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REARRANGEMENT OF 2,2-DISUBSTITUTED CYCLOHEXANE-1,3-DIONES IN POLYPHOSPHORIC ACID

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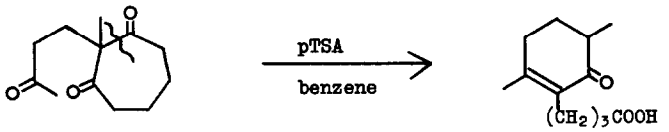
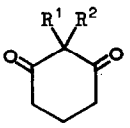
Current interest[2,3] in the Robinson-Mannich annelation of cyclohexane-1,3-dione prompts us to report an aspect of acid catalysed reactions of 2,2-disubstituted cyclohexane-1,3-diones using polyphosphoric acid[4].

The effect of various acids on 2,2-disubstituted cycloalkane-1,3-diones has been reported to result in cleavage to the keto acids or their derivatives. Thus Selvarajan et al[5] have treated trione 1 with p-toluenesulphonic acid to give mainly the keto acid 2. Similar cleavages have been achieved using boron trifluoride[6] and sulphuric acid[7]. We wish to report some novel compounds derived from 1,3-diones using polyphosphoric acid and to suggest a mechanism for their formation.

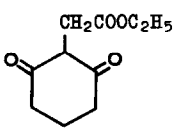


1 2

The diones 3a and 3b are readily available[8,9] while 3c (37%, b.p. 94°/0.025 mm) and 3d (40%, m.p. 55.5-56.5°) were obtained from the diketo ester 4 by reaction with ethyl bromoacetate[9] and 1-diethylaminopentan-3-one[10] respectively. 2-Ethoxycarbonylmethylene-2-methylcyclohexane-1,3-dione (3b) was added to a vigorously stirred syrup of polyphosphoric acid at an oil bath temperature of 90°. This temperature was maintained for 0.75 hr, the solution cooled and ice added. The product was extracted with chloroform and purified



3a $R^1 = R^2 = CH_3$
3b $R^1 = CH_3$; $R^2 = CH_2COOC_2H_5$
3c $R^1 = R^2 = CH_2COOC_2H_5$
3d $R^1 = CH_2COOC_2H_5$; $R^2 = CH_2CH_2COCH_2CH_3$



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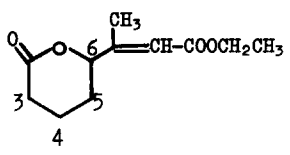
by preparative TLC (silica gel) to give a colourless oil (48%, b.p. 125°/0.25 mm), which analysed for $C_{11}H_{16}O_4$ (M^+212). The IR spectrum showed the presence of lactone, ester and double bond groups [$\nu_{max}^{CCl_4}$ 1768, 1734 and 1647 cm^{-1}] while the UV spectrum showed a high intensity absorption [λ_{max}^{EtOH} 209 nm (ε_{app} 12900)]. Complete structural assignment of the compound as lactone ester 5 was achieved by NMR spectroscopy ($CDCl_3$). Both the ethyl group of the ester and the ring methylene groups were readily assigned; δ1.23 (t, J = 7Hz, 3H), 4.06 (q, J = 7Hz, 2H), 2.32 (t, J = 6Hz, 2H, H_3), 1.5 - 2.0 ppm (m, 4H, H_4 and H_5). Absorptions for an olefinic methyl and an olefinic proton were observed at δ2.03 (s, 3H) and 5.72 (m, 1H) respectively and a broad singlet atδ4.79 (1H)



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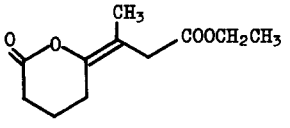

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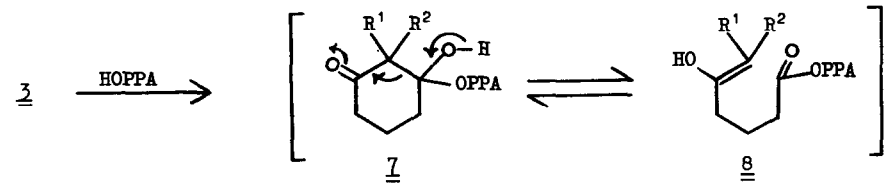
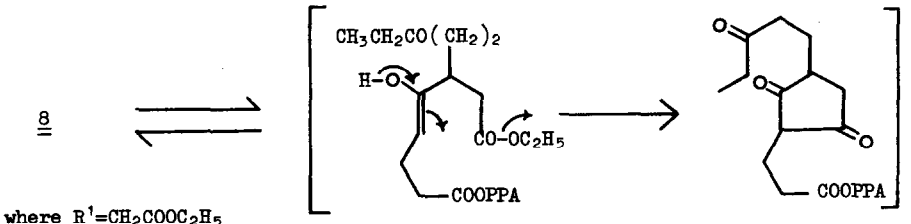
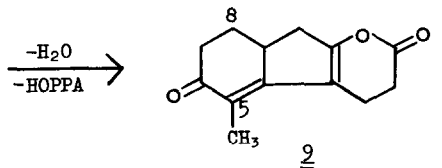
was assigned as the methine proton H_6; coupling between H_6 and the olefinic proton was demonstrated by double resonance experiments. It is probable that this compound results from the isomeric enol lactone 6, the latter being isomerised to 5 in the acidic medium.

Surprisingly, polyphosphoric acid treatment of dione 3d gave the cyclisation product 9 (34%, m.p. 131-132°) which analysed for $C_{13}H_{14}O_3$ (M^+218). The IR spectrum showed the presence of lactone, enone and double bond groups [$\nu_{max}^{CCl_4}$1823, 1677 (inf.) and 1656 cm^{-1}]. The UV spectrum exhibited a conjugated chromophore [λ_{max}^{EtOH} 213 (ε app6480), 231 (ε 5450), 238 (inf.) (5120) and 306.5 nm (20150)] while the NMR spectrum showed only two salient features, absorptions at δ1.70 (broad s, 2H) attributable to the methylene protons H_8 and δ1.84 (s, 3H) assigned as the olefinic methyl protons H_5. A complex region at δ2.1 - 3.2 ppm resulted from methylenes in allylic positions or adjacent to carbonyl groups. Hydrogenation of 9 showed the presence of two double bonds and simultaneously cleaved the lactone to the saturated acid [mass spectrum of methyl ester M^+238]. A plausible mechanism for the formation of





where $R^1=CH_2COOC_2H_5$
$R^2=CH_2CH_2COCH_2CH_3$



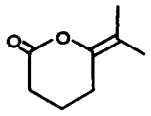
Scheme A

where HOPPA = Polyphosphoric acid

9 is outlined in Scheme A. It is probable that the intermediate 8 is also involved in the above rearrangement of dione 3b. Isomer 6 would be derived from 8 merely by a displacement of the polyphosphoric acid moiety.

Compound 3a under similar polyphosphoric acid conditions was recovered unchanged; this could be attributed to a deactivating effect of the two methyl groups. A similar effect could also account for the fact that in the case of dione 3b no cyclisation involving the ester group (as in Scheme A) was observed. It has been shown[11], however, that under photolytic conditions the same molecule (3a) rearranges in high yield to the enol lactone 10.

An unexpected product, dilactone 11 (64%, m.p. 134.5 - 135°), was obtained when diester 3c was reacted with polyphosphoric acid. This substance analysed for $C_{10}H_{10}O_5$ (M^+210) and its IR spectrum displayed absorptions $\nu_{max}^{CCl_4}$ 1829, 1813 and 1729 cm^{-1} attributable to lactone and ketone groups. The NMR spectrum confirmed structure 11



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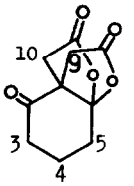

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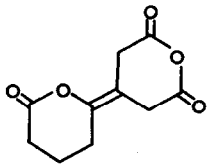

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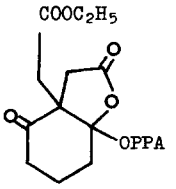

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rather than isomeric structures (e.g. 12 the counterpart of 6). Absorptions for the cyclohexane methylenes were easily identified $\delta(CDCl_3)$: 1.91 (m, 2H, H_4), 2.30 (t, J = 6Hz, 2H, H_5), 2.58 ppm (t, J = 6Hz, 2H, H_3) while a pair of doublets at δ2.83 and 3.15 ppm (J = 18Hz, 4H) showed the presence of two pairs of non-equivalent geminal protons at C_9 and C_{10}. The mechanism of formation of 11 may be rationalised by involving the intermediate 13 which then undergoes hydrolysis and lactonisation.

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