Note

A novel and convenient method for the removal of a nitrate group at the anomeric position

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The azidonitration¹ of galactals provides nitrates of derivatives of 2-azido-2deoxy- α,β -D-galactopyranose. As thioglycosides are efficient glycosyl donors, a onestep conversion of anomeric nitrates into alkyl or aryl 1-thioglycoside derivatives is desirable.

On attempted S_N^2 displacement of the nitrate group in 3,4,6-tri-O-acetyl-2azido-2-deoxy- α -D-galactopyranosyl nitrate¹ (1) with thiophenoxide, denitration was observed². This reaction contrasts with the S_N^2 displacement of a nitrate group at the anomeric position with sodium alkoxides³ or potassium O-ethyl dithiocarbonate⁴. We now report an optimised methodology for the removal of nitrate groups from azidonitrates.

Treatment of the azidonitrate 1 or 2^5 in acetonitrile with thiophenol (3 equiv.) at room temperature for ~5 min in the presence of N,N-diisopropylethylamine (1 equiv.) gave, after column chromatography, the corresponding hemiacetal derivatives 3^6 and 4^7 in yields of 94 and 90%, respectively. Similar treatment of 2-azido-6-O-benzyl-2-deoxy--3,4-O-isopropylidene- α -D-galactopyranosyl nitrate⁸ (5) gave the hemiacetal 6 (92%). When 5 reacted⁷ with sodium nitrite in aqueous 1,4-dioxane at 80° for ~6 h, extensive decomposition of the acid-sensitive compound occurred. Likewise, denitration of 3-O-acetyl-2-azido-4,6-O-benzylidene-2-deoxy- α -D-galactopyranosyl nitrate⁴ (7) afforded 8 in almost quantitative yield. These reactions are not restricted to the *galacto* series. Denitration of 2-azido-3-O-benzyl-4,6-O-benzylidene-2-deoxy- β -D-glucopyranosyl nitrate⁹ (9) provided the corresponding hemiacetal 11 (93%), and the α anomer⁹ 10 gave similar results.

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The denitration of nitrate esters by sulfide ions has been described and discussed¹⁰. Recently, potassium thioacetate in dry N,N-dimethylformamide has been proposed¹¹ as a reagent to deprotect various sugar nitrates. We believe that the mild, efficient, and simple procedure described above will be a useful addition to the azido-nitration route to 2-azido-2-deoxyglycosyl donors.



EXPERIMENTAL

General methods. — Elemental analyses were performed at the Service Central d'Analyse (C.N.R.S., Vernaison). ¹H-N.m.r. spectra were recorded with Bruker AC-250 and AM-400 spectrometers for solutions in CDCl₃ (internal Me₄Si). Reactions were monitored by t.l.c. on Silica Gel 60 F_{254} (Merck) with detection by charring with sulfuric acid. Flash column chromatography was performed on Silica Gel 60 (230–400 mesh, Merck). Mass spectrometry was performed with a Nermag R10-10 spectrometer.

General procedure for denitration. — A solution of the azidonitrate (0.5 mmol) in acetonitrile (3 mL) and thiophenol (0.15 mL, 1.5 mmol) was treated at room temperature with N,N-diisopropylethylamine (87 μ L, 0.5 mmol). When t.l.c. showed that the starting material had disappeared (usually after 5 min), the mixture was concentrated and the residue was subjected to column chromatography.

The following products were obtained by the above procedure. The structures of the known compounds were verified by 'H-n.m.r. spectroscopy.

3,4,6-Tri-O-acetyl-2-azido-2-deoxy- α,β -D-galactopyranose (3). — Denitration of 1¹, followed by column chromatography (1:1 hexane-ethyl acetate), gave known⁶ 3 (94%).

2-Azido-3,4,6-tri-O-benzyl-2-deoxy- α , β -D-galactopyranose (4). — Denitration of 2⁵, followed by column chromatography (from 5:1 \rightarrow 3:1 hexane-ethyl acetate), gave first an uncharacterised compound (5%), presumably phenyl 2-azido-3,4,6-tri-O-benzyl-2-deoxy-1-thio- β -D-galactopyranoside. ¹H-N.m.r. data: δ 7.58–7.16 (m, 20 H, 4 Ph), 4.87 and 4.52 (2 d, 2 H, J 11.4 Hz, PhCH₂), 4.72 and 4.66 (2 d, 2 H, J 11.6 Hz, PhCH₂), 4.48 and 4.42 (2 d, 2 H, J 11.7 Hz, PhCH₂), 4.40 (d, 1 H, J 10.1 Hz, H-1), 3.94 (dd, 1 H, J_{3,4} 2.6, J_{4.5} ~0.5 Hz, H-4), 3.84 (dd, 1 H, J_{2,3} 9.8 Hz, H-2), 3.66–3.54 (m, 3 H, H-5,6a,6b), 3.42 (dd, 1 H, H-3). C.i. (ammonia)-mass spectrum: m/z 568 (M + 1)⁺, 585 (M + 18)⁺.

Eluted second was known⁷ 4 (90%).

2-Azido-6-O-benzyl-2-deoxy-3,4-O-isopropylidene-α,β-D-galactopyranose (6). — Denitration of 5⁸, followed by column chromatography (3:1 hexane–ethyl acetate that contained 0.5% of triethylamine), gave 6 (92%). ¹H-N.m.r. data (CDCl₃ + D₂O): δ 7.41–7.32 (m, 5 H, Ph), 5.32 (d, 0.6 H, $J_{1,2}$ 3.5 Hz, H-1α), 4.69 and 4.57 (2 d, 1.2 H, J 12.0 Hz, PhC $H_2\alpha$), 4.68 and 4.57 (2 d, 0.8 H, J 12.0 Hz, PhC $H_2\beta$), 4.56 (d, 0.4 H, $J_{1,2}$ 8.5 Hz, H-1β), 4.51 (ddd, 0.6 H, $J_{4,5}$ 2.5, $J_{5,6a}$ 4.0, $J_{5,6b}$ 8.0 Hz, H-5α), 4.43 (dd, 0.6 H, $J_{2,3}$ 8.5, $J_{3,4}$ 5.5 Hz, H-3α), 4.16 (dd, 0.6 H, H-4α), 4.08 (dd, 0.4 H, $J_{3,4}$ 5.5, $J_{4,5}$ 2.2 Hz, H-4β), 3.99 (ddd, 0.4 H, $J_{5,6a}$ 4.0, $J_{5,6b}$ 8.0 Hz, H-5β), 3.94 (dd, 0.4 H, $J_{2,3}$ 8.0 Hz, H-3β), 3.85–3.72 (m, 2 H, H-6a,6b), 3.44–3.39 (m, 1 H, H-2), 1.58 and 1.36 (2 s, 2.4 H, 2 Meβ), 1.55 and 1.37 (2 s, 3.6 H, 2 Meα).

Anal. Calc. for C₁₆H₂₁N₃O₃: C, 57.30; H, 6.31. Found: C, 57.43; H, 6.31.

3-O-Acetyl-2-azido-4,6-O-benzylidene-2-deoxy- α , β -D-galactopyranose (8). — Denitration of 7⁴, followed by column chromatography (1:1 hexane-ethyl acetate that contained 0.5% of triethylamine), gave 8 (97%). ¹H-N.m.r. data: δ , amongst others, 5.54 (s, 1 H, PhCH), 5.47 (d, 0.7 H, $J_{1,2}$ 3.5 Hz, H-1 α), 5.36 (dd, 0.7 H, $J_{2,3}$ 11.0, $J_{3,4}$ 3.4 Hz, H-3 α), 4.76 (dd, 0.3 H, $J_{2,3}$ 10.8, $J_{3,4}$ 3.4 Hz, H-3 β), 4.63 (d, 0.3 H, $J_{1,2}$ 8.0 Hz, H-1 β).

Anal. Calc. for C₁₅H₁₇N₃O₆: C, 53.73; H, 5.11. Found: C, 54.09; H, 5.36.

2-Azido-3-O-benzyl-4,6-O-benzylidene-2-deoxy- α,β -D-glucopyranose (11). — Denitration of 9°, followed by column chromatography (20:1 dichloromethane-acetone that contained 0.5% of triethylamine), gave 11 (93%). ¹H-N.m.r. data: δ , amongst others, 5.60 (s, 0.4 H, PhCH α), 5.58 (s, 0.6 H, PhCH β), 5.28 (d, 0.4 H, $J_{1,2}$ 3.5 Hz, H-1 α), 4.64 (d, 0.6 H, $J_{1,2}$ 8.0 Hz, H-1 β).

Anal. Calc. for $C_{20}H_{21}N_3O_5$: C, 62.65; H, 5.52. Found: C, 62.48; H, 5.50. Denitration of 10⁹ gave similar results.

REFERENCES

- 1 R. U. Lemieux and R. M. Ratcliffe, Can. J. Chem., 57 (1979) 1244-1251.
- 2 A. Marra, F. Gauffeny, and P. Sinaÿ, Tetrahedron, 47 (1991) 5149-5160.
- 3 H. Paulsen and M. Paal, Carbohydr. Res., 135 (1984) 53-69; J.-C. Jacquinet and P. Sinaÿ, ibid., 159 (1987) 229-253; H. Paulsen, U. von Deessen, and H. Tietz, ibid., 137 (1985) 63-77; G. Catelani, A. Marra, F. Paquet, and P. Sinaÿ, ibid., 155 (1986) 131-140.

- 4 A. Marra, L. K. Shi Shun, F. Gauffeny, and P. Sinaÿ, Synlett, 8 (1990) 445-448.
- 5 K. Briner and A. Vasella, Helv. Chim. Acta, 70 (1987) 1341-1356.
- 6 H. Paulsen and B. Sumfleth, Chem. Ber., 112 (1979) 3203-3213.
- 7 G. Grundler and R. R. Schmidt, Liebigs Ann. Chem., (1984) 1826-1847.
- 8 A. Marra, X. Dong, M. Petitou, and P. Sinaÿ, Carbohydr. Res., 195 (1989) 39-50.
- 9 C. Tabeur and P. Sinaÿ, unpublished data.
- 10 R. T. Merrow, S. J. Cristol, and R. W. van Dolah, J. Am. Chem. Soc., 75 (1953) 4259-4265.
- 11 N. Rakotomanomana, J. M. Lacombe, and A. A. Pavia, 15th Int. Carbohydr. Symp., Yokohama, August 12-17, 1990, p. A050.