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THE VILSMEIER-HAACK REACTION-VI[1]
REACTION OF PHOSPHORYL CHLORIDE-DIMETHYLFORMAMIDE WITH SCHIFF BASES AND AZINES

M.A. Kira, Z.M. Nofal and K.Z. Gadalla
National Research Centre, Dokki, Cairo, UAR

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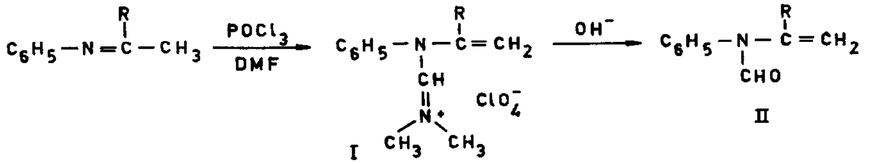
Acetophenone anil reacted with one mole of $POCl_3$-DMF, in DMF[2], and afforded after treatment with perchloric acid, the salt Ia, m.p. 160°, which upon alkaline hydrolysis gave the N-formylenamine IIa[3], m.p. 130°. The structure of IIa was inferred from its IR (1660 cm^{-1}) and NMR spectra ($CDCl_3$): signals at 4.5 and 4.7 τ (= CH_2), 2.7 τ (ten protons) and 1.4 τ (N-CHO). p-Methylacetophenone behaved similarly and afforded the enamine IIb, m.p. 115° (NMR in $CDCl_3$; τ values at 7.74, three proton; 4.4 and 4.8, one proton each; 2.5, nine protons, and 1.15, one proton, Expectedly, these enamines are stable towards the action of strong aqueous alkali, but are readily hydrolysed to the corresponding ketones by dilute acids. This represents a novel synthesis for enamines thereby obtainable in yields of over 90%.



a : R = C_6H_5 b : R = p-$CH_3O.C_6H_4$

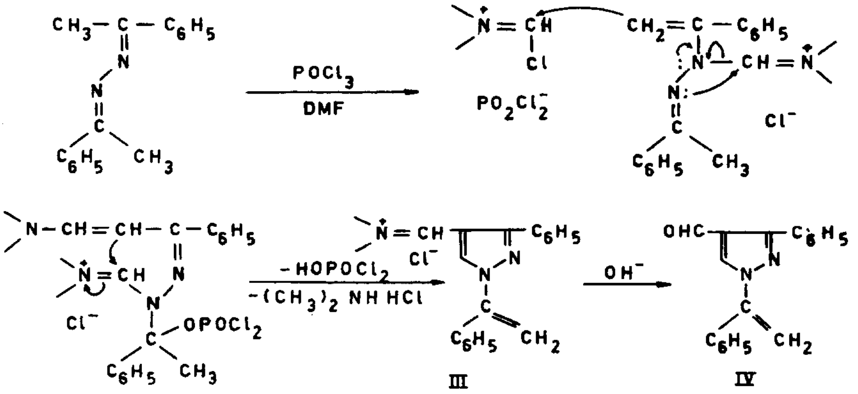
This reaction conceivably takes place by an addition of the acid chloride-amide adduct[4] to the azomethane double bond followed by elimination of dichlorophosphoric acid.

On the other hand reaction of acetophenone azine[2] with two moles of $POCl_3$-DMF gave, via the perchlorate salt III, m.p. 228°, the pyrazole carboxaldehyde IV, m.p. 62°, in an almost quantitative yield. It gave 2,4-dinitrophenylhydrazone and semicarbazone derivatives, melting points 220° and 235°, respectively. Supporting evidence for the structure of IV was derived from IR (1690 cm^{-1}) and NMR ($CDCl_3$) data: τ values at 4.15 and 4.8 (= CH_2), 2.6 (ten protons), 2.1 (5-H proton) and 0.6 (aldehydic proton). *p*-Nitro-, *p*-methoxy- and *p*-methylacetophenone azines afforded the corresponding pyrazole aldehydes, melting points 184°, 105° and 116°, in 40, 90 and 95% yields, respectively.

The cyclisation of ketone azines to pyrazole aldehydes is obviously analogous to the recently reported cyclisation of ketone[5] and α-ketoester[6] phenylhydrazones as well as ketone semicarbazones[2] to 1,3- and 1-substituted pyrazole-4-carboxaldehydes. It has been proposed[5] that the methyl group of acetophenone phenylhydrazone is the site of attack by two acid chloride-amide carbonium ions. The validity of this assumption has now been disproved by subjecting acetophenone N,N-diphenylhydrazone to a similar reaction and isolating a product m.p. 235°, obtained in a 40% yield, which was characterised as 1,2-diphenylindole-4-carboxaldehyde. It gave 2,4-dinitrophenylhydrazone and semicarbazone derivatives with melting points 185° and above 300°, respectively, and exhibited carbonyl absorption at 1640 cm^{-1}. Its NMR ($CDCl_3$) showed a multiplet at 2.5 τ (fourteen protons) and an aldehydic proton at 0.1 τ .

Furthermore, the present study showed that pyrazoles are not intermediates in this reaction, since 1,3-diphenylpyrazole-4-carboxaldehyde was readily obtained (80% yield) from a reaction with acetophenone phenylhydrazone, but only in meagre yield (9%) from 1,3-diphenylpyrazole[7] under identical conditions. Likewise, *p*-nitroacetophenone phenylhydrazone afforded 1-phenyl-3-*p*-nitrophenylpyrazole-4-carboxaldehyde in excellent yield, while 1-phenyl-3-*p*-nitrophenylpyrazole[7] was recovered unchanged under similar conditions of reactions.

From these observations and by analogy to the reaction of $POCl_3$-DMF with acetophenone anil, *vide supra*, it now seems that the reaction of this reagent with ketone hydrazones, semicarbazones and azines involve initial addition to the C = N double bond with the formation of an intermediate as illustrated by the adjoining scheme. In the reaction of acetophenone N,N-diphenylhydrazone, where migration of the CH = $\overset{+}{N}<$ group is not possible, a Fischer Indole-type reaction[8] would feasibly occur giving 1,2-diphenylindole which subsequently reacts with excess of the reagent to form the corresponding aldehyde.



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