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Preliminary communication

Saccharide 1,3,4-oxadiazole analogs. A novel method for cyclization of saccharide aroylhydrazides

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1,3,4-Oxadiazoles are compounds of significant biological and industrial importance[1,2]. In one approach, saccharide 1,3,4-oxadiazole analogs are synthesized by the action of acid chlorides or acid anhydrides on the tetrazole derivative[3]. Other approaches for their synthesis are by oxidative cyclization of the acetyl derivatives of *aldehydo* sugar aroylhydrazones using mercuric oxide and iodine[4], and from aldaric bis(aroylhydrazide) acetates by treatment with phosphoryl chloride[5], triethyl orthoformate[6] or thionyl chloride[7].

We now report the synthesis of 2-(D-*glycero*-D-*gulo*-1,2,3,4,5,6-hexa-*O*-acetylhexitol-1-yl)-5-phenyl-1,3,4-oxadiozole (3) by the simultaneous acetylation–cyclization of D-*glycero*-D-*gulo*-heptonic benzoylhydrazide (1) by a novel method using trifluoroacetic acid and acetyl bromide, reagents convenient for the acetylation of acid- and base-labile compounds[8]. The methods previously reported[4–7] implied protection of the hydroxyl groups of the saccharide residue by acylation, before cyclization. Trials to protect the hydroxyl groups of 1 by acetylation or benzoylation by the normal acylating agents resulted in the removal of the hydrazide residue and separation of 1-acyl-2-benzoylhydrazine. However, on stirring compound 1 (0.1 g) with trifluoroacetic acid (5 mL) at 0° with dropwise addition of acetyl bromide (2 mL), and then keeping the solution for 25 h at room temperature and evaporating it under diminished pressure, the last traces of acids being removed by repeated addition and evaporation of toluene, compound 3 was obtained. Its i.r. spectrum lacked the NH and CONH absorption of the parent compound 1, and showed the carbonyl ester absorption at 1755–1750 cm^{-1}, and new bands at 1355 and 940 cm^{-1} characteristic[9,10] of the oxadiazole ring. Its n.m.r. spectrum (60 MHz) showed the presence of six acetyl groups at δ 1.92–2.25. The sugar protons appeared as a multiplet at δ 1.92–2.25, and the phenyl protons, as a multiplet at δ 7.20–8.30. The imino proton signals, at δ 10.02 and 10.50, of the starting material 1 were absent for compound 3. Its mass spectrum showed the molecular ion peak at *m/z* 578, in agreement with the molecular formula $C_{26}H_{30}N_2O_{13}$. The base peak appeared at *m/z* 176, corresponding to 2-(hydroxymethyl)-5-phenyloxadiazole (4). The

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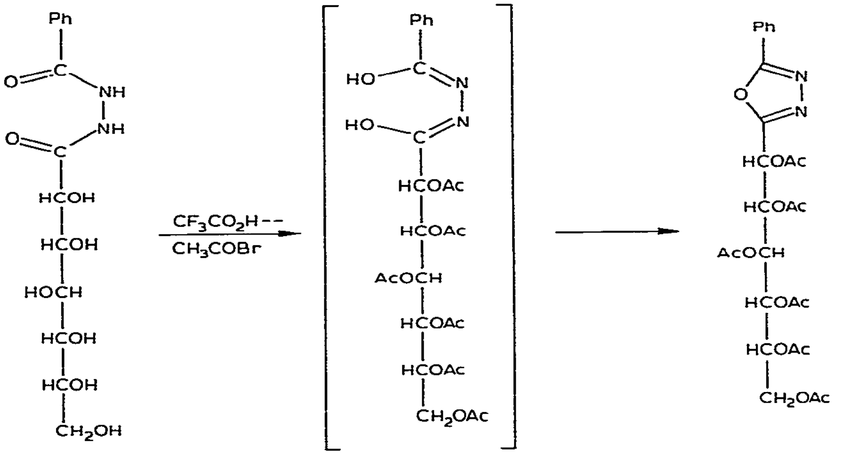

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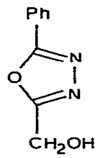
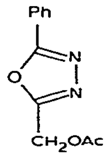


4

m/z 176 (100)



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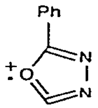
m/z 218 (95)



6

m/z 145 (43)

strong peaks at *m/z* 218 [corresponding to 2-(acetoxymethyl)-5-phenyloxadiazole (5)] and *m/z* 145 [corresponding to the 5-phenyloxadiazole ion (6)] confirmed the presence in compound 3 of the 1,3,4-oxadiazole ring (which may be formed *via* the dienol acetate intermediate 2).

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