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THE VILSMEIER-HAACK REACTION - III
CYCLIZATION OF HYDRAZONES TO PYRAZOLES

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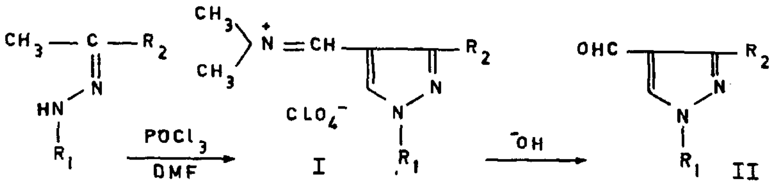
In continuation to our work on the potentialities of the Vilsmeier reaction in heterocyclic synthesis[1], we report here a new synthesis of pyrazoles.

Acetophenone phenylhydrazone reacts[2] with two moles of DMF-POCl$_3$ adduct[3] in DMF at 70-80° for six hours with formation of the immonium perchlorate Ia (m.p. 250°)* in 96% yield. On alkaline hydrolysis, Ia afforded 1,3-diphenylpyrazole-4-carboxaldehyde (IIa) m.p. 140° (2,4-dinitrophenylhydrazone, m.p. 271° and oxime m.p. 173°). The structure of IIa was established by combustion analysis (IR: 1680 cm^{-1}, CO; no NH) and NMR spectra (CDCl$_3$) [two broad signals (τ = 2.5 and 2.2, each 5 protons, and two sharp ones, τ = 1.4 and 0.4, each one proton (C-5H and CHO)].

Similarly, acetone phenylhydrazone gave the immonium salt Ib, m.p. 230°, in 77% yield. The latter on alkaline hydrolysis afforded IIb, m.p. 53°.

On the other hand, when desoxybenzoin was subjected to a similar cyclization reaction, it gave in 45% yield a compound with m.p. 88°. From a consideration of its combustion values and IR spectrum (NH absent), this compound may well be 1,3,4-triphenylpyrazole. From the pyrolysis of 1,2-diphenyl-1,3,4,6-tetraphenylpyridazine, Smith[4] obtained a product (m.p. 185°) for which the structure of 1,3,4-triphenylpyrazole was assigned on the basis of analytical data only.

The presence of a p-nitro-group on either of the two phenyl groups in acetophenone phenylhydrazone did not hinder this reaction. Thus, p-nitroacetophenone phenylhydrazone afforded, in 72% yield, the aldehyde IIc, m.p. 165° (IR: 1690 cm^{-1}, CO; NH absent; semicarbazone, m.p. 315 dec.). Similarly, acetophenone p-nitrophenylhydrazone gave, in 90% yield, the aldehyde IId, m.p. 210° (IR: 1680 cm^{-1}, CO; NH absent; 2,4-dinitrophenylhydrazone derivative, m.p. 300° dec.).



a, $R_1 = R_2 = C_6H_5$
b, $R_1 = C_6H_5$; $R_2 = CH_3$
c, $R_1 = C_6H_5$; R_2 = p-$C_6H_4NO_2$
d, R_1 = p-$C_6H_4NO_2$; $R_2 = C_6H_5$

A possible mechanism for this reaction consists in two successive attacks of the $POCl_3$-DMF available carbonium ions at the methyl group of acetophenone phenylhydrazone followed by subsequent cyclization to IIa with elimination of one dimethylamine molecule. This argument appears to be favoured by the observation that the use of only one mole of $POCl_3$ gave IIa in ca. 50% yield together with the remainder of acetophenone phenylhydrazone with no trace of 1,3-diphenylpyrazole.

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REFERENCES

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* All melting points are not corrected.