Preliminary communication

A new synthesis of the cyclitol ring-system

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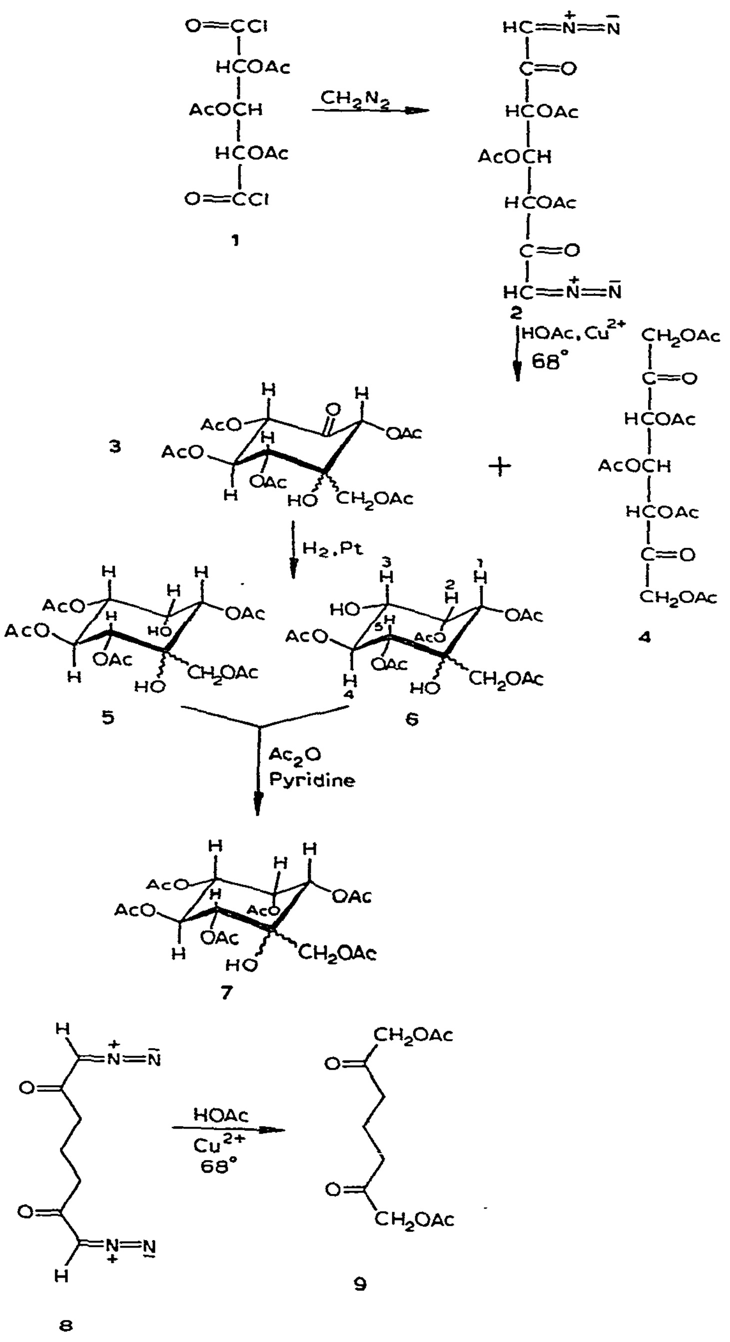
Delta-dicarbonyl monosaccharides constitute a class of sugars for which few specific examples are known, either from natural or synthetic sources. During a synthesis designed to give one such δ-dicarbonyl monosaccharide, *xylo*-2,6-heptodiulose, a unique cyclization of a bisdiazomethyl ketone (2) to a cyclose (3) occurred.

Tri-*O*-acetyl-xylaryl dichloride[2] (1), was converted with diazomethane into the light yellow, crystalline, bisdiazomethyl ketone (2), (60%, m.p. 118–120°)★ A solution of the diketone in glacial acetic acid containing 0.1% of cupric acetate was heated to 68° until evolution of nitrogen was complete (~ 45 min). A white crystalline solid, isomeric with the 2,6-heptodiulose pentaacetate 4, crystallized when the reaction mixture was cooled to room temperature (35%, m.p. 239–241°). This compound gave a positive Scherer's test for a cyclitol (by a spot-test modification[3]), and its i.r. and mass spectra were consistent with a structure such as 3; i.r. (KBr disc) 3515 (s, O–H) and 1725 cm^{-1} (s and broad, C=O). No molecular ion $[M^{\ddagger}]$ (*m/e* 418) was observed in the mass spectrum of 3 but a strong $[M^{\ddagger} -42]$ peak resulted from the loss of the elements of ketene. The very low solubility of 3 in common organic solvents precluded the recording of its n.m.r. spectrum.

Catalytic hydrogenation of 3 in glacial acetic acid for 25 h at 50° over platinum black yielded two white crystalline compounds, 5 (60%, m.p. 160–162°) and 6 (5%, m.p. 209–210°), separated by fractional crystallization from ethanol. Presumably compound 6 is derived from 5 by migration of one acetyl group. The i.r. spectra of 5 and 6 (KBr discs) were similar, and both showed broad absorptions characteristic of O–H and C=O stretching vibrations; for 5 3440 (s) and 1740 cm^{-1} (s), for 6 3460 (s) and 1725 cm^{-1} (s). The n.m.r. spectrum of 6 ($CDCl_3$, 220 MHz) firmly established the conformation of all of the ring protons for compounds 3 and 5–7; δ 2.04, 2.11, 2.18

★ All new compounds gave correct elemental analyses and showed optical rotations of zero.



(three acetyl groups), δ 2.08 (two acetyl groups), 2.86 (s, O–H), 3.82 and 3.90 (each d, 1, J 11.0 Hz, CH_2–O), 5.05 (d, 1, $J_{1,2}$ 3.5 Hz, H–1), 5.16 (d, 1, H–5), 5.53 (d of d, 1, $J_{3,4}$ 10.0 Hz, $J_{4,5}$ 10.0 Hz, H–4), 5.68 (d of d, 1, $J_{2,3}$ 3.5 Hz, H–2). Both 5 and 6 underwent acetylation to give a common cyclitol hexaacetate 7, (m.p. 189–191°). The hydrogenation reaction-mixture also afforded the hexaacetate 7 directly (80%). The configuration at the carbon atom bearing the tertiary hydroxyl group in compounds 3 and 5–7 is unknown, but is presently being investigated.

The crystalline heptodiulose pentaacetate 4 (5%, m.p. 90–92°) was obtained after column chromatography (silica gel) of the mother liquors from the acetolysis reaction; i.r. (KBr disc) no O–H stretching vibration, 1750 cm^{-1} (s, C=O). The n.m.r. spectrum of 4 ($CDCl_3$, 60 MHz) was uncomplicated; δ 2.15 (a single peak from the five acetyl groups), 4.8 (s, 4, terminal CH_2–), 5.48 (d, 2, $J_{3,4} = J_{4,5}$ 4 Hz, H–3 and H–5), 5.75 (t, 1, $J_{3,4}$ 4 Hz, H–4). Compound 4 is the first reported example of a 2,6-heptodiulose.

The success of the unique cyclization, perhaps arising from a dicarbene generated from 2, results in part from the presence of the acetoxyl groups along the carbon chain. When 1,7-bisdiazo-2,6-heptanedione[4] (8), which lacks the acetoxyl groups, was treated with gracial acetic acid and cupric acetate, a high yield (70%) of the acyclic diketone 9 precipitated directly from the reaction mixture.

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