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**Preliminary communication**

# The synthesis of derivatives of 3-amino-2,3,6-trideoxy-3-*C*-methyl-L-*xylo*-hexopyranose, the novel branched-chain amino sugar of antibiotic A35512B

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In a recent approach[1,2] to branched-chain amino sugars of biological interest, we opted for a synthetic strategy that should lead to derivatives of all the stereoisomeric 3-amino-2,3,6-trideoxy-3-*C*-methyl-L-hexopyranoses from a common precursor. Thus, the reaction of the temporarily protected methyl 2,6-dideoxy-α-L-*erythro*-hexopyranosid-3-ulose[1,3] **1** with potassium cyanide under conditions of kinetic control gave the cyanohydrin **2**, which could be transformed, *via* the spiro-aziridine **3**, into methyl 3-acetamido-2,3,6-trideoxy-3-*C*-methyl-α-L-*arabino*-hexopyranoside[2] (**4**). Inversion of the configuration at C-4 of **4** affords[4] the corresponding α-L-*lyxo* derivative **5**, namely, methyl *N*-acetyl-α-L-vancosaminide[5]. We now report the synthesis from **1**[3] of the stereoisomers **6** and **7** in which the amino group at the branch-point is axially disposed. Interest in these sugars is heightened by the recent discovery[6] of 3-amino-2,3,6-trideoxy-3-*C*-methyl-L-*xylo*-hexopyranose (**8**) as the sugar component of A35512B, a new Gram-positive antibiotic isolated from *Streptomyces candidus*[7].

Previous work[1] has shown that **1** reacts with potassium cyanide under equilibrating conditions to form the cyanohydrin **9**, which readily furnished **10** on mesylation. Treatment of **10** with lithium aluminium hydride in *refluxing* ether gave two products in roughly equal proportions, one of which was the spiro-aziridine **11**†. A methanolic solution of both products was subjected to hydrogenolysis over Raney nickel (30 atmos., 70 h), whereafter acetylation yielded, *inter alia*, the methyl-branched amino sugar **12**, b.p. 115–118° (bath)/0.1mm Hg, $[\alpha]_D$ −116° (*c* 1, chloroform), in moderate yield over the three stages. Deprotection of **12** in refluxing 1.5 M methanolic hydrogen chloride for 90 min gave, after acetylation (acetic anhydride in pyridine), virtually only the α-glycoside **13** (79%), $[\alpha]_D$ −88.5 ±3° (*c* 0.75, chloroform). *O*-Deacetylation of **13** furnished methyl 3-acetamido-2,3,6-trideoxy-3-*C*-methyl-α-L-*ribo*-hexopyranoside (**6**, 80%), m.p. 133–135° (from ethyl

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†Little, if any, of **11** was produced when the reaction was conducted at room temperature. In this case, *N*-acetylation of the reaction product(s) and chromatography yielded a compound, m.p. 100.5–102.5° (from ethyl acetate–hexane), $[\alpha]_D$ −140° (*c* 0.6, chloroform), which, although devoid of methanesulphonyloxy and hydroxyl groups, was shown (i.r. spectroscopy) to contain an NHAc group. Unlike the formation of the spiro-aziridine **3**[2], the reduction of **10** with lithium aluminium hydride is far from straightforward and is the subject of continuing investigations.

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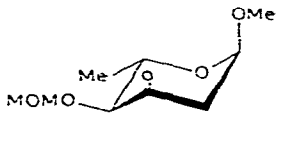
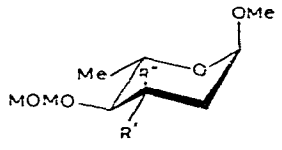
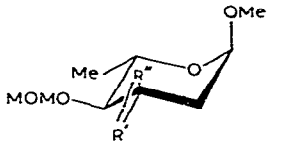


1

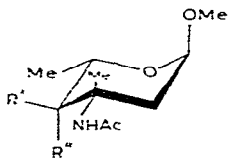
MOM = $CH_2OMe$



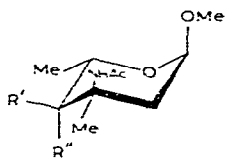
2 R′ = CN, R″ = OH
9 R′ = OH, R″ = CN
10 R′ = OMs, R″ = CN



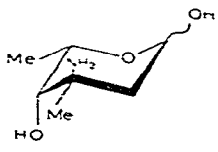
3 R′ = NH, R″ = $CH_2$
11 R′ = $CH_2$, R″ = NH



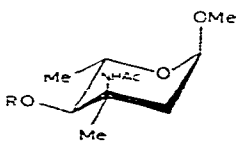
4 R′ = OH, R″ = H
5 R′ = H, R″ = OH



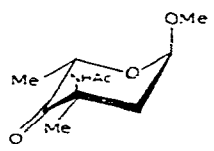
6 R′ = OH, R″ = H
7 R′ = H, R″ = OH



8



12 R = MOM
13 R = Ac



14

acetate–hexane), $[\alpha]_D$ −26° (*c* 1.7, chloroform), whose $^{13}C$ n.m.r. spectrum was indistinguishable from that of the D enantiomer* [lit.[8] m.p. 134–135°, $[\alpha]_D$ +41° (chloroform)].

Oxidation of **6** with pyridinium chlorochromate[9] in dichloromethane in the presence of 3 Å molecular sieves[10] gave **14** (87%), m.p. 149–150.5° [from ethyl acetate–light petroleum (b.p. 60–80°)], $[\alpha]_D$ −238° (*c* 1.1, chloroform), $\nu_{max}$ 1730 $cm^{-1}$ (C=O), which, on reduction with L-Selectride[11], afforded methyl 3-acetamido-2,3,6-trideoxy-3-*C*-methyl-α-L-*xylo*-hexopyranoside (**7**, 82%), m.p. 151–153° (from ethyl acetate–hexane), $[\alpha]_D$ −85° (*c* 1, chloroform). T.l.c. (dichloromethane–acetone, 1:1) readily distinguished between **6** and **7**, and showed that only traces of **6** were formed on reduction of **14**. In keeping with other glycosidic derivatives of **8**[6], p.m.r. spectroscopy revealed H-4 of **7** as a singlet. An alternative route to derivatives of **8** from a non-carbohydrate precursor has been outlined recently[12].

Regardless of the need to improve the yield of the spiro-aziridine **11**, the facility to prepare the branched-chain amino sugars **4**–**7** from a common precursor is advantageous

*The D enantiomer of **6** was recently prepared[5], along similar lines, from methyl 4,6-*O*-benzylidene-2-deoxy-α-D-*erythro*-hexopyranosid-3-ulose.

from a synthesis standpoint, and manipulation of the functional groups of **6** and **7** could lead to other sugars of biological interest.

New compounds had elemental analyses and/or spectroscopic properties in agreement with the structures assigned.

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REFERENCES

1 J. S. Brimacombe, R. Hanna, M. S. Saeed, and L. C. N. Tucker, *Carbohydr. Res.*, 100 (1982) C10–C13.
2 J. S. Brimacombe, A. S. Mengech, K. M. M. Rahman, and L. C. N. Tucker, *Carbohydr. Res.*, in press.
3 J. S. Brimacombe, R. Hanna, M. S. Saeed, and L. C. N. Tucker, *J. Chem. Soc., Perkin Trans. 1*, submitted for publication.
4 H. I. Ahmad, J. S. Brimacombe, A. S. Mengech, and L. C. N. Tucker, *Carbohydr. Res.*, 93 (1981) 288–293.
5 W. D. Weringa, D. H. Williams, J. Feeney, J. P. Brown, and R. W. King, *J. Chem. Soc., Perkin Trans. 1*, (1972) 443–446; A. W. Johnson, R. M. Smith, and R. D. Guthrie, *ibid.*, (1972) 2153–2159.
6 M. Debono and R. M. Molloy, *J. Org. Chem.*, 45 (1980) 4685–4687.
7 K. Michel, R. M. Shah, and R. L. Hamill, *Conference on Antimicrobial Agents and Chemotherapy, 17th*, New York, 1977, Abstr. 41.
8 T. That Thang, F. Winternitz, A. Olesker, A. Lagrange, and G. Lukacs, *Chem. Commun.*, (1979) 153–154.
9 E. J. Corey and J. Suggs, *Tetrahedron Lett.*, (1975) 2647–2650.
10 J. Herscovici and K. Antonakis, *Chem. Commun.*, (1980) 561–562.
11 H. C. Brown and S. Krishnamurthy, *J. Am. Chem. Soc.*, 94 (1972) 7159–7161; S. Krishnamurthy, *Aldrichimica Acta*, 7 (1974) 55–60.
12 G. Fronza, C. Fuganti, P. Grasselli, and G. Pedrocchi-Fantoni, *Tetrahedron Lett.*, (1981) 5073–5076.