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Preliminary communication

A novel route to terminal chlorodeoxy sugars

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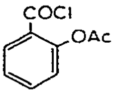
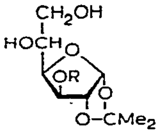
Several methods[1,2] have been described for the syntheses of chlorodeoxy sugars and nucleosides, many of which have considerable chemical and biological interest. We now describe a new synthesis of terminal chlorodeoxy sugars based on the anomalous reaction of acetylsalicyloyl chloride (1) with diols in the absence of hydrogen chloride acceptors[3].

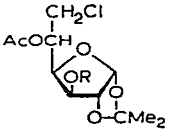
Treatment of 3-*O*-acetyl-1,2-*O*-isopropylidene-α-D-glucofuranose[4] (2) {m.p. 120–121°, $[\alpha]_D^{20}$ −21° (*c* 3.2, water)} with 1 in anhydrous *p*-dioxane at room temperacute for 48 h, followed by alumina column chromatography, gave 60–85% of 3,5-di-*O*-acetyl-6-chloro-6-deoxy-1, 2-*O*-isopropylidene-α-D-glucofuranose** (5) {m.p. 117–118°, $[\alpha]_D^{20}$ +4° (*c* 7.5, chloroform)}, which was identical (m.p., m.m.p., $[\alpha]_D$, and i.r. and p.m.r. spectra) with 5 prepared from 6-chloro-6-deoxy-1,2:3,5-di-*O*-isopropylidene-α-D-glucofuranose[1] by mild hydrolysis (80% acetic acid) followed by acetylation.



1



2 R = Ac
3 R = Ts
4 R = CONHPh



5 R = Ac
6 R = Ts
7 R = CONHPh

Similarly, syrupy 1,2-*O*-isopropylidene-3-*O*-toluene-*p*-sulphonyl-α-D-glucofuranose[5] (3) {$[\alpha]_D^{20}$ −12° (*c* 3.16, chloroform), homogeneous on t.l.c.} and 1,2-*O*-isopropylidene-3-*O*-phenylcarbamoyl-α-D-glucofuranose {4, prepared by the action of phenyl isocyanate–pyridine on 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose, followed

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[**] Satisfactory elemental analyses were obtained for all new compounds described in this communication.

by mild hydrolysis of the 5,6-*O*-isopropylidene group; m.p. 87–88°, $[\alpha]_D^{20}$ −6° (*c* 14, ethanol)}were converted into 5-*O*-acetyl 6-chloro-6-deoxy derivatives **6** {m.p. 75–76°, $[\alpha]_D^{20}$ −43° (*c* 0.56, chloroform), 75%} and **7** {m.p. 138–139°, $[\alpha]_D^{20}$ −47° (*c* 6.5, chloroform), 60–80%}, respectively.

In addition to **5** and **6**, in some experiments, small amounts of the 5,6-diacetates of **2** and **3**, respectively, were formed and were readily isolable by column chromatography on alumina. Furthermore, the reaction of **1** with **4** also gave the 6-acetate (max. yield 30%).

The H-6 resonances (100 MHz, ~15% solutions in $CDCl_3$, HMDS as internal standard) of **5** (τ6.18, *q*, $J_{5,6}$ 3.0 Hz, H-6; τ6.33 *q*, $J_{5,6'}$, 4.7 Hz, H-6'; $J_{6,6'}$ 12.5 Hz) occurred at higher field than the signals for the corresponding protons of 3,5,6-tri-*O*-acetyl-1,2-*O*-isopropylidene-α-D-glucofuranose (τ 5.56, *q*, $J_{5,6}$ 2.5 Hz, H-6; τ 6.04, *q*, $J_{5,6'}$ 6.0 Hz, H-6'; $J_{6,6'}$ 12.5 Hz) and illustrate the known deshielding effects of the various substituents[6]

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