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Preliminary communication

Nitroxide spin-labelling of amino and carboxyl groups of monosaccharide derivatives, mediated by dicyclohexylcarbodiimide

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Although the major thrust of our studies of sugars by the spin-labelling method[1] has thus far been directed to polysaccharide systems[2], there is a pressing need for further methods[3] whereby monosaccharides can be covalently spin-labelled. In the present Communication, we report the use and limitations of dicyclohexylcarbodiimide (**1**) for coupling sugars and piperidin-1-oxyl derivatives *via* an amide linkage.

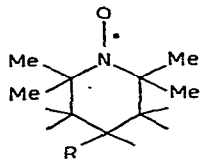
In a typical reaction, methyl 3,4,6-tri-*O*-acetyl-2-amino-2-deoxy-β-D-glucopyranoside[4] (**2**) was treated with 4-carboxy-2,2,6,6-tetramethylpiperidin-1-oxyl (**3**, 1.1 molar equiv.) and **1** (1.2 molar equiv.) in dry dichloromethane for 1 h at 0°, and subsequently for 16 h at 20°. Conventional processing[5], followed by column chromatography on alumina, afforded, in addition to the anticipated product (**4**)* {52% yield, m.p. 139°, $[\alpha]_D^{25}$ +6.8° (*c* 1.6, $CHCl_3$)}, the *N*-acylurea derivative **5** (21% yield, m.p. 185°).

In like fashion, two products were formed from the reaction of 4-amino-2,2,6,6-tetramethylpiperidin-1-oxyl (**6**) with uronic acids. Thus, 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranuronic acid[6] (**7**) reacted with **6** in the presence of **1** to give the *N*-acylurea **8** in 12% yield {m.p. 132°, $[\alpha]_D^{25}$ −94.5° (*c* 0.5, $CHCl_3$)}, along with the desired product **9** in 47% yield; m.p. 167°, $[\alpha]_D^{25}$ −100.9° (*c* 1.1, $CHCl_3$).

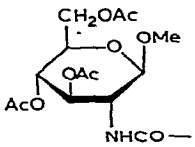
Although the yields of spin-labelled sugars obtained in this way are acceptable, the formation of *N*-acylurea by-products, which is characteristic[7] of dicyclohexylcarbodiimide-mediated coupling-reactions involving sterically hindered reactants (in this case, the nitroxides **3** and **6**), constitutes a limitation to this approach to spin-labelling of sugars.

We routinely use high-resolution ^1H- and ^{13}C-n.m.r. spectroscopy to characterize spin-labelled sugars, following reduction[8] with aqueous sodium dithionite ($Na_2S_2O_4$).

*All compounds reported herein had elemental, microanalytical data in accord with the structures assigned.



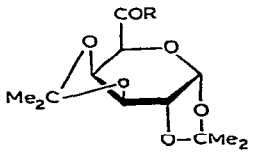
3 R = $-CO_2H$



4 R =

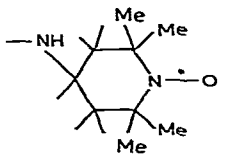
5 R = $-CON(C_6H_{11})CONHC_6H_{11}$

6 R = $-NH_2$



7 R = OH

8 R = $-N(C_6H_{11})CONHC_6H_{11}$



9 R =

ACKNOWLEDGMENT

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