Synthesis of the Carbazole Alkaloid Hyellazole

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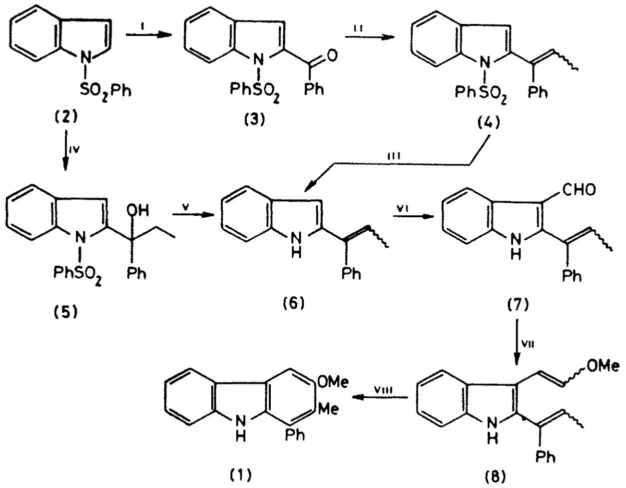
Summary Hyellazole, a new carbazole alkaloid, was synthesized *via* cyclisation of a 2,3-bis-vinylindole derivative.

We report here the first total synthesis of hyellazole (**1**),[1] a new carbazole alkaloid, isolated from the blue-green alga *Hyella caespistosa*, based upon the intramolecular cyclisation of a triene system. For this purpose, the 2,3-bis-vinylindole (**8**) was prepared as follows. Lithiation of *N*-phenylsulphonylindole (**2**) with lithium di-isopropylamide (LDA), followed by addition of benzoic anhydride afforded the 2-benzoylindole (**3**)[2] (72%). Wittig reaction



Reagents and conditions (LDA = lithium di isopropylamide THF = tetrahydrofuran) i LDA THF 0 °C 0 5 h (PhCO)$_2$O, −78 °C, then room temp 4 h ii, $Ph_3P^+Et\ Br^-$ Bu^{n}Li THF, 0 °C, 0 5 h, (**3**), −30 °C then room temp 2 h, iii, NaOH–H$_2$O–EtOH–dioxan, 48 h iv, LDA, THF, 0 °C, 0 5 h, PhCOEt, −78 °C, then room temp , 4 h v, NaOH–H$_2$O–EtOH–dioxan, 2 h, vi, POCl$_3$, dimethylformamide, 45 °C, 1 h, vii, Ph_3P^+-CH$_2$OMe Br$^-$, Bu^{n}Li, THF, 0 °C, 0 5 h, (**7**), −30 °C, then room temp , 3 h, viii, xylene, reflux, 40 h, 5% Pd–C

of (**3**) with triphenylphosphonium ethylide gave the *N*-phenylsulphonyl-diene (**4**,† 73%, 1 : 1 mixture of *E*- and *Z*-isomers), m p 142—143 °C, δ (CDCl$_3$) 1 57 and 1 88, each d, *J* = 7 Hz) Hydrolysis of (**4**) yielded (**6**) in 80% yield as a mixture of *E*- and *Z*-isomers, δ (CDCl$_3$) 1 65 and 1 94 (each d, *J* = 7 Hz) In contrast, hydrolysis of the alcohol (**5**), obtained by condensation of (**2**) with propiophenone under the same conditions as above, gave exclusively the *E*-isomer of (**6**), 76% from (**2**), m p 88—89 °C, δ (CDCl$_3$) 1 94 (d, *J* = 7 Hz) Vilsmeier reaction of the diene (**6**) easily afforded the aldehyde (**7**) (85%), m p 182—183 °C, δ (CDCl$_3$) 9 74 (s) Wittig reaction of (**7**) with methoxymethylenetriphenylphosphorane afforded the desired triene compound (**8**) ‡ Compound (**8**) thus obtained was cyclised by heating in the presence of 5% Pd-C to give hyellazole (**1**) in 21% yield from (**6**) This synthetic carbazole derivative was identical spectroscopically with natural hyellazole [1]§

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† All new compounds gave satisfactory elemental analyses and spectral data except (**8**)

‡ The triene (**8**), δ (CDCl$_3$) 3 45 and 3 53 (each s, OMe), was used without purification because it polymerized on silica gel chromatography

§ Synthetic hyellazole (*cf* ref 1) δ (CD$_3$COCD$_3$) 3 95 (s, OMe) and 2 15 (s Me), ^{13}C n m r δ (CDCl$_3$) 152 7 (s), 139 5 (s), 133 3 (s), 129 9 (d), 128 8 (d), 127 5 (d), 125 5 (s), 125 0 (d) 123 8 (s), 123 7 (s), 120 3 (s), 119 9 (d), 118 9 (d), 110 6 (d), 100 3 (d), and 56·2 (q) p p m (JEOL-FX 100 spectrometer)

[1] J H Cardellina II M P Kirkup, R E Moore, J S Mynderse, K Seff, and C J Simmons *Tetrahedron Lett* , 1979, 4915
[2] R J Sundburg and H F Russel, *J Org Chem* , 1973, **38**, 3324 In our work, LDA was used instead of Bu^{t}Li