

Preparation and Rearrangement of Some α -Hydroxy-aldehydes

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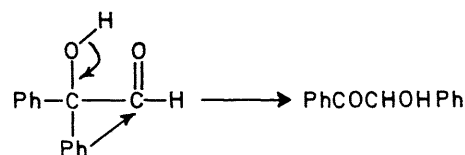
Summary 2-Cycloalkyl-2-hydroxy-2-phenylacetaldehydes, prepared by oxidation of the corresponding 2-cycloalkyl-2-phenylethane-1,2-diols with acetic anhydride in dimethyl sulphoxide, undergo acid-catalysed rearrangements in boiling heptane to give cycloalkenyl benzyl ketones.

THE acid-catalysed rearrangements of α -hydroxy-acetaldehydes and α -hydroxy-ketones (the so-called acyloin rearrangements¹) although well known, have been less studied than others such as the pinacol rearrangement.² We now report the synthesis and preliminary studies of the rearrangements of diphenylhydroxyacetaldehyde [(4), m.p. 45° (monomer), 165° (dimer)], 2-cyclohexyl-2-hydroxy-2-phenylacetaldehyde [(5), m.p. 91–93° (monomer)], and 2-cyclopentyl-2-hydroxy-2-phenylacetaldehyde [(6), m.p. 74–77° (monomer)].†

The α -hydroxy-aldehydes (4, 5, and 6) were prepared by oxidation of the corresponding 2,2-disubstituted-ethane-1,2-diols, PhCROHCH₂OH, (1; R=H), (2; R=cyclohexyl), and (3; R=cyclopentyl) with Ac₂O–Me₂SO. Yields were 50–70%, and small quantities of acetates and thiomethyl ethers were also formed in the oxidation procedure. The diols were prepared by lithium aluminium hydride reduction of the corresponding 2,2-disubstituted-2-hydroxyacetic acid esters. Since methyl benzilate is available commercially and since the ethyl esters of 2-cyclohexyl- and 2-cyclopentyl-2-hydroxy-2-phenylacetic acids were prepared conveniently by reaction in sequence of phenylmagnesium bromide and cyclohexyl(or cyclopentyl)magnesium bromide with diethyl oxalate (and by other methods³) this procedure provides a convenient synthesis of α -hydroxy-aldehydes.

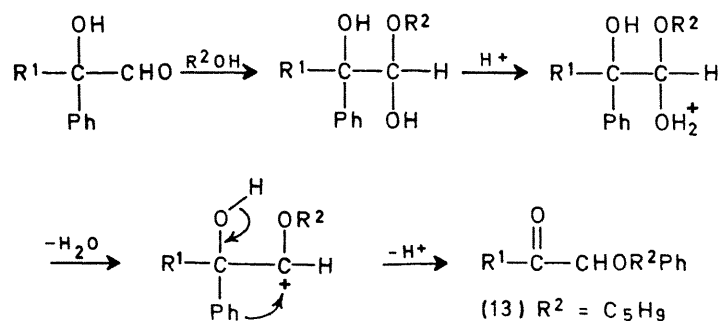
reported recently by Russell and Ochrymowycz.⁵ The monomer (R_F 0.63) and the dimer (R_F 0.3) were separated by chromatography over silica in ether:light petroleum (1:4).

It has been reported that when (4), either as the monomer or dimer, is heated in ethanol containing a few drops of concentrated sulphuric acid a ready rearrangement occurs with the formation of benzoin as the main product. A mechanism for this rearrangement is shown in Scheme 1.¹



SCHEME 1

We have found that the rearrangement of (4) to benzoin also occurred in boiling heptane in the presence of toluene-*p*-sulphonic acid, but under these conditions rapid oxidation of benzoin to benzil was observed. However, under similar conditions compounds (5) and (6) did not afford the expected PhCHOHCOR (7; R=cyclohexyl) and (8; R=cyclopentyl) as the main products, but instead were converted in high yield into the cycloalkenyl derivatives PhCH₂COR, (11; R=cyclohexenyl) and (12; R=cyclopentenyl), respectively. From the reaction mixtures small quantities of the benzoin analogues (7) and (9; PhCOCHOHR, R=cyclohexyl) [from (5)] and (8) and (10; PhCOCHOHR, R=cyclopentyl) [from (6)] were also isolated.



SCHEME 2

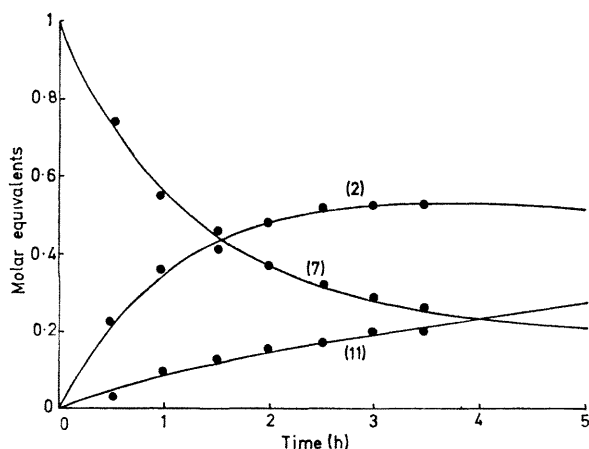
Whereas (5) and (6) existed as stable crystalline monomers (as shown by n.m.r. and i.r.), (4) existed as a stable dimer, m.p. 165° (from ethanol) and as an unstable monomer, m.p. 45° (from light petroleum) which on storage in air decomposed over a period of a few days into benzophenone and formic acid. The monomer was reported previously⁴ to be an oil; the m.p. of the dimer is in agreement with that

Evidence that the rearrangement of diphenylhydroxyacetaldehyde to benzoin proceeds *via* an acetal intermediate and that the first stage of the rearrangements (5) → (11) and (6) → (12) proceed by a similar mechanism, was obtained as follows. The rate of conversion of (5) into (11) was much slower in dry heptane containing anhydrous toluene-*p*-sulphonic acid than when a small quantity of

† All the compounds described had elemental analyses and n.m.r. and i.r. spectra consistent with the assigned structures.

water was present; this is consistent with the mechanism shown in Scheme 2 ($R^2 = H$) involving water in acetal formation. In the presence of *n*-pentanol but without water the only product from (5) was (13; $R^2 = C_5H_9$). This provided clear evidence for the mechanism of the initial rearrangement of 2-substituted-2-hydroxy-2-phenylacetaldehydes and showed that in (5), and probably in (6), the migrating group was phenyl and not cycloalkyl.

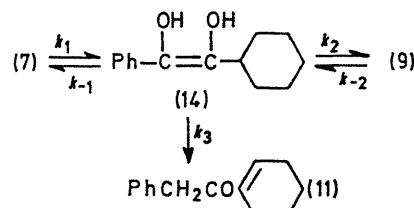
The presence of (8) and (10) as well as (7) and (9) in the reaction mixtures when (5) and (6), respectively, were heated in hexane containing toluene-*p*-sulphonic acid is to be expected since (7) and (9), and (8) and (10) may obviously be interconverted under acidic conditions *via* an enol intermediate [*e.g.* (14), Scheme 3].



FIGURE

That the immediate precursor of (11) was the enol intermediate (14) was established through a study of the rates of formation of (9) and (11) from (7) and of (7) and (11) from (9). The reactions were followed by cooling the

reaction solution [initial concentration of (9) or (7) $9.2 \times 10^{-4}M$, toluene-*p*-sulphonic acid $2.1 \times 10^{-3}M$ in heptane under reflux] to room temperature, separating the precipitated acid by centrifugation, and measuring the electronic spectra between 210 and 290 nm on a Unicam SP700A. The relative concentrations of (7), (9), and (11) were calculated from the absorbances at the analytical wavelengths 219, 242, and 281 nm. The relevant molar absorptivities at these wavelengths are:—(7) 7150, 374, and 354; (9) 3160, 13400, and 1030; (11) 11500, 5700, and 36. The enol (14) could not be detected by t.l.c. and was assumed not to be in sufficient concentration to contribute to the absorption. The data were analysed using a Solatron HS7-1 Analogue computer to simulate the various possible



SCHEME 3

kinetic schemes and to obtain estimates of the rate parameters. The data are consistent with reaction Scheme 3 in which the enol (14) is the immediate precursor of (11) and not with schemes in which (11) is formed directly from (7) and/or (9). The mechanism of this rearrangement is as yet unknown. The Figure gives data for a reaction in which (7) was the starting material. The full lines are those simulated on the analogue computer using the relative rates $k_1 = 1$, $k_{-1} = 26$, $k_2 = 16$, $k_{-2} = 0.29$, $k_3 = 5.2$. Absolute rates may be obtained by multiplying these values by $4.3 \times 10^{-4} s^{-1}$.

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¹ C. K. Ingold, "Structure and Mechanism in Organic Chemistry," G. Bell & Sons, London, 1969, page 728.

² E. S. Gould, "Mechanism and Structure in Organic Chemistry," Holt, Rinehart and Winston, New York, p. 637.

³ S. B. Coan, B. Jaffe, and D. Papa, *J. Amer. Chem. Soc.*, 1956, **78**, 3701; H. A. Smith, D. M. Alderman, jun., C. D. Shacklett, and C. M. Welch, *ibid.*, 1949, **71**, 3772; W. G. Kenyon, R. B. Meyer, and C. R. Houser, *J. Org. Chem.*, 1963, **28**, 3108.

⁴ S. Danilov, *Ber.*, 1927, **60B**, 2390.

⁵ G. A. Russell and L. A. Ochrymowycz, *J. Org. Chem.*, 1969, **34**, 3618.