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Preliminary communication

2-Deoxy branched-chain amino sugars. Methyl 3-*C*-aminoethyl-2-deoxy-α-D-*arabino*-hexopyranoside*

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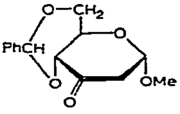
Interest in the general chemistry of the amino sugars[1,2] stems partly from the fact that they occur as components of many antibiotics[3-7]. An account of the methods of synthesis of amino sugars has already been given[1-3]. Recently, branched-chain amino sugars have been synthesized by application of the Wittig reaction to 3-oxo sugars[8] and by application of the nitromethane synthesis[9] to oxo sugars[10]. In addition, nitroethane has been condensed with "sugar dialdehydes" to afford novel branched-chain amino sugars[11].

We now report on a new route to the synthesis of branched-chain amino sugars, namely, by a base-catalyzed addition of acetonitrile to oxo sugars.

The following example is cited. To a stirred solution of lithium amide in liquid ammonia (from 0.220 g of lithium in 125 ml of ammonia containing a few crystals of ferric nitrate) cooled to −50 to −60°, was added anhydrous acetonitrile (31 ml), followed by a solution of methyl 4,6-*O*-benzylidene-2-deoxy-α-D-*erythro*-hexopyranosid-3-ulose[12] (1) (1.240 g) in anhydrous tetrahydrofuran (40 ml). The mixture was kept at −50° for 3 h (or until all starting material was consumed as evidenced by monitoring by t.l.c. (Silica gel G, 95:5 chloroform–ethyl acetate). Ammonium chloride was added to neutralize the lithium amide, and the ammonia was allowed to evaporate. The residue was partitioned between an equal mixture of water and dichloromethane. The dichloromethane layer was washed with water and then dried over sodium sulfate. Evaporation of the solvent left a solid (1.400 g, 95%) which was recrystallized from ethyl acetate–petroleum ether (b.p. 35–60°) to yield methyl 4,6-*O*-benzylidene-3-*C*-cyanomethyl-2-deoxy-α-D-*arabino*-hexopyranoside (2, 1.100 g, 75%), m.p. 170°, $[\alpha]_D^{22}$ +69° (*c* 1, chloroform); ν_{max} (5mM, CCl_4) 3500 (OH),



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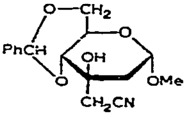

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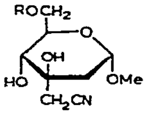
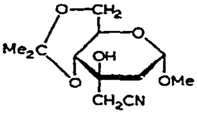


3 R=H
4 R=Ts



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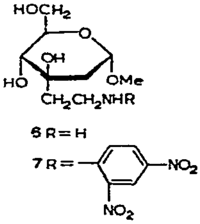

6 R=H
7 R=

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[*] Dedicated to Professor F. Micheel in celebration of his 70th birthday.
[**] Doctoral student of Professor Micheel, 1966–69.

2200 cm^{-1} (C≡N). Compound 2, in methanol, was debenzylidenated over Dowex-W 50-X8 (H$^+$) resin for 4 h (the reaction must be stopped when a trace of starting material is still present to prevent anomerization of the glycoside). The product was chromatographed on silica gel with 5:5:1 benzene–ethyl acetate–methanol to give methyl 3-*C*-cyanomethyl-2-deoxy-α-D-*arabino*-hexopyranoside (3, 95%), m.p. 103° (from ethyl acetate–petroleum ether (b.p. 35–60°)], $[\alpha]_D^{22}$ +129° (*c* 1, methanol).

The configuration of C-3 of compound 3 was deduced from the following facts. Reaction of 3 with an equimolar mixture of acetone and 2,2-dimethoxypropane in the presence of di-*p*-nitrophenyl hydrogen phosphate[13] gave exclusively methyl 3-*C*-cyanomethyl-2-deoxy-4,6-*O*-isopropylidene-α-D-*arabino*-hexopyranoside (5), m.p. 89°, $[\alpha]_D^{22}$ +79° (*c* 1, chloroform); τ (methyl sulfoxide-d_6) 5.42 (singlet, tertiary OH), which disappeared on addition of D_2O. Selective sulfonylation of 3 with an equimolar amount of toluene-*p*-sulfonyl chloride in pyridine at 0° gave a product which was separated by preparative t.l.c. (90:5:0.5 dichloromethane–ethyl acetate–ethanol) to afford the 6-sulfonate (4) (55%), m.p. 107–108° (from ethyl acetate–hexane), $[\alpha]_D^{23}$ +65° (*c* 2, chloroform); τ (methyl sulfoxide-d_6) 5.50 (singlet, tertiary OH), 4.8 (doublet, secondary OH), both peaks disappeared on addition of D_2O. The 6-toluene-*p*-sulfonate 4 did not react with acetone[13], thus indicating the presence of a *trans* glycol group on C-3 and C-4. Surprisingly, 4 reacted with sodium methoxide in methanol to give the 6-*O*-methyl derivative of 3, m.p. 105–107°, $[\alpha]_D^{22}$ +113° (*c* 1, dichloromethane); ν_{max} (5mM, CCl_4) 3490, 3540 cm^{-1} (OH) (the normal OH bands indicate no intramolecular H bonds[14]).

Reduction of 3 in the presence of ammonia, with 5% rhodium-on-alumina as catalyst[15], gave the title compound 6 as a syrup (90%) which was characterized as the *N*-2,4-dinitrophenyl[16] derivative 7, m.p. 85–87°, $[\alpha]_D^{22}$ +75° (*c* 1, methanol).

Studies of the application of acetonitrile to 1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofuranos-3-ulose and the use of the branched-chain amino sugars as intermediates in the synthesis of nucleosides containing branched-chain amino sugars will be reported in a future communication.

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REFERENCES

1 A. B. Foster and M. Stacey, *Advan. Carbohyd. Chem.*, 7 (1952) 247.
2 A. B. Foster and D. Horton, *Advan. Carbohyd. Chem.*, 14 (1959) 213.
3 W. G. Overend, *Chem. Ind.* (London), (1963) 342.
4 J. D. Dutcher, *Advan. Carbohyd. Chem.*, 18 (1963) 259.
5 J. J. Fox, K. A. Watanabe, and A. Block, *Progr. Nucleic Acid Res. Mol. Biol.*, 5 (1966) 251.
6 J. S. Brimacombe, *Angew. Chem. Intern. Ed. Engl.*, 8 (1969) 401.
7 L. Hough and A. C. Richardson, in S. Coffey (Ed.), *Rodd's Chemistry of Carbon Compounds*, Vol. 1, Part F, Elsevier, Amsterdam, 1967.
8 A. Rosenthal and D. A. Baker, *Tetrahedron Lett.*, (1969) 397.
9 H. H. Baer, *Advan. Carbohyd. Chem.*, 24 (1969) 67.
10 G. J. Lourens, *Tetrahedron Lett.*, (1969) 3733; A. Rosenthal and K. S. Ong, *ibid.*, (1969) 3981; A. Rosenthal, K. S. Ong, and D. A. Baker, *Carbohyd. Res.*, 13 (1970) 113; A. Rosenthal and K. S. Ong, *Can. J. Chem.*, in press.

11 S. W. Gunner, W. G. Overend, and N. R. Williams, *Chem. Commun.*, (1964) 1523.
12 A. Rosenthal and P. Catsoulacos, *Can. J. Chem.*, 46 (1968) 2868.
13 A. Hampton, *J. Amer. Chem. Soc.*, 83 (1961) 3640, and references therein.
14 K. N. Slessor and A. S. Tracey, *Can. J. Chem.*, 47 (1969) 3989, and references therein.
15 M. Freifelder, *J. Amer. Chem. Soc.*, 82 (1960) 2386.
16 M. L. Wolfrom, Yen-Lung Hung, and D. Horton, *J. Org. Chem.*, 30 (1965) 3394.