m*, 1272*m*, 1156*s*, 1110*s*, 1035*m*, 1004*m*, 973*m*, 948*w*, 940*w*, 905*m*, 880*w*, 861*m*, 835*w*. ^{1}H-NMR: 7.60–7.20 (*m*, 15 arom. H); 5.24 (*d*, $J = 6.2$, H–C(2)); 4.92 (*dd*, $J = 3.5$ and 2.0, H–C(4)); 4.79 (*dd*, $J = 6.2$ and 2.0, H–C(3)); 3.61 (*dd*, $J = 10.8$ and 3.5, H–C(5)); 3.25 (*dd*, $J = 10.8$ and 3.5, H–C(5')); 1.40 (*s*, CH_3); 1.28 (*s*, CH_3). ^{13}C-NMR: 143.05 (*s*); 128.46 (*d*); 127.90 (*d*); 127.22 (*d*); 124.49 (*s*); 115.88 (*s*); 90.25 (2*d*); 87.47 (*s*); 80.78 (*d*); 62.73 (*t*); 25.78 (*q*); 24.95 (*q*). MS: 497 (3), 496 (2), 495 (6), 418 (8), 258 (5), 244 (22), 243 (100), 183 (6), 182 (8), 165 (24), 105 (11), 43 (5). Anal. calc. for $C_{27}H_{26}ClNO_6$ (495.97): C 65.38, H 5.28, Cl 7.14, N 2.82; found: C 65.60, H 5.01, Cl 7.40, N 2.93.

*1,5-Anhydro-2,3-*O*-isopropylidene-1-*C*-nitro-β-*D*-ribofuranose* (**11**). The treatment of 1 g (4.8 mmol) of **5** as described for the preparation of **6** gave, after chromatography (100 g SiO_2, AcOEt/hexane 1:2) 870 mg (83%) of **11** as a colourless solid. Recrystallization from CH_2Cl_2/hexane, m.p. 68–69°, $[M]_D^{25} = -170°$. IR: 3030*w*, 2980*m*, 2940*m*, 2910*m*, 1570*s*, 1457*w*, 1377*s*, 1347*w*, 1304*m*, 1154*s*, 1140*s*, 1100*s*, 1054*s*, 1044*s*, 973*s*, 943*m*, 910*w*, 865*s*.

^{1}H-NMR: 4.89 (*d*, *J* = 3.6, H–C(4)); 4.78 and 4.66 (*AB*, *J* = 5.0, H–C(2), H–C(3)); 3.95 (*dd*, *J* = 7.3 and 3.6, H–C(5)); 3.72 (*d*, *J* = 7.3, H–C(5')); 1.49 (*s*, CH_3); 1.33 (*s*, CH_3). ^{13}C-NMR: 119.82 (*s*); 114.64 (*s*); 80.65 (*d*); 80.49 (*d*); 77.96 (*d*); 66.22 (*t*); 25.90 (*q*); 25.61 (*q*). *MS*: 202 (26), 159 (4), 99 (4), 88 (8), 85 (20), 69 (28), 59 (24), 58 (5), 57 (6), 43 (100), 41 (57). Anal. calc. for $C_8H_{11}NO_6$ (217.18): C 44.24, H 5.10, N 6.44; found: C 44.51, H 5.09, N 6.21.

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