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A ONE STEP SYNTHESIS OF 4-OXO-Δ^2-PYRROLINES FROM IMINOESTERS[1]

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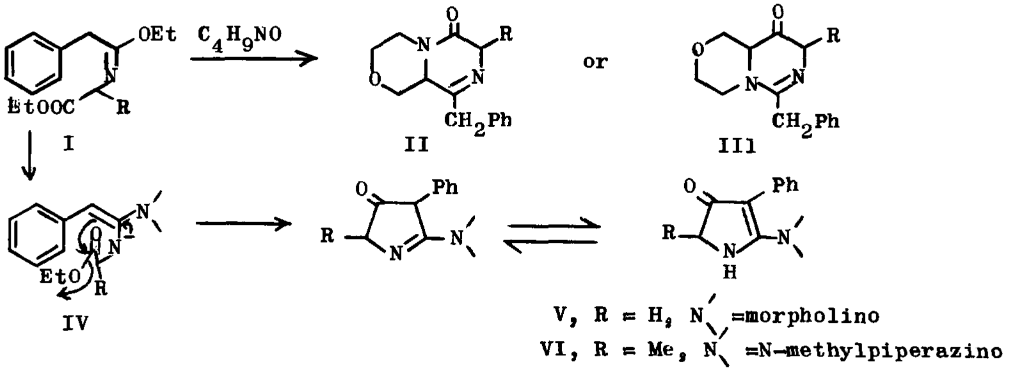
Kjaer[2] reported that the reaction of ethyl α-ethoxy-β-phenylethylideneaminoacetate (I: R = H) with morpholine led to the formation of unexpected products, and he proposed that the data could be best presented by structure II or III. However, on mechanistic consideration it was difficult to visualise the functionalisation of one of the morpholine methylenes under the mild experimental conditions used and, therefore, the assigned structure II or III seemed untenable. This prompted us to reinvestigate this reaction.



V, R = H, N< =morpholino
VI, R = Me, N< =N-methylpiperazino

On repetition of the work the product, mp 219°, mol. formula $C_{14}H_{16}N_2O_2$, as reported by Kjaer was obtained. Evidence presented below, however, shows that the product does not have structure II or III and we propose that the product in fact is 2-morpholino-3-phenyl-4-oxo-Δ^2-pyrroline (V: R = H, N< = morpholino).

Structures II and III for this product were ruled out on the basis of the following facts: (a) absence of benzylic protons and the presence of all the

8 protons of morpholine in the nmr spectrum, (b) presence of NH in the ir spectrum, and (c) recovery of the unchanged compound after boiling it with 6N HCl for 5 hr. On the other hand structure V was supported by the spectroscopic results [ir (KBr), ν_{max}: 3200, 1620 cm^{-1}; uv (MeOH), λ_{max}: 227, 292 mμ; nmr (CF_3COOH): 6.50–6.83 (m, 8H), 5.04 (s, 2H), 2.80–3.17 (m, 5H)], together with the isolation of benzoic acid on alkaline $KMnO_4$ oxidation.

V could exist in either the hydroxy or 4-keto form. On the basis of spectroscopic evidence previous authors[3,4] have favoured the 4-oxo structure for such compounds. Unambiguous support for this was forthcoming from the nmr spectrum of VI. The nmr spectrum ($CDCl_3$) of VI showed *inter alia* the following signals: 8.74 (d, J = 8, $C\underline{H}_3$), 6.40 (deformed q, changing to a sharp q after D_2O shake, $C\underline{H}$, J = 8), 3.2 (broad hump, exchangeable with D by D_2O shake, $N\underline{H}$).

The formation of V by the reaction of I with morpholine could be rationalized in the following way. A simple nucleophilic displacement reaction of I with morpholine furnishes the Schmidt ester (IV), which could be geometrically well positioned to undergo cyclization to V. The facile nature of cyclization was evident from the formation of V even at room temperature.

An extension of this reaction (I: R = Me, Ph, CH_2Ph) with other amines like piperidine, N-methyl- and N-phenylpiperazine indicated that this method could provide a general route for the synthesis of substituted 4-oxo-Δ^2-pyrrolines.

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References

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Note:- nmr spectra were recorded on Varian A-60D instrument using TMS as internal reference, the chemical shifts are expressed in τ.