

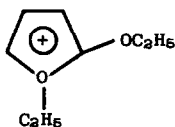
BASE CLEAVAGE OF 5-CHLORO-2-PENTANONE ACETALS

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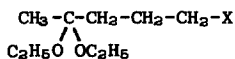
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The difference in rate of alkaline hydrolysis of 1,1-diethoxy-4-chlorobutane and 1,1-diethoxy-5-chloropentane has been ascribed (1) to anchimeric assistance of an ethoxyl group, as in I. There was, however, no supporting evidence from the reaction products. Hughes and Speakman (2) have found that in the reaction of the dimethyl acetal of 2,3,5-tri-O-benzyl-4-tosyl-D-ribose with tetrabutylammonium benzoate in N-methylpyrrolidone, transfer of a methoxyl group to C-4 occurred, thus convincingly demonstrating methoxyl participation.



I



II X = Cl

III X = OOCCH₃

We allowed 1-chloro-4,4-diethoxypentane (II) and tetraethylammonium acetate, obtained as (approximately) a dihydrate, to react in N-methylpyrrolidone at 70°. The former compound was prepared in 62% yield from 5-chloro-2-pentanone (3); b.p. 85-88°/20 mm, n_D²⁵ 1.4323; found 55.6% C, 9.5% H, 18.6% Cl, 44.2% OC₂H₅. IR-bands at 943, 1055, 1073, 1088 and 1130 cm⁻¹ (acetal), 1290 and 1308 cm⁻¹ (CH₂Cl). NMR-spectrum: triplet at δ_{TMS} 1.1 (J = 7.0 Hz) (CH₃-CH₂-O), overlapping singlet at δ 1.2 (CH₃-C-), combined (9H); multiplet at δ 1.7 (4H) (-C-CH₂-CH₂-C-); overlapping quartet (J = 7.0 Hz) and multiplet at δ 3.2-3.7, combined (6H) (-CH₂Cl and CH₃-CH₂-O). Tetraethylammonium acetate was prepared according to Steigman and Hammet (4); it contained 86.4% CH₃COON (C₂H₅)₄, determined by potentiometric titration.

From the reaction an ester was isolated in 46% yield, which was shown to be 1-acetoxy-4,4-diethoxypentane (III); b.p. 125-128°/20 mm, n_D²⁵ 1.3912, found 60.5% C, 9.9% H, 40.8% OC₂H₅.

IR-bands at 1055 and 2980 cm^{-1} (OC_2H_5) and 1240 and 1745 cm^{-1} (acetate). NMR-spectrum: broad peak (15 Hz) at δ 4.0 (2H) $-\text{CH}_2-\text{O}-\text{C}=\text{O}$; quartet ($J = 7.0$ Hz) at δ 3.41 (4H) ($\text{CH}_3-\text{CH}_2-\text{O}$); singlet at δ 1.97 (3H) ($\text{CH}_3-\text{C}=\text{O}$); multiplet at δ 1.62 (4H) ($-\text{C}-\text{CH}_2-\text{CH}_2-\text{C}-$); singlet at δ 1.21 (3H) ($\text{CH}_3-\overset{\text{O}}{\underset{\text{O}}{\text{C}}}$); triplet ($J = 7.0$ Hz) at δ 1.10 (6H) ($\text{CH}_3-\text{CH}_2-\text{O}$).

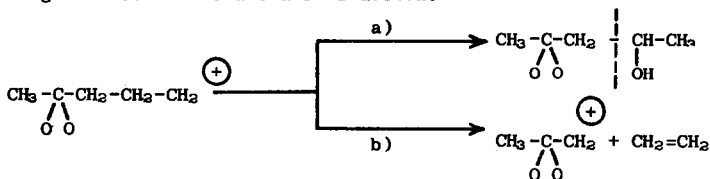
The aqueous liquors from the work-up were acidified, and heated with 2,4-dinitrophenylhydrazine. The resulting mixture of the DNPH's of 5-hydroxy-2-pentanone and acetone was separated by chromatography on silica gel. IR and NMR-spectra, m.p. and elemental analyses were in agreement.

In another experiment the reaction product from 0.79 mmole II with 1.60 mmole tetraethylammonium acetate dihydrate (an arbitrarily chosen excess) was converted to 5-hydroxy-2-pentanone-DNPH (0.26 mmole) and acetone-DNPH (0.35 mmole). Products of ethoxyl transfer could not be found.

The formation of acetone-DNPH was unexpected. Compound III gave on prolonged heating with 2,4-dinitrophenylhydrazine in ethanol 5-hydroxy-2-pentanone-DNPH only, which was relatively stable to prolonged heating in acidified aqueous 2,4-dinitrophenylhydrazine solution. This pointed to formation of a water-soluble product from which acetone-DNPH was eventually derived in the reaction of II with tetraethylammonium acetate, or with the associated water.

Normant and Feugeas (5) have described the reaction of the ethylene acetal of 5-chloro-2-pentanone with nucleophiles, including hydroxide ion and methoxide. The hydroxy acetal obtained with hydroxide was hydrolysed by acid to 5-hydroxy-2-pentanone in 32% yield overall. Unspecified amounts of 2,3-dihydro-5-methylfuran, under certain circumstances a dehydration product of the hydroxyketone, were obtained. This reaction was re-examined. The aqueous alkaline solution obtained on heating 2.04 mmole 2-methyl-2(3-chloropropyl)-1,3-dioxolane (6) with 1 g KOH in 10 ml water at 105°C was diluted to 50 ml with water. A 10 ml portion was acidified with 4 N HCl and treated with 2,4-dinitrophenylhydrazine. 5-Hydroxy-2-pentanone-DNPH (0.25 mmole) and acetone-DNPH (0.18 mmole) were obtained. In a more recent publication (7) Novak and Tarbell too apparently failed to appreciate the competing reaction when, repeating the work of Normant and Feugeas (5), they treated the ethylene acetal of 5-chloro-2-pentanone with methoxide ion.

The reactions described must proceed by one route to give the expected derivative of 5-hydroxy-2-pentanone, and by a second to give a product from which acetone is derived. Obviously a C-C bond must be broken. We suggest that either a) the acetals of 4-hydroxy-2-pentanone are intermediates, which by a process of hydrolytic or oxidative splitting (8) could give rise to the acetals of acetone



or more probably, b) heterolytic fragmentation (9) may lead to the acetals of acetone or hydroxyacetone from which acetone is subsequently formed (10).

Acetaldehyde, a possible product of a retro-aldol type splitting, or of a true acid-catalysed retro-aldol reaction of 4-hydroxy-2-pentanone, was not observed. The mild conditions in the reaction with tetraethylammonium acetate dihydrate might be reconciled with catalysis by the tetraethylammonium ion and the increased activity of anions, in this case OH^{\ominus} , in the aprotic solvent N-methylpyrrolidone (11), but for the case of aqueous alkali the reaction temperature was still much lower than that required for an oxidative splitting (8) via path a). Assuming fragmentation via b), and as far as we are aware this would be the first example of such a fragmentation involving an acetal (9), the implied reduction at a following stage presents features of its own.

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