

THE CHEMISTRY OF DELTA DICARBONYL SUGARS.

THE BASE CATALYZED CYCLIZATION OF A xylo-HEPTO-2,6-DIULOSE TO AN UNUSUAL CYCLOHEXENONE¹

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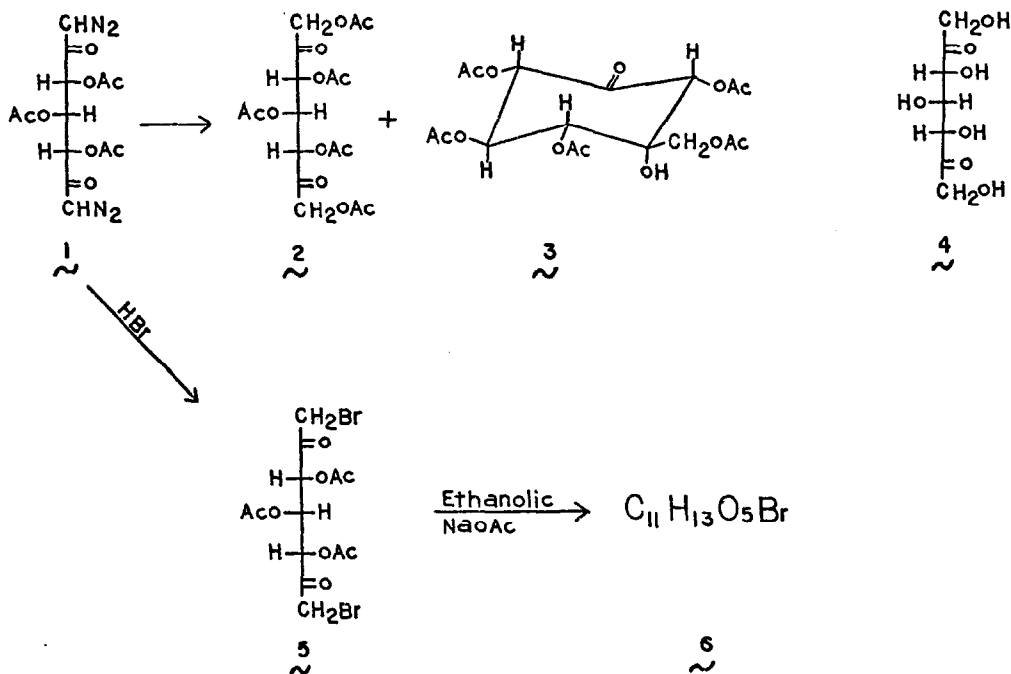
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In 1968 Kiely and Fletcher reported the base catalyzed cyclization of the simple, un-protected, δ -dicarbonyl monosaccharide, D-xylo-hexos-5-ulose, to the all trans 2,4,6/3,5-pentahydroxycyclohexanone^{3,4}. This transformation served as a chemical model for the cyclization step in the biosynthetic conversion of D-glucose 6-phosphate to L-myo-inositol 1-phosphate, and also pointed to the potential use of this class of monosaccharides as synthetic precursors to the cyclohexanone ring system. In anticipation of applying this intramolecular aldol condensation to similar systems, we undertook the synthesis of a seven carbon δ -dicarbonyl monosaccharide, i.e., xylo-hepto-2,6-diulose (4). A key step in the preparation of 4 was to have been the addition of acetic acid to the carbene generated from the bisdiazomethyl ketone 1. The expected acyclic pentaacetate (2) was obtained in only 10% yield while a unique penta-acetylated cyclose (3), formed by a carbene initiated cyclization, was the major isolated product (35-40%)^{5,6}. We now report the results of our most recent efforts to prepare 2.

Treatment of an ether suspension of the diketone 1 with gaseous hydrogen bromide gave 5 as the only detectable organic product, m.p. 84-85°; $\nu_{\text{max}}^{\text{KBr}}$ 1750 cm⁻¹ (C=O) but no O-H stretching; n.m.r. signals (CDCl₃, 220 MHz) at δ 2.08 (s, three acetyl groups), 4.13 (s, 4, CH₂Br), 5.64 (d, 2, J_{3,4} = J_{4,5} 4.0 Hz, H-3 and H-5), and 5.70 (t, 1, J_{3,4} 4.0 Hz, H-4). The mass spectrum of 5 showed a strong [M + 1] two bromine isotropic cluster at 459, 461, and 463 mass units.

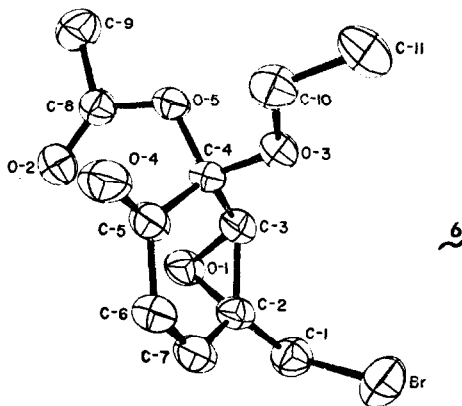
Stirring an ethanolic solution of the dibromide (5) with suspended anhydrous sodium acetate for 15-30 minutes at room temperature resulted in the formation of a monobromo compound 6 (C₁₁H₁₃O₅Br, m.p. 78-80°) isolated as the predominant product (50%) after purification by

silica gel column chromatography. However, none of the acyclic diketone **2** was detected in the reaction mixture. The essential structural features of **6** were revealed in its i.r. and n.m.r. spectra; $\nu_{\text{max}}^{\text{KBr}}$ 1750 (ester C=O) and 1700 cm^{-1} (α, β -unsaturated C=C): n.m.r. signals (CDCl_3 , 220 MHz) at δ 1.18 (t, 3, J 7.0 Hz, OCH_2CH_3), 2.08 (s, 3, one acetyl group), 3.52 and 3.77 (each was an unresolved multiplet from the nonequivalent methylene protons of OCH_2CH_3), 3.52 (s, 2, isolated CH_2Br), 4.22 (s, 1, oxirane H), 6.15 (d, 1, J 10.0 Hz, vinyl H) and 7.23 (d, 1, J 10.0 Hz, α -keto vinyl H). No molecular ion or $[\text{M} + 1]$ peak was observed in the mass spectrum of **6**, but the spectrum did have a number of major peaks resulting from ions containing single bromine atoms; i.e., $[\text{M}-29]$, $[\text{M}-43]$, and $[\text{M}-59]$ corresponding to the loss of ethyl, acetyl, and acetoxy fragments respectively. The structure of **6** was finally resolved by x-ray crystallography.

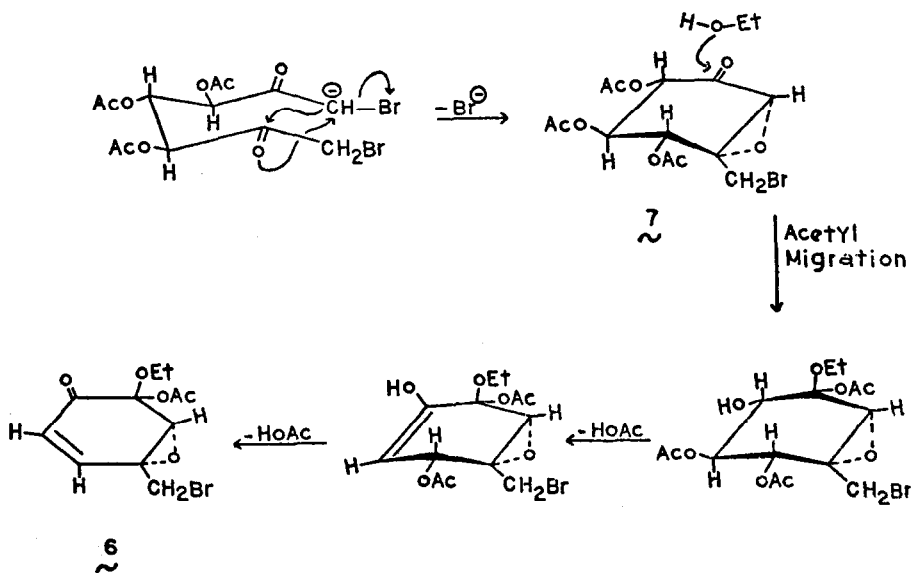


Triclinic crystals of **6** were obtained from 95% ethanol. The space group is $\bar{P}1$ with two molecules per unit cell of dimensions $a = 9.718(4)$, $b = 10.683(11)$, $c = 7.926(16) \text{ \AA}$, $\alpha = 118.86(9)$, $\beta = 98.55(14)$ and $\gamma = 109.10(5)^\circ$. Three-dimensional intensity data were collected on an automated diffractometer by use of nickel-filtered copper radiation, a scintillation detector, and a θ - 2θ scanning technique. All 2059 independent reflections

with $2\theta \leq 128^\circ$ were measured. A trial structure for 6 was obtained by the heavy-atom method and was refined by least-squares. Final cycles of refinement included positional and anisotropic temperature parameters for all nonhydrogen atoms, and a secondary extinction parameter. The final R index ($(\Sigma ||F_o| - |F_c||) / \Sigma |F_o|$) based on all reflections is 0.076.



The mechanism we propose for the transformation of 5 to 6 involves initially, generation of a carbanion from which arises a neutral but transient oxirane intermediate 7. There then



follows sequentially, nucleophilic attack of 7 by a mole of solvent, an acetyl migration step, and finally elimination of two moles of acetic acid to give 6. The conversion of 5 to 6 represents another illustration of the remarkable tendency for xylo configurational δ -dicarbonyl monosaccharides to undergo cyclization to homocyclic six-membered rings.

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References and Footnotes

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