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HYDROGEN BONDING IN ORGANIC SYNTHESIS II: THE INTERMOLECULAR SELF-CONDENSATION OF 2,4-PENTANEDIONE TO 3-HYDROXY-2,5,7-TRIMETHYLCYCLOHEPTA-2,4,6-TRIENONE

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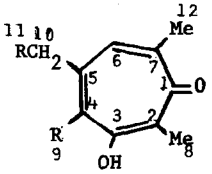
Few examples of the self-condensation of β-diketones are known, 2,4,6-heptanetrione self-condenses under carefully controlled conditions, a reaction that is pH sensitive.[1] All other attempts to date, to effect the self-condensation of β-diketones have failed.[2]

Alkali metal and tetraalkylammonium fluorides have been used for a variety of purposes in preparative organic chemistry, for example, for fluorination[3,4] or in a number of elimination reactions[5-9]. Our own investigations into the applications of potassium fluoride to organic synthesis have shown that fluoride anion acts as a source of electron density in hydrogen bonds formed with a number of protic organic compounds and thereby provides a fast and efficient route to condensation products formed between such compounds and alkyl halides.[10-12]

We have now found that KF has a remarkable capacity to enable intermolecular self-condensations of the following type to proceed.



I. R = H

II. R = Ph

Potassium fluoride (11.62 g, 0.2 mol) and 2,4-pentanedione (10.0 g, 0.1 mol) were stirred together in N,N-dimethylformamide (40 g) at room temperature. Sampling and ^{1}H n.m.r. analysis showed the presence of 100% enol in the mixture. The mixture was refluxed for 16 h, after which time the product was precipitated by adding water. It was filtered, washed with water and recrystallised from pentane as yellow needles of 3-hydroxy-2,5,7-trimethylcyclohepta-2,4,6trienone (I) (5.25 g, 0.032 mol, 64%) m.p. 55-6°C (Found: C: 73.12; H: 7.39. Calc. for $C_{10}H_{12}O_2$: C: 73.2; H: 7.38%. m/e(relative intensity) 164(M$^+$,41), 150(9), 149(100), 121(4), 93(50), 91(28), 77(32), 43(26). I.r. shows ν at 1620(C=O) and 1595 cm^{-1})C=C). ^{1}H n.m.r. resonances at δ 2.23 (s,3H,Me), 2.53(s,3H,Me), 2.59(s,3H,Me), 6.48(s,1H,CH), 6.59(s,1H,CH) and 12.36 p.p.m. (s,br,1H,OH). ^{13}C n.m.r. resonances at δ 21,484(C-10), 24.467(C-12), 33.109(C-8), 116.797(C-4), 119.292(C-5), 124-526(C-6), 139.620(C-7), 146.133(C-2), 163.783(C-3) and 205.414 p.p.m. (C-1)[13]). When the same reaction was carried out using 1-phenyl-2,4-pentanedione (3.53 g, 0.02 mol), refluxing for 16 h, followed by separation procedures similar to those described above provided 5-benzyl-3-hydroxy-2,7-dimethyl-4-phenylcyclohepta-2,4,6-trienone (II) (1.63 g, 0.0052 mol, 52%) m.p. 124°C (Found: C: 83.55; H: 6.35. Calc. for $C_{22}H_{20}O_2$:

C: 83.54; H: 6.33%. m/e(relative intensity) 317(12), 316(M^+,49), 302(26), 301(100),239(5), 182(9), 165(8), 91(26). I.r. shows ν at 1615 (C=O) and 1600 cm^{-1} (C=C). ^1H n.m.r. resonances at δ 2.53(s,3H,Me), 2.64(s,3H,Me), 3.69(s,2H,CH_2), 6.53(s,1H,CH), 7.18(m,10H,Ph) and 12.5 p.p.m. (s,br,1H,OH). ^{13}C n.m.r. resonances at δ 24.10(C-12), 33.170(C-8), 29.278(C-10), 119.710(C-5), 124.584(C-6), 126.109, 127.509, 128.361, 128.482, 128.908, 130.308(C-9,11), 139.520(C-7), 141.711(C-4), 146.220(C-2), 162.895(C-3) and 205.712 p.p.m. (C-1)[13]).

There are a number of interesting features of this condensation in particular with regard to the nature of the reaction and to the choice of fluoride.

(1) 2,4-Pentanedione is converted to 100% enol on treatment with KF/D.M.F. at room temperature, this compares to the 80% enol found in the pure liquid. ^1H n.m.r. analysis of the β-ketone in the presence of KF alone (ca. 10 mole%, larger concentrations of KF having no further effect on the composition) shows about 86% enol whereas treatment of the β-diketone with D.M.F. alone appeared to actually reduce the amount of enol present compared to that in the pure liquid.

(2) Infra-red analysis of a concentrated solution of tetra-n-butylammonium fluoride in 2,4-pentanedione shows a shift in ν_s(OH) of greater than 1000 cm^{-1} compared to that for the pure β-diketone. This is indicative of strong anionic H-bonding.[11]

(3) Refluxing a mixture of KF and 2,4-pentanedione (1:2 mole ratio) alone provides only 5% conversion to I after some 16 h. Condensation does not take place on refluxing a solution of 2,4-pentanedione in D.M.F. for several days.

(4) Condensation is limited to the fluoride salt; potassium chloride or bromide do not yield any noticeable amount of condensation product.

Fluoride appears to be capable of enolising the β-diketones and thereafter forming a strong H-bond to the enol hydroxy--this H-bond will have the effect of enhancing the electron density at the hydroxyl oxygen.[11] D.M.F. is necessary to encourage total enolisation and to provide fast and efficient reaction to the self-condensation product--this is probably due to the small but significant solubility of KF in D.M.F. and to the ability of the D.M.F. to solvate the metal cation and hence provide a more reactive fluoride anion. We hope to carry out further investigations on this and related reactions and to discuss possible reaction mechanisms at a later date.

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13. Mass spectra were recorded on an AEI MS-30 double beam mass spectrometer. Infra-red spectra were recorded on a Perkin-Elmer 237B Spectrometer. ^1H n.m.r. spectra were recorded on a Varian A-60 spectrometer and ^{13}C n.m.r. spectra on a Brüker WP-60FT (15.08 MHz) spectrometer using broad band decoupling facilities. All n.m.r. spectra were recorded in $CDCl_3$ solution with T.M.S. as internal reference.