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THE REACTION OF DIAZOMETHANE WITH DOUBLE BONDS.- PART III (1). A STEPWISE AND IMPROVED BUCHNER-CURTIUS-SCHLOTTERBECK REACTION

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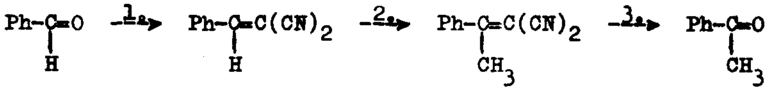
METHYLKETONES can be obtained from the parent aldehydes and diazomethane, the so-called Buchner-Curtius-Schlotterbeck reaction (2), but from a preparative view-point the general usefulness of the method is hampered by several factors: slowness of the reaction (3), variable yields depending on the solvent (4), and simultaneous formation of closely related by-products as the epoxide and the aldehyde homolog (2).

We wish now to report a convenient three-steps procedure for the preparation of acetophenone from benzaldehyde, which can be considered as the prototype of an improved Buchner-Curtius-Schlotterbeck synthesis of methylketones. The three steps are extremely fast, clean and smooth and the overall yield is practically quantitative. The reaction sequence is as follows:



$$\mathrm{Ph{-}\underset{H}{C}{=}O} \xrightarrow{1.} \mathrm{Ph{-}\underset{H}{C}{=}C(CN)_2} \xrightarrow{2.} \mathrm{Ph{-}\underset{CH_3}{C}{=}C(CN)_2} \xrightarrow{3.} \mathrm{Ph{-}\underset{CH_3}{C}{=}O}$$

I II III IV

Step 1. Knoevenagel condensation of the aldehyde with malononitrile.- Benzalmalononitrile (II) (m.p. 84.5-85°) is obtained in quantitative yield by adding a catalytic amount of glycine to a (satured) 70% aqueous alcoholic solution of benzaldehyde containing an equimolecular amount of malononitrile. In this context it should be mentioned that the use, in Knoevenagel condensations, of bifunctional catalysts such as aminoacids, first introduced by Dakin (5) and later on discussed in several papers (6), does not seem to have had the widespread generalisation that their effectiveness deserve.

Step 2. Direct methylation with diazomethane.- Dropwise addition, at room temperature, of an equimolecular ether solution of diazomethane into a dry ether solution of benzalmalononitrile, followed by removal of the solvent, gives a 100% yield of α-cyano-β-phenylcrotononitrile (III) (m.p. 94-95°). During the addition of diazomethane, a vigorous evolution of nitrogen takes place. The ease of reaction towards diazomethane of benzalmalononitrile as compared with benzaldehyde, reflects the increase in acidity of the pertinent hydrogen when a dicyanomethylen substituent is present instead of an oxo group. Step 2 is a further example of the direct methylation of trisubstituted ethylenes which is being studied in this Laboratory (1).

Step 3. Hydrolysis of the dicyanomethylene derivative.- Treatment of α-cyano-β-phenylcrotononitrile with an excess of 33% aqueous solution of sodium hydroxide, at 40-50°, followed by extraction with ether and distillation, affords pure acetophenone (b.p. 202°; m.p. 19-20°; IR spectrum identical with that of a pure specimen) in practically quantitative yield (99%).

It can be seen that α-cyano-β-phenylcrotononitrile represents the dicyanomethylene derivative of acetophenone. Its easy conversion into the ketone is in line with the work of Carrié and Bargain (7) and with the preconized use of this type of derivatives for the protection of oxo groupings (8).

Further work on the scope and limitations of the method is in progress.

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