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Preliminary communication

The synthesis of branched-chain amino sugars from *C*-methylene sugars: a re-assignment of structure

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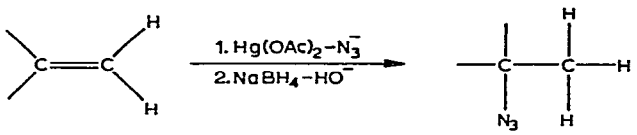
We have recently reported[1] an approach to the synthesis of branched-chain amino sugars involving treatment of a terminal alkene **1** with mercury(II) acetate in the presence of azide ion[2]. Regiospecific addition to the alkenic bond furnishes an organomercury(II) adduct which can be reduced with sodium borohydride to the alkyl azide **2**. Application of this procedure to 1,2:5,6-di-*O*-isopropylidene-3-*C*-methylene-α-D-*ribo*-hexofuranose (**3**) gave[1] a product, b.p. ~79°/0.4 mmHg, $[\alpha]_D$ –15° (*c* 1.2, chloroform), which, based on correlations made with work reported by Bourgeois[3], was tentatively assigned the *allo* configuration **4**. Subsequent investigations have shown that this assignment of structure is in error and that the product of the foregoing reactions is 3-azido-3-deoxy-1,2:5,6-di-*O*-isopropylidene-3-*C*-methyl-α-D-glucofuranose (**5**).

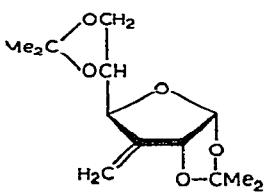


1 **2**

On partial hydrolysis with 70% acetic acid at room temperature, **5** afforded the diol **6**, m.p. 67–68.5° (from cyclohexane), $[\alpha]_D$ –1.5° (*c* 1, chloroform), which was transformed into the dimethanesulphonate **7**, m.p. 80–82° (from ethanol–light petroleum*), $[\alpha]_D$ –11° (*c* 1, chloroform), in the usual way. Hydrogenation of **7** in methanol over a platinum catalyst and *N*-acetylation of the resulting amine furnished a compound, m.p. 45–50° (from cyclohexane–carbon tetrachloride), $[\alpha]_D$ –17.5° (*c* 0.3, chloroform), containing, *inter alia*, only *one* methanesulphonyloxy group (n.m.r. evidence) and exhibiting no i.r. absorptions attributable to an NH group, although an *N*-Ac group (ν_{max} ~ 1650 cm^{-1}) was present[4,5]. This compound was identified as 3,6-acetylepimino-3,6-dideoxy-1,2-*O*-iso-

*Light petroleum refers to the fraction having b.p. 40–60°.

propylidene-5-*O*-methanesulphonyl-3-*C*-methyl-α-D-glucofuranose (**8**) on the basis of spectroscopic and analytical data; its formation by the route **7** → **9** → **10** → **8** is indicated.



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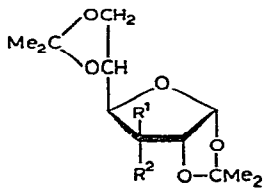
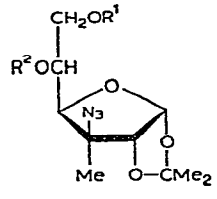
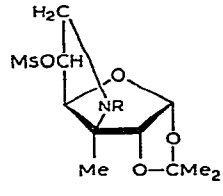


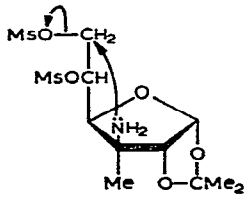
4 R^1 = Me; R^2 = N_3
5 R^1 = N_3; R^2 = Me
16 R^1 = NHAc; R^2 = Me



6 R^1 = R^2 = H
7 R^1 = R^2 = Ms
11 R^1 = Ts; R^2 = H
12 R^1 = Ts; R^2 = Ms



8 R = Ac
10 R = H



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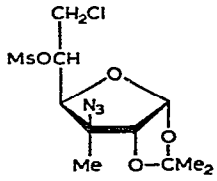

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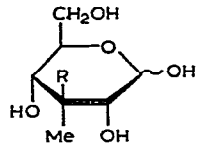

14 R = N_3
15 R = NH_2

Unequivocal evidence for the structure **8** was obtained following conversion of the diol **6** into 3-azido-3-deoxy-1,2-*O*-isopropylidene-5-*O*-methanesulphonyl-3-*C*-methyl-6-*O*-toluene-*p*-sulphonyl-α-D-glucofuranose (**12**), $[\alpha]_D$ +7° (*c* 1.1, chloroform), by way of the 6-toluene-*p*-sulphonate **11**, m.p. 100–102° (from ethanol–light petroleum), $[\alpha]_D$ +8° (*c* 1, chloroform). Catalytic hydrogenation of **12** furnished the 3,6-epimine derivative **10**, m.p. 138–139° (from ethanol–cyclohexane), $[\alpha]_D$ +40° (*c* 0.9, chloroform), with loss of the toluene-*p*-sulphonyloxy group from C-6. *N*-Acetylation of **10** then gave **8**, which was identical (m.p., and i.r. and n.m.r. spectra) with that obtained previously. Methanesulphonylation of the monosulphonate **11** also furnished a chlorine-containing compound that was identified as 3-azido-6-chloro-3,6-dideoxy-1,2-*O*-isopropylidene-5-*O*-methanesulphonyl-3-*C*-methyl-α-D-glucofuranose (**13**), m.p. 100–101° (from ether–light petroleum), $[\alpha]_D$ –68° (*c* 0.8, chloroform), since it yielded the *N*-acetylepimine derivative **8** on catalytic hydrogenation and acetylation. In view of the stereochemistry involved, participation by the amino group in the foregoing reactions can only occur with the D-*gluco* isomer, thereby providing indisputable evidence for the structure of **5** and its derivatives.

Complete hydrolysis (0.5M hydrochloric acid at 50°) of **5** gave 3-azido-3-deoxy-3-*C*-methyl-D-glucopyranose (**14**), m.p. 166–168° (dec.) (from ethanol–benzene), $[\alpha]_D$ +51° (*c* 1, methanol), which afforded 3-amino-3-deoxy-3-*C*-methyl-D-glucopyranose (**15**), m.p. 155–157° (from methanol–benzene), $[\alpha]_D$ +18 ±1° (*c* 0.5, water), on hydrogenation in methanol over a platinum catalyst. The physical constants of **15** are in reasonably close

agreement with those {m.p. 158–160°, $[\alpha]_D$ +22° (*c* 1, water)} reported[6] for a branched-chain amino sugar obtained, *inter alia*, by way of cyclization of periodate-oxidized methyl α-D-glucopyranoside with nitroethane. The chemical evidence cited above confirms the D-*gluco* configuration tentatively assigned[6,7], on the basis of chemical-shift data, to *N*-acetylated glycosides derived from **15**.

In our previous communication, the branched-chain acetamido sugar **16** (now correctly assigned) was shown to be identical with a compound prepared by Bourgeois[3] using an alternative route. However, it is now clear that a number of the branched-chain amino sugars reported in Bourgeois' communication must be accorded the D-*gluco* configuration*.

New compounds gave elemental analyses and spectroscopic data compatible with the structures assigned.

ACKNOWLEDGMENTS

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REFERENCES

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Added in proof: Dr. Bourgeois has kindly informed us that he has reached the same conclusion with regard to the structures of the branched-chain amino sugars reported in his original communication (ref. 3).