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Preliminary communication

An approach to the synthesis of branched-chain amino sugars from *C*-methylene sugars

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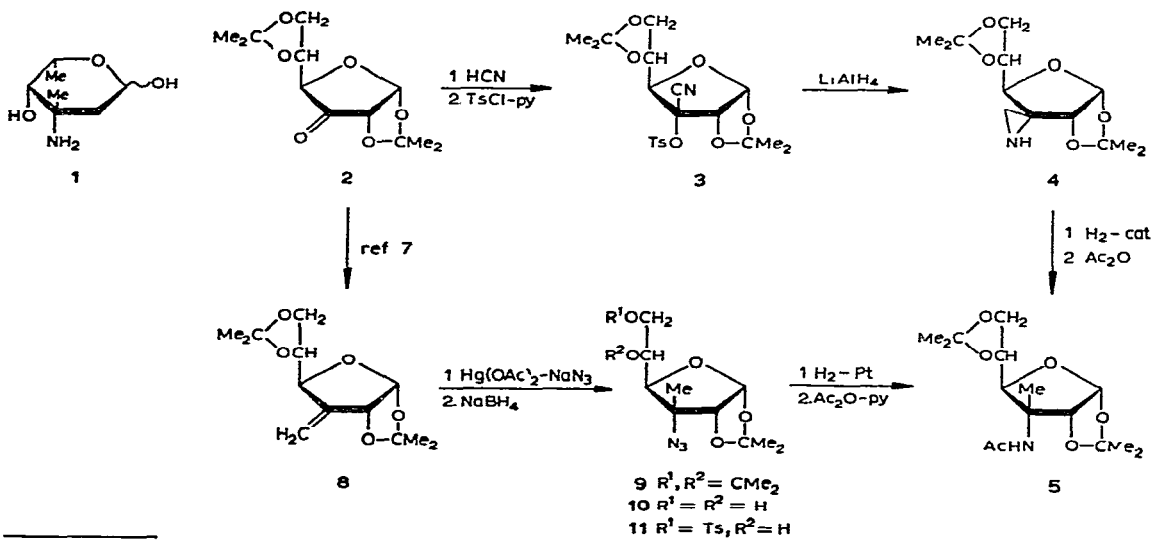
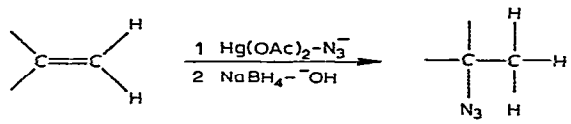
The introduction into sugars of an amino group at a tertiary carbon atom, such as occurs in the antibiotic sugar vancosamine[1] (3-amino-2,3,6-trideoxy-3-*C*-methyl-L-*lyxo*-hexose; **1**), poses an intriguing synthetic problem Although such amino groups have been introduced[2] into the pyranose ring by reduction of the nitro sugars resulting from cyclization of "dialdehydes" with nitroethane, considerable difficulties attend the assignment of structure to the various stereoisomers obtained[3] For example, a structure has been assigned to only one of the eight possible stereoisomers arising from cyclization of periodate-oxidized methyl α-L-rhamnopyranoside with nitroethane[4]. A method that limits the number of stereoisomers formed would represent a considerable advance Such a method has been reported recently by Bourgeois[5], who prepared 3-acetamido-3-deoxy-1,2 5,6-di-*O*-isopropylidene-3-*C*-methyl-α-D-allofuranose (**5**), m p 103 5–105°, $[\alpha]_D$ −19° (chloroform), by the sequence **2**→**3**→**4**→**5***



*Although the structure assigned to **5** by Bourgois[5] is assumed to be correct in this communication, a rigorous proof of the stereochemistry at C-3 has yet to be provided for **5** and its progenitors,

We have obtained **5** by a different route, based on the reaction of a terminal alkene **6** with mercuric acetate in the presence of azide ion in 50% aqueous tetrahydrofuran[6]. Regiospecific addition to the alkenic bond leads to an adduct which can be reduced with sodium borohydride to the alkyl azide **7***.



6 7

Application of this sequence of reactions to 1,2 5,6-di-*O*-isopropylidene-3-*C*-methylene-α-D-*ribo*-hexofuranose[7] (**8**) afforded a single product, b p. ~79°/0 4mmHg, $[\alpha]_D$ −15° (*c* 1 2, chloroform), which was isolated after chromatography on silica gel While n m r. and i r spectroscopy readily confirmed the general structural features of this product, Bourgeois' results[5] allowed its stereochemistry to be assigned as 3-azido-3-deoxy-1,2 5,6-di-*O*-isopropylidene-3-*C*-methyl-α-D-allofuranose (**9**) Thus, catalytic reduction of the azido group and *N*-acetylation of the resulting amine transformed **9** into **5**, m p 106–108°, $[\alpha]_D$ −19° (*c* 1, chloroform), which was identical with the compound obtained by the aziridine route

It appears that initial attack on the alkenic bond of **8** occurs preferentially from the *exo*-direction with respect to the bicyclic ring-system, requiring subsequent attack of azide ion at C-3 from the *endo*-direction However, it is not certain whether steric or other factors control the stereochemistry in the first step, and work to establish this point is in progress Nevertheless, the method appears to hold promise for the synthesis of branched-chain amino sugars, particularly as a number of 3-*C*-methylene compounds related to **8** are available from the corresponding hexofuranos-3-uloses

Partial hydrolysis of the azide **9** with 70% acetic acid furnished 3-azido-3-deoxy-1,2-*O*-isopropylidene-3-*C*-methyl-α-D-allofuranose (**10**), m p 67–68 5°, $[\alpha]_D$ −1 5° (*c* 1, chloroform), from which a monosulphonate **11**, m p 100–102°, $[\alpha]_D$ +8° (*c* 0 9, chloroform), was obtained following treatment with toluene-*p*-sulphonyl chloride (1 mol) in pyridine Both **10** and **11** should be amenable to synthetic manipulations of the type carried out with related systems[8]

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

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*The addition reaction with alkenes is normally carried out at 50–90°. There is no danger from the formation of mercuric azide *in situ* if the instructions given in reference 6 are followed.

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