Photochemical Preparation of Dihydro-pyrrolo[2,1-*b*][3]benzazepines. A *Cephalotaxus* Alkaloid Synthon[1]

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Summary Irradiation of the *N*-(*o*-iodophenylethyl)methylenepyrrolones (**1a**,**b**) provides the dihydro-pyrrolo[2,1-*b*][3]benzazepines (**2a**,**b**), one of which (**2a**) is converted into the *Cephalotaxus* alkaloid synthon (**5**).

We report on the photochemical synthesis of the dihydro-pyrrolo[2,1-*b*][3]benzazepines (**2a**,**b**)† from the readily available methylenepyrrolone derivatives (**1a**,**b**). Our results represent a new photochemical reaction of pyrrolone derivatives[2] and provide a new entry into the heterocyclic system (**2**) which represents an advanced synthon of the biosynthetically intriguing[3] *Cephalotaxus* alkaloids, *e.g.*, cephalotaxine (**3**). As a result of the promising antitumour activity of several members of this class of alkaloids, there has been intense synthetic activity in this area which has culminated in two total syntheses.[4]

The maleimide (**4a**), conveniently prepared in two steps[5] from 3,4-methylenedioxy-β-phenethylamine[6] and maleic anhydride, was iodinated (I_2, CF_3CO_2Ag, CH_2Cl_2)[7] to give (**4b**) (71%). Grignard reaction[8] of (**4b**) with MeMgI in ether–benzene followed by dehydration (TsOH, C_6H_6, room temp.) provided the somewhat unstable methylenepyrrolone

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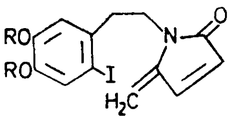
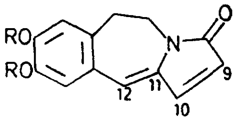
† All new compounds show satisfactory elemental analysis and i.r., n.m.r., and mass spectral data consistent with their structures.

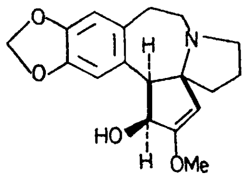


(1)

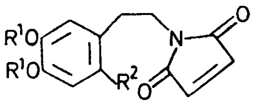


(2)

a: R,R = $-CH_2-$
b: R = R = Me

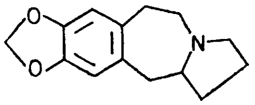


(3)



(4)

a; $R^1,R^1 = -CH_2-, R^2 = H$
b; $R^1,R^1 = -CH_2-, R^2 = I$



(5)

(**1a**) (70% overall). Irradiation (253·7 nm, C_6H_6, Et_3N, room temp., Rayonet apparatus) of (**1a**) followed by preparative t.l.c. gave the tricyclic product (**2a**) (46%), λ_{max} (EtOH) 263 (ϵ 8130) and 375 nm (15,150);[9] τ ($CDCl_3$) 2·93 (d, 1H, J 5·5 Hz, 10-H), 3·82 (d, 1H, J 5·5 Hz, 9-H), and 3·93 (s, 1H, 12-H); M^+, m/e 241. Chemical confirmation of structure was obtained by successive hydrogenation (H_2, PtO_2, MeOH) and $LiAlH_4$ reduction to give the tertiary amine (**5**), hydrochloride m.p. 264—266 °C (decomp.), identical i.r. and n.m.r. spectra with those of material prepared by Dolby *et al.*[10] Compound (**5**) has been previously converted[4b,10] into its corresponding C-11–C-12 enamine which served[4a] as a key intermediate in the synthesis of cephalotaxine (**3**).

Following similar procedures, compound (**1b**) was also prepared and, upon irradiation, afforded the analogous photoproduct (**2b**) (28%). These results coupled with our previous report[11] demonstrate the utility of *ortho*-halogenophenethylenamide photocyclization in heterocyclic and alkaloid synthesis.

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