An Intramolecular, Aldehyde–Enamine Condensation

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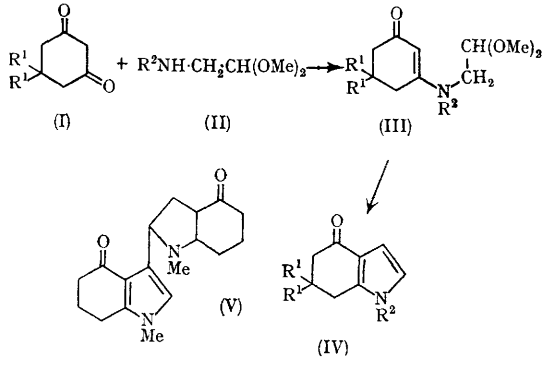
WE report an intramolecular, enamine–aldehyde condensation leading to 4,5,6,7-tetrahydro-4-oxoindoles.

Condensation of a 1,3-cyclohexanedione (I; R^1 = H or Me) with an aminoacetaldehyde dimethyl acetal (II; R^2 = H, Me, or $PhCH_2$) in benzene and in the presence of a toluene-*p*-sulphonic acid catalyst yielded, after azeotropic removal of water, an intermediate oxo-enamine (III) as an oil. The n.m.r. spectrum of (III) was in agreement with the structure and the compound quenched fluorescence on a t.l.c. layer. Treatment of (III) with cold 3N-hydrochloric acid gave the 4,5,6,7-tetrahydro-4-oxoindoles (IV) in reasonable yields (see Table). The remarkable stability of the enamine portion of (III) to dilute acid is presumably due to its conjugated nature.[1] More concentrated acid led to the formation of dimers similar to (V) while less concentrated acid yielded no products. When R^2 was hydrogen, chromatography over silica gel was required for the isolation of the indoles. In the cases where R^2 was benzyl, attempts to debenzylate by hydro genolysis were not successful.

4,5,6,7-Tetrahydro-4-oxoindoles have been prepared previously from 1,3-cyclohexanediones through a 4,5,6,7-tetrahydro-4-oxobenzo[*b*]furan intermediate[2] and their conversions to 4-hydroxyindoles and other derivatives have been carried out.[3] In two cases (R^1 = H, R^2 = $PhCH_2$ and R^1 = H, R^2 = H) we have also aromatized the ketones to known indoles.

4,5,6,7-*Tetrahydro*-4-*oxoindoles* (IV)

R^1	R^2	Yield (%)	M.p. (lit.)
H	H	48—50	184—186 (188—190^2)
Me	H	25—30	182—183
H	$PhCH_2$	65—70	78—80 (80—81·5^3)
H	Me	75	84—86 (85—86^2)
Me	Me	79	106—107



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[1] P. Crabbe, B. Halpern, and E. Santos, *Tetrahedron*, 1968, **24**, 4299, and references therein.

[2] H. Stetter and R. Lauterbach, *Annalen*, 1962, **655**, 20.

[3] W. A. Remers and M. J. Weiss, *J. Amer. Chem. Soc.*, 1965, **87**, 5262.