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A NEW METHOD FOR THE CARBALKOXYLATION OF KETONES

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Ketones can be carbalkoxylated in the α-position by reaction with either diethyl carbonate, EtO.CO.OEt, or diethyl oxalate, EtO.CO.CO.OEt, in the presence of such bases as sodium ethoxide or sodium hydride (1). We have found it advantageous to use as reagent ethyl diethoxyphosphinyl formate, $\mathrm{EtO.CO.P(=O)(OEt)_2}$ (2). The primary product obtained from this compound and a ketone $\mathrm{R.CO.CH_2R'}$ in the presence of sodium hydride, is undoubtedly $[\mathrm{R.CO.CR.CO.P(=O).(OEt)_2}]^-\mathrm{Na^+}$; like all α-oxophosphonates it is very susceptible to acidic cleavage (3), which is best carried out by pouring the reaction mixture into an alcohol, containing a slight excess of an anhydrous acid (a little more than required for the neutralization of the above sodium derivative).

$$[\mathrm{R.CO.CR'.CO.P(=O).(OEt)_2}]^- \mathrm{Na^+} + \mathrm{R''OH} \xrightarrow{\mathrm{H^+}} \mathrm{R.CO.CHR.COOR''} + \mathrm{H - P(=O)(OEt)_2}$$

The overall yield in this "one-step" reaction lies between 70 and 80% in the cases studied so far.

Example. To the suspension of sodium hydride (5 g. of a 5% suspension in paraffin oil) in dibutyl ether (150 ml.), 21.2 g.

(0.1 mole) of freshly distilled ethyl diethoxyphosphinylformate (2) was added, followed by 9.8 g. of cyclohexanone in small portions. (If the stirred solution does not develop a yellow coloration, 2 to 3 drops of methanol are added). The reaction mixture was held at below 30° for 1 hr. and heated at 50-60° *in vacuo*, so as to distil of about 10 ml. of the solvent together with the ethanol liberated in the reaction. Then the mixture was cooled at below 30° and, after one more hour, poured into 200 ml. of anhydrous ethanol, containing 15 g. (0.15 mole) of conc. sulphuric acid; the temperature rose to 50-55°. After 30 mins., the product was poured into 500 ml. of water and extracted three times with 150 ml. of benzene. Washing with saturated sodium chloride solution, drying and distillation gave 12 g. (71%) of ethyl cyclohexanone-2-carboxylate, b.p. 93-94° (1 mm); it was identified as its cupric chelate, m.p. 178° (4).

Analogously, the following reactions were carried out :

Acetone → ethyl acetoacetate, cupric chelate of m.p. 92-93° (5); yield, 68%.

Acetophenone → ethyl benzoylacetate, cupric chelate of m.p. 200-201° (6); yield, 74%.

Diethylketone → ethyl α-propionyl-propionate, N-phenyl-pyrazolone of m.p. 112° (7); yield, 81%.

2-Methyl-cyclohexanone → ethyl 2-methylcyclohexanone-6-carboxylate, semicarbazone, m.p. 140° (8); yield, 67%.

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