Synthesis of 3,4-Dideoxy-3,4-*C*-cyanomethylene Pyranosides: A New Class of Cyclopropanated Sugars

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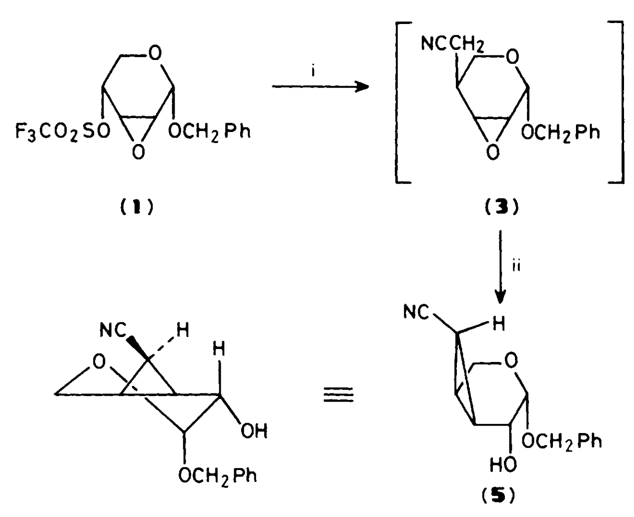
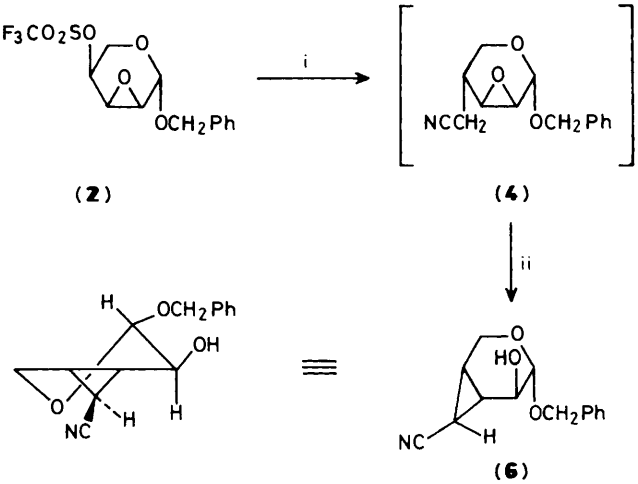
A new class of 3,4-cyclopropanated sugars (**5**) and (**6**) has been synthesized by reacting the sugar triflates (**1**) and (**2**) with the nitrile-stabilized carbanion of acetonitrile.

Although a number of 2,3-cyclopropanated sugars have been synthesized,[1,2] no example of 3,4-cyclopropanated sugars could be found despite careful sifting of the literature. We now report a novel approach to these compounds which not only have biochemical interest but can also serve as chiral templates in the synthesis of natural products.

The previous successes in the synthesis of a number of carbohydrate derivatives *via* displacement of the trifluoromethanesulphonyloxy (triflyl) group[3,4] prompted us to investigate the similar reaction with a nitrile stabilized carbanion.[5] When the known[3] benzyl 4-*O*-trifluoromethanesulphonyl-2,3-anhydro-α-D-ribopyranoside (**1**) and benzyl 4-*O*-trifluoro-



Scheme 1. *Reagents*: i, LiCH$_2$CN, HMPA, THF; ii, LDA.



Scheme 2. *Reagents*: i, LiCH$_2$CN, HMPA, THF; ii, LDA.

methanesulphonyl-2,3-anhydro-β-L-ribopyranoside (**2**) were treated with lithio acetonitrile [obtained from MeCN and lithium di-isopropylamide (LDA)], in the presence of an additional equivalent of LDA, 3,4-dideoxy-3,4-(*exo*-*C*-cyano)-methylene-β-L-arabinopyranoside (**5**) and benzyl 3,4-dideoxy-3,4-(*exo*-*C*-cyano)-methylene-α-D-arabinopyranoside (**6**) were isolated in 53 and 49% yield respectively.

In a typical experiment, acetonitrile (3.1 mmol) was added to a solution of LDA (3.3 mmol) in dry tetrahydrofuran (THF) at −78 °C under N$_2$, followed by hexamethylphosphoramide (HMPA, 3.3 mmol) after 15 min. A solution of the triflate (**1**) or (**2**), (3.0 mmol) in THF was pre-cooled to −78 °C and transferred through a double-ended needle to the above solution. After 10 min a solution of LDA (3.3 mmol) in THF, and HMPA (3.3 mmol) were successively added. After stirring at −78 °C for an additional period of 15 min, the reaction was quenched by adding a saturated aqueous solution of ammonium chloride. The solvent was evaporated *in vacuo*, and the residue was partitioned between water and CH$_2$Cl$_2$. After usual work-up the crude product was purified on a column of silica gel using n-hexane–ether (1 : 2) as eluent, to afford the pure cyclopropanated compounds (**5**)[†] or (**6**).[‡] The formation of the products is explained by initial displacement of the triflyl group by the lithio acetonitrile to give the intermediate cyanomethyl derivative (**3**) or (**4**) followed by the alkylation of their monolithiated derivatives, with the *trans*-oriented oxirane.

The cyano group on the newly formed chiral centre was exclusively *exo* oriented as shown by the coupling constant $J_{3,6} = J_{4,6}$ 4.9 Hz,[1] in both cases. The two different conformations $^0H_1$ and $^1H_0$ can be safely assigned to the compounds (**5**) and (**6**) based on the chemical shift of H-1.[6]

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[†] *Selected data* for (**5**): white needles from diethyl ether–n-hexane, m.p. 91—92 °C; $[\alpha]_D^{20}$ +10.7 (*c* 1, CHCl$_3$); i.r. (KBr): 3410 (OH), 2214 cm^{-1} (CN); field desorption mass spectrometry (f.d.m.s.): *m/z* = 245; ^{1}H n.m.r. (400 MHz, CDCl$_3$): δ 7.36 (m, 5H, Ar-H), 4.63 (dd, 2H, J_{gem} 11.6 Hz, OCH_2Ph), 4.68 (d, 1H, $J_{1,2}$ 5.1 Hz, H-1), 4.03 (dd, 1H, $J_{5',4}$ 3 Hz, $J_{5',5}$ 11.9 Hz, H-5'), 3.73—3.74 (m, 2H, H-5 and H-2), 2.71 (d, 1H, $J_{OH,2}$ 10.1 Hz, O*H*, exchanges with D$_2$O), 1.77 (dd, 1H, $J_{3,6}$ 4.9 Hz, $J_{3,4}$ 9.5 Hz, H-3), 1.72 (m, 1H, H-4), 1.31 (t, 1H, $J_{6,3} = J_{6,4}$ 4.9 Hz, H-6); ^{13}C n.m.r. (100 MHz, CDCl$_3$) δ 120.4 (CN), 93.0 (C-1), 70.1 (CH$_2$Ph), 62.9 (C-2), 55.1 (C-5), 23.6 (C-3), 19.3 (C-4), 5.2 (C-6); satisfactory elemental analysis obtained.

[‡] *Selected data* for (**6**): colourless needles from ether–n-hexane, m.p. 85—87 °C; $[\alpha]_D^{20}$ +8 (*c* 1, CHCl$_3$); i.r. (KBr): 3500 (OH), 2210 cm^{-1} (CN); f.d.m.s.: *m/z* = 245; ^{1}H n.m.r. (400 MHz, CDCl$_3$ saturated with D$_2$O): δ 7.37 (m, 5H, Ar-H), 4.61 (dd, 2H, J_{gem} 11.7 Hz, -OCH_2Ph), 4.19 (d, $J_{1,2}$, 5.6 Hz, H-1), 4.07 (d, 1H, $J_{5',5}$ = 12.2 Hz, H-5'), 3.97 (dd, 1H, $J_{5,4}$ 3Hz, $J_{5',5'}$ 12.2 Hz, H-5), 3.71 (d, 1H, $J_{2,1}$ 5.7 Hz, H-2), 1.71-1.78 (overlapping multiplets, 2H, H-3 and H-4), 1.65 (t, 1H, $J_{6,3} = J_{6,4}$ 4.9 Hz, H-6); ^{13}C n.m.r. (100 MHz, CDCl$_3$) δ 120.3 (CN), 102.1 (C-1), 70.5 (-OCH$_2$Ph), 65.8 (C-2), 61.7 (C-5), 24.2 (C-3) 19.6 (C-4), 5.3 (C-6); satisfactory elemental analysis obtained.

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