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NEIGHBOURING GROUP EFFECT IN 4-CHLOROBUTANAL AND 1,1-DIETHOXY-4-CHLOROBUTANE

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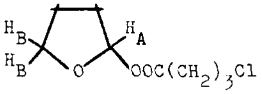
A recent publication on the solvolytic cyclisation of 4-chlorobutyrophenone and 5-chlorovalerophenone1) has prompted us to describe related observations. While preparing 4-chlorobutanal (Ia)2) and 5-chloropentanal (Ib)3) by the Rosenmund reduction of 4-chlorobuteroyl chloride and 5-chlorovaleroyl chloride in xylene we isolated from the former a higher boiling reaction product, b.p. 116-117°/2 mm, in yields varying from 5-25%, to which we assigned the structure 2(4-chlorobuteroyloxy)tetrahydrofuran (II).

$Cl(CH_2)_nCHO$

Ia $n = 3$

Ib $n = 4$



II

$Cl(CH_2)_nCH(OC_2H_5)_2$

IIIa $n = 3$

IIIb $n = 4$

The IR spectrum of the compound showed a strong band near 1130 cm^{-1} suggesting an ether group, and a carbonyl stretching band at 1750 cm^{-1}. The proton magnetic resonance spectrum was consistent with the formulation of the compound as II. A 20% solution in carbon tetrachloride showed a one proton triplet at $\delta = 6.55$4) (J = 5 cps) assigned to H_A, and two overlapping triplets at $\delta = 3.63$, J = 5 cps, (4 protons) assigned to the $-CH_2-Cl$ and H_B protons. There were also a 2 proton (distorted, "second order") triplet

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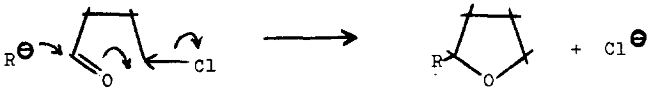
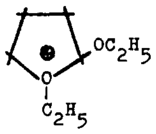
at δ = 2.58 ($J \sim 6$ cps) assigned to the $-CH_2-\underset{O}{\underset{\|}{C}}-O-$ protons, and a 6 proton complex centred at about 2.1 accounting for the remaining hydrogens. The compound decomposed slightly on distillation, resembling 2-benzoyloxytetrahydrofuran[5,6], which could not be purified sufficiently for elemental analysis.

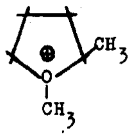
Compound II could have been formed by nucleophilic attack of an anion $R^{\ominus}$ (R = $OOC(CH_2)_3Cl$, whose source may be 4-chlorobutyric acid or its anhydride formed from the acid chloride and water, or from the derived aldehyde and atmospheric oxygen during the Rosenmund reduction[7]) on the carbonyl carbon atom, with ring formation and expulsion of a chloride ion:



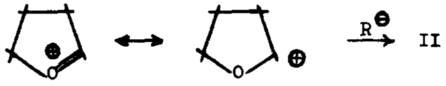
A mechanism similar to this was proposed for the ring closure of 3,4-dibromo-1-phenyl-2-benzyl-2,3-dimethyl-1-butanone with alkali[8], but a second possible mechanism was suggested by the following result. When 1,1-diethoxy-4-chlorobutane (IIIa)[2] and 1,1-diethoxy-5-chloropentane (IIIb, b.p. 74°/2 mm, $n_D^{22.9}$ 1.4318, found 55.6% C; 9.7% H; 18.0% Cl; 43.2% OC_2H_5), were hydrolysed with potassium hydroxide in ethylene glycol, a much greater rate of elimination of chloride ion from IIIa was observed than from IIIb. The reason for this difference may be neighbouring group participation of an ethoxyl group in IIIa, then the intermediacy of a cyclic oxonium ion (IV) of the type V postulated in the acetolysis of 4-methoxypentyl-p-bromobenzenesulphonate. This latter reaction led to 4-methoxypentyl-1-acetate and 5-methoxypentyl-2-acetate, i.e. with rupture of both the ring oxygen-to-carbon bonds in V[9].



IV



V



VI

In the same way, the formation of II from Ia in the presence of 4-chlorobutyrate ion might proceed via the cyclic oxonium ion VI.

Direct evidence for IV was sought in the products of the reaction. Alkali hydrolysis of 1,1-diethoxy-4-chlorobutane, however, gave only 1,1-diethoxy-4-hydroxybutane (90% yield), which was identified by its conversion to the 2,4-dinitrophenylhydrazone of 4-hydroxybutanal[10], without formation of 1,4-diethoxy-1-hydroxybutane or 4-ethoxybutanal. That there was no transfer of ethoxyl was confirmed in the reaction of sodium acetylide with IIIa and IIIb in liquid ammonia giving 1,1-diethoxy-5-hexyne (b.p. 72-74°/10 mm, $n_D^{20.4}$ 1.4275, found 69.7% C; 10.3% H; 52.9% OC_2H_5) and 1,1-diethoxy-6-heptyne (b.p. 76°/5 mm, n_D^{22} 1.4292, found 71.1% C; 11.1% H; 51.3% OC_2H_5), which were unaccompanied by branched chain compounds. The yields were 88% and 73% based on IIIa and IIIb used up in the reaction, or 65% and 69% without this correction, after approximately 48 hours. This is in contrast to the apparently complete transfer of a methoxyl group in the reaction of the dimethyl acetal of 2,3,5-tri-O-benzyl-4-tosyl-D-ribose with tetra-n-butylammonium benzoate in N-methylpyrrolidone[11], where, however, the postulated cyclic oxonium intermediate may be stabilised by solvation.

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