INTRAMOLECULAR CLAISEN CONDENSATION OF KETO ESTERS CATALYSED BY POTASSIUM TRIPHENYLMETHOXIDE

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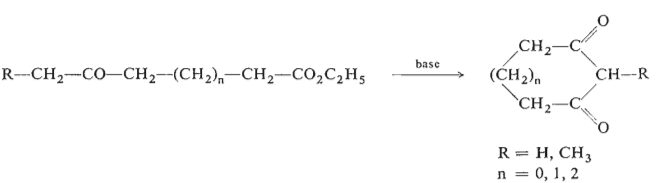
Potassium triphenylmethoxide was found to be a suitable catalyst for the preparation of 1,3-cyclopentanedione and 1,3-cyclohexanedione from ethyl 4-oxopentanoate and ethyl 5-oxohexanoate, respectively. Under identical conditions, ethyl 6-oxoheptanoate and ethyl 6-oxooctanoate afforded 2-acetylcyclopentanone and 2-propionylcyclopentanone. Reactions, catalysed by potassium triphenylmethoxide afford higher yields than those catalysed by other alcoholates.

Intramolecular Claisen condensation of keto esters represents one of the synthetic ways leading to monocyclic β-diketones. This method was used in the preparation of 1,3-cyclohexanedione and its derivatives[1-6]. The yields of 1,3-cyclohexanedione range from 27% (sodium ethoxide as catalyst)[1] to 80% (sodium methoxide as catalyst)[6]. Ethyl 4-oxopentanoate does not afford 1,3-cyclopentanedione[7,8] and unsuccessfull attempts to cyclise ethyl 4-oxohexanoate[7] and ethyl 4-oxo-2-methylpentanoate[9] have also been reported. On the other hand, ethyl 4-oxohexanoate gave[10,11] 2-methyl--1,3-cyclopentanedione in 78% yield when potassium 2-methyl-2-propoxide was used and the reaction was performed under high dilution.

The aim of the present paper was to investigate the possibilities of preparation of 1,3-cyclopentanedione, 1,3-cyclohexanedione and 1,3-cycloheptanedione from the corresponding keto esters and to study the effect of the nature and quantity of the base and of the concentration of the substrate on the yield of the dione.



The starting 4-oxopentanoic acid was prepared by degradation of glucose[12], 5-oxohexanoic acid was synthesised starting from ethyl acetoacetate and acrylonitrile *via* ethyl 2-(2-cyanoethyl)-3-oxobutanoate[13]. 6-Oxoheptanoic acid was obtained by oxidation of 1-methylcyclohexanol with chromium trioxide in sulphuric acid; in acetic acid[14] no oxidation occurred. 6-Oxooctanoic acid was synthesised using the Hünig method[15,16]. The yield of the last step – alkaline cleavage of 2-propionylcyclopentanone to 6-oxooctanoic acid – was raised from 50%[16] to 85% using 5% sodium hydroxide and a prolonged reaction time (7 h). The keto acids were esterified according to ref.[17].

Optimum conditions for the intramolecular condensation were sought in the case of ethyl 4-oxopentanoate[18]. Catalysts which are commonly used in Claisen and Dieckmann condensations (sodium methoxide, sodium ethoxide, sodium 2-methyl-2-propoxide, lithium N-methylaniline) were not suitable for the preparation of 1,3-cyclopentanedione. The use of potassium 2-methyl-2-propoxide afforded only 5–10% of the cyclisation product. However, potassium triphenylmethoxide proved to be a very suitable catalyst which gave 1,3-cyclopentanedione in 60% yield. This catalyst is soluble in xylene and the reaction thus proceeds in a homogeneous medium. Generally, an excess of the basic catalyst increases the yield of the Claisen condensation. In our case, the use of a smaller than threefold molar excess of base lowered the yield and when a smaller than twofold excess was used the intramolecular condensation did not practically take place. Of the solvents investigated – benzene, toluene and xylene – the last one proved to be the most advantageous one because of the above-mentioned solubility of potassium triphenylmethoxide in this solvent. The reaction must be carried out under conditions of high dilution. Concentration, given in the Experimental, is the maximum concentration and higher concentrations lead to lower yields of the cyclisation products. On the other hand, larger amounts of xylene did not affect the yields.

Under conditions given for the preparation of 1,3-cyclopentanedione, ethyl 5-oxohexanoate afforded quantitative yield of 1,3-cyclohexanedione. Ethyl 6-oxoheptanoate and ethyl 6-oxooctanoate cyclised under formation of five-membered rather than seven-membered ring, affording thus 2-acetylcyclopentanone and 2-propionylcyclopentanone, respectively. Neither larger excess of the catalyst nor variation in temperature, solvent or reaction time led to the formation of 1,3-cycloheptanedione. Similarly to other catalysts, also potassium triphenylmethoxide converted the mentioned esters into compounds containing the more stable five-membered ring[19–21].

EXPERIMENTAL

6-Oxoheptanoic Acid

A solution of chromium trioxide (220 g; 2·2 mol) in concentrated sulphuric acid (200 ml) and water (660 ml) was added dropwise at 30—35°C to a stirred and cooled mixture of 1-methylcyclohexanol (114 g; 1·0 mol), concentrated sulphuric acid (200 ml) and water (660 ml). The mixture was then stirred at 30—35°C for 2 h and set aside overnight at room temperature. The organic acid was continuously extracted, the ether evaporated and the residue distilled, yielding 57·5 g (40%) of 6-oxoheptanoic acid, b.p. 120—123°C/1 Torr, m.p. 32—34°C.

Reaction of Keto Esters with Potassium Triphenylmethoxide

A solution of ethyl ester of the given keto acid (0·1 mol) in xylene (200 ml) was added dropwise under nitrogen during 3 h to a boiling solution of potassium triphenylmethoxide[22] prepared from potassium (12 g; 0·30 g-atom) and triphenylmethanol (91 g; 0·35 mol) in xylene (800 ml). The reaction mixture was then refluxed for 4 h, cooled to 0°C and water (300 ml) was added. The separated triphenylmethanol was filtered and washed twice with water (50 ml). The layers in the filtrate were separated, the organic layer washed three times with water (50 ml) and the aqueous extracts combined and acidified by addition of 20% hydrochloric acid (pH 3).

a) Water was distilled *in vacuo* and the residue sublimed at 130°C/0·01 Torr. The sublimate was crystallised from ethyl acetate, washed with ether and again sublimed. The yield and m.p of the obtained 1,3-cyclopentanedione were identical with those obtained by the method *b*).

b) The aqueous layer was continuously extracted with chloroform for 24 h, the organic layer was dried over sodium sulphate and the solvent was evaporated. The residue was sublimed and isolated as described under *a*), affording 1,3-cyclopentanedione, m.p. 153—154°C, in accord with the literature[23]; yield 60%.

c) The aqueous layer was continuously extracted with chloroform for 10—12 h, the extract was dried over sodium sulphate and taken down. The solid residue was crystallised from benzene or ethyl acetate, yielding quantitative amount of 1,3-cyclohexanedione, melting at 105—106°C, in accord with the literature data[24].

d) The aqueous layer was extracted with ether, the extract was dried over sodium sulphate, taken down and the residue distilled; 2-acetylcyclopentanone: yield 70%, b.p. 93°C/15 Torr; 2-propionylcyclopentanone: yield 80%, b.p. 108°C/15 Torr.

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