

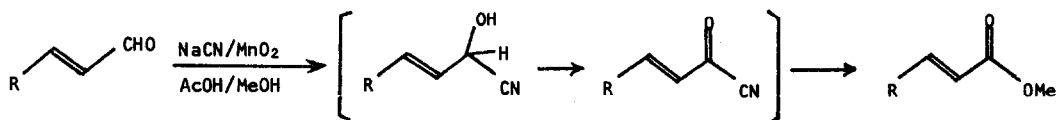
COREY OXIDATION OF AN ALDEHYDO 2,3-DIDEOXY-HEX-2-ENOSE TRIACETATE¹

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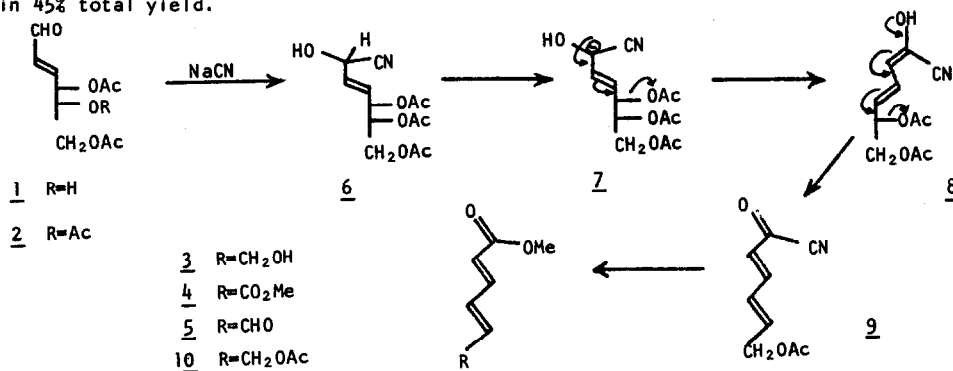
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In a recent communication from this laboratory it was reported that the unsaturated aldehyde 1 could be obtained from triacetyl glucal by hydrolysis with boiling aqueous dioxan². This reaction has been found to be general for acetylated glycols³, and in exploring prospects for the aldehydes so obtained, it was noted that the aldonic acids derivable from them would contain an α,β -unsaturated carboxyl grouping reminiscent of that found in ascorbic acid⁴, and other carbohydrates of biological importance⁵. A method for oxidation of 1 seemed to be the elegant process developed recently by Corey⁶ and summarised in Scheme I. However, when applied to the aldehyde, the oxidation took a course (Scheme II) which appears to have been triggered by the presence of an acetoxy function at the γ -position.



The fully acetylated aldehyde 2 (1.0 g; 3.7 mmole) was stirred with a mixture of sodium cyanide (0.8 g; 16.3 mmole), acetic acid (3 ml; 3.7 mmole) and manganese dioxide (5.75 g; 66.0 mmole) in methanol for twelve hours at room temperature. Filtration and evaporation of the methanol afforded a residue which was partitioned between ether and water. The ether phase yielded a syrup which was fractionated on a silica column to give two crystalline substances 3 and 4 in 45% total yield.



For 3: mp 55-56°C. $C_7H_{10}O_3$. M^+ $m/e=142$ (Calcd: C, 59.15; H, 7.05. Found: C, 59.02; H, 6.83). λ_{max}^{256} . $\mu_{max}^{-1620, 1650, 1705, 3300\text{ cm}^{-1}}$. NMR ($CDCl_3$, TMS) τ 6.92 (OCH₃); \sim 5.65 (H-6, H¹-6); 4.1 (H-2); 3.2-3.8 (H-4, H-5); 2.6 (H-3) $J_{23}=15$. For 4: mp 157-159°C. $C_8H_{10}O_4$ (Calcd: C, 56.5; H, 5.88. Found: C, 56.8; H, 5.73). λ_{max}^{257} . $\mu_{max}^{-1610, 1710\text{ cm}^{-1}}$. NMR ($CDCl_3$, TMS) τ 6.2 (OCH₃); 3.9 (H-2, H-5); 2.6 (H-3, H-4). $J_{23}=J_{45}=13\text{ Hz}$; $J_{24}=J_{35}=3\text{ Hz}$.

The hydroxyester 3 was hydrogenated to give methyl 6-hydroxyhexanoate, an authentic sample of which was prepared from 6-hexanolactone by methanolysis. Compound 3 was a primary reaction product since it could be obtained in a pure state by treatment of 2 with sodium cyanide in methanol for two hours. On oxidation with manganese dioxide in methanol 3 gave an isolable aldehyde 5 (τ 0.13, $J_{12}=6\text{ Hz}$) which with the Corey reagents⁶ then gave the diester 4.

This sequence permits a rationalisation for the course of oxidation of 2. The cyanohydrin 6 instead of being oxidised (c.f. Scheme 1) is deprotonated to give a stabilised "acyl carbanion equivalent"⁷ 7 such as that operative in a benzoin condensation. The carbanion 7 is dissipated by loss of the γ -acetoxy group and the resulting dienol 8 ketonises by ejection of the δ -acetoxy group. The resulting α -ketonitrile 9 is then methanolised to give ester 10 the acetate group of which is hydrolyzed to give 3. The latter suffers the fate described in the last paragraph.

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