A Novel Two-stage Route to the 2a,5a-Diazacyclopenta[*jk*]fluorene Ring System

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The title ring system has been synthesised by phosphoryl chloride mediated cyclisation of the condensation product of tryptamine with diketene.

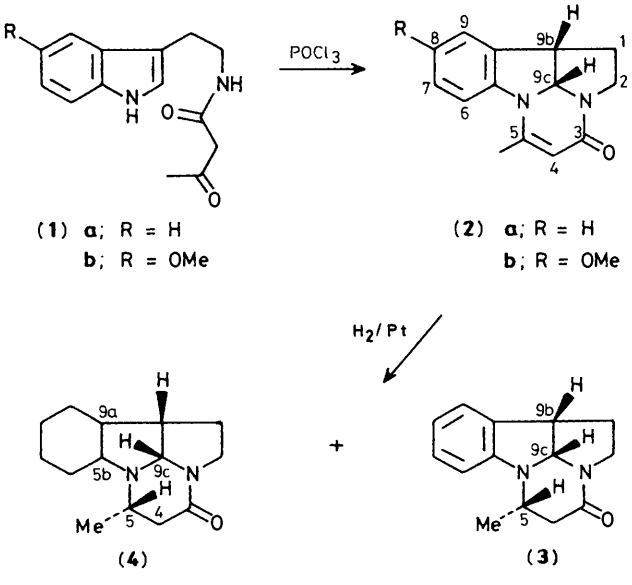
In connection with studies[1] of the cyclisation of *N*-acyltryptamines to form spirocyclic systems related to indole alkaloids, we synthesised *N*-acetoacetyltryptamine (**1a**), m.p. 77—78 °C, in 80% yield by treatment of tryptamine with diketene in tetrahydrofuran at 20 °C for 2 h.

Treatment of the amide (**1a**) in dichloromethane with phosphoryl chloride (1.1 equiv.) (under nitrogen) gave, after 24 h, (±)-1,2,9b,9c-tetrahydro-5-methyl-3*H*-2a,5a-diazacyclopenta[*jk*]fluoren-3-one (**2a**), M^+, *m/z* 226 (73%), as an oil after chromatography. The diazafluorenone, which slowly reverted to the amide (**1a**) on standing in the laboratory atmosphere, showed $\lambda_{max.}$ 230 and 326.5 nm (EtOH) and $\nu_{max.}$ 1630 cm^{-1}.

The ^1H n.m.r. spectrum of (**2a**) showed a doublet at δ 5.5 (*J* 8 Hz) as expected for 9c-H (*cf.* ref. 2) whilst the characteristic low-field indolyl-4-H signal [δ 7.62 for (**1a**)] had moved upfield to δ 6.98 in keeping with the indoline structure. The remaining protons were assigned from decoupling experiments. In the ^{13}C n.m.r. spectrum, the 9b- and 9c-C signals could be seen as doublets at δ 45.1 and 79.0 and most of the indoline ring carbon signals could be assigned from earlier work.[3]

Hydrogenation of the diazafluorene (**2a**) over platinum oxide at atmospheric pressure gave the amine (**3**) (59%) as a colourless crystalline solid, m.p. 142 °C. Its u.v. and ^1H n.m.r. spectra showed the expected changes from those of (**2a**). The 5-methyl group in (**3**) appeared as a 3-proton doublet (*J* 7 Hz) at δ 1.6 and its α-configuration was demonstrated by a nuclear Overhauser enhancement (n.O.e.) difference spectrum. Thus saturation of the 9c proton (δ 5.15, d, *J* 6.4 Hz) gave 7 and 6% enhancements of the 9b-H and 5-H signals respectively.

Smaller amounts (15%) of the perhydro derivative (**4**), m.p. 102—104 °C, were also obtained in the hydrogenation; the latter showed M^+, *m/z* 234, and only end absorption in the u.v. Assignments for most of the signals in the ^1H n.m.r. spectrum were obtained from a homoscalar 2D ^1H n.m.r. experiment.[4] An n.O.e. difference spectrum showed that saturation of the 5β proton at δ 3.55 gave a 5% enhancement of the 4-H signal and a 6.5% enhancement of the doublet at δ 4.70 due to the 9c-H, thus confirming the same α-methyl configuration as in (**3**). The stereochemistry of the 5b,9a ring junction in (**4**) was not determined, but it is likely that *cis*-addition of hydrogen occurs on the catalyst surface from the same side as for the 4,5 bond leading to a *cis–cis* configuration.

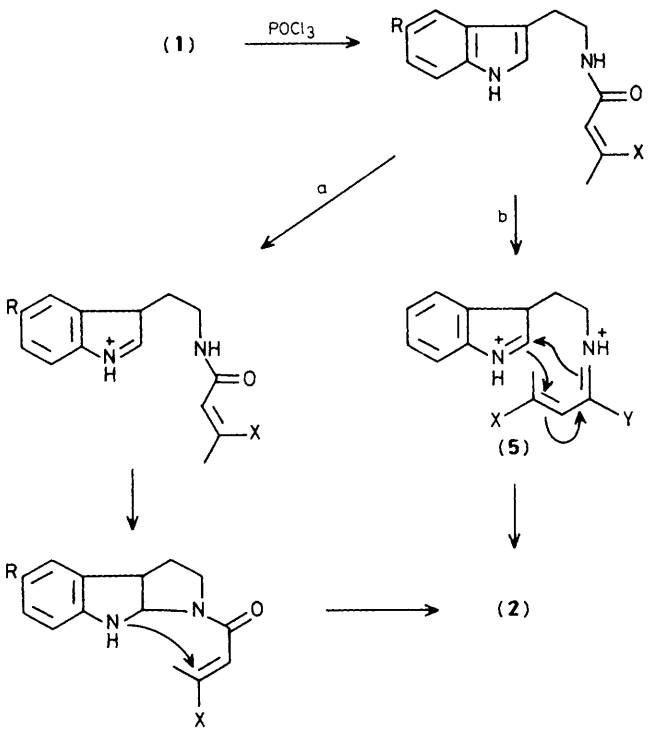


(**1**) **a**; R = H
b; R = OMe

(**2**) **a**; R = H
b; R = OMe

(**4**)

(**3**)



♦ X = $OPOCl_2$, Cl
Y = O^-, $OPOCl_2$, Cl

Scheme 1

Treatment of 5-methoxytryptamine with diketene as above gave the methoxy amide (**1b**), obtained as an oil in almost quantitative yield after chromatography. The amide (**1b**) was cyclised under similar conditions to those for (**1a**) giving the 8-methoxy analogue (**2b**) as a stable, crystalline solid, m.p. 122 °C (68%). Its structure was confirmed by its spectroscopic properties and by satisfactory elemental analysis.

This facile approach to an unusual tetracyclic system contrasts favourably in yield and simplicity with the only other reported preparation.[5] The course of the present cyclisation may be explained as shown in Scheme 1, part a. Activation of the ketone by phosphoryl chloride releases hydrogen chloride which can protonate the indole 3-position. Nucleophilic attack by the amide nitrogen on the resulting indolenine gives the tetrahydropyrrolo[2,3-*b*]indole and final cyclisation occurs *via* nucleophilic addition of the indoline nitrogen to the unsaturated amide systems, followed by elimination. An alternative explanation (arising from a comment by a referee) is that intermediates of type (**5**) might be formed (Scheme 1, path b) and then undergo electrocyclic ring closure; hydrolysis and elimination during work-up and chromatography would then lead to the tetracyclic products (**2**).

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