

## A New Efficient Synthesis of the 3-Methoxycarbazole Alkaloid Hyellazole

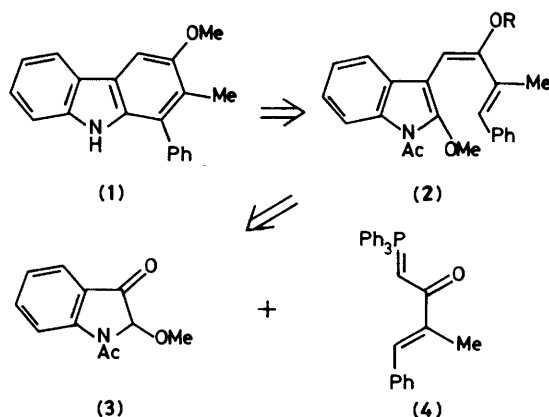
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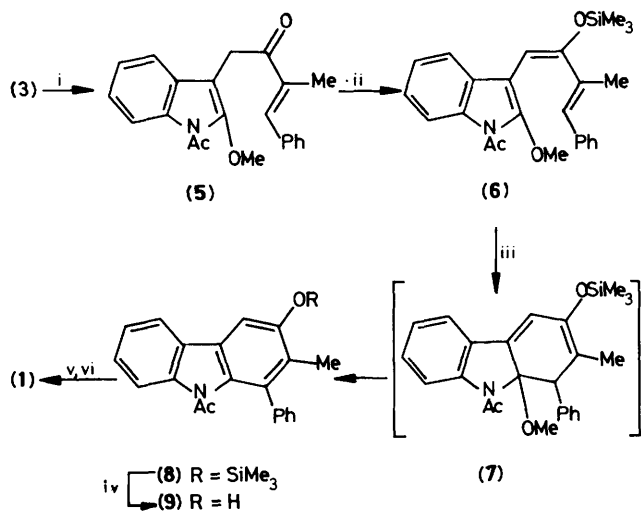
A short synthesis of hyellazole (1) based on a new method of benzannulation of indoles which involves cyclization of 3-buta-1,3-dienylindole (6) is described.

Current interest in the chemistry of polysubstituted 3-methoxycarbazoles such as hyellazole,<sup>1</sup> carbazomycins,<sup>2</sup> and so on<sup>3</sup> has continued to grow because of their physiological activities. Although 3-methoxycarbazoles have been synthesized by electrocyclic closure of 3-( $\beta$ -methoxyvinyl)-2-vinylindoles<sup>4</sup> and Diels-Alder reaction of 3-( $\beta$ -methoxyvinyl)indoles with dienophiles in the presence of dehydrogenating agents,<sup>5</sup> in the dehydrogenation step the methoxy group is concomitantly lost to give 3-demethoxycarbazoles. We now report a new synthesis of a 3-methoxycarbazole alkaloid, hyellazole (1), based on the strategy shown in Scheme 1. This approach, which involves a ring closure of a 3-buta-1,3-dienylindole (2) without the loss of the methoxy group at the 3-position of hyellazole (1) has surprisingly found little use in the carbazole synthesis to date.<sup>6</sup>

The starting 2-methoxyindolin-3-one (3) is readily available by our previously described method.<sup>7</sup> The phosphonium ylide



Scheme 1



**Scheme 2.** Reagents and conditions: i, (4), dioxane, reflux, 7 h; ii, Me<sub>3</sub>SiI, HMDS, CH<sub>2</sub>Cl<sub>2</sub>, -20 °C, then room temp., 2 h; iii, decaline, reflux, 5.5 h; iv, Bu<sub>4</sub>N<sup>+</sup>F<sup>-</sup>, aq. tetrahydrofuran, 0 °C, 10 min.; v, Me<sub>2</sub>SO<sub>4</sub>, 50% NaOH, Bu<sub>4</sub>N<sup>+</sup>HSO<sub>4</sub><sup>-</sup> (cat.), C<sub>6</sub>H<sub>6</sub>, room temp., 10 min.; vi, 50% NaOH, Bu<sub>4</sub>N<sup>+</sup>HSO<sub>4</sub><sup>-</sup> (cat.), C<sub>6</sub>H<sub>6</sub>, reflux, 1.5 h.

(4) was prepared by the usual procedure<sup>8</sup> from triphenylphosphine and 1-chloro-3-methyl-4-phenylbut-3-en-2-one.<sup>9</sup> Wittig reaction of (3) with (4) gave the 3-(2-oxobut-3-enyl)indole (5) in 74% yield,†‡ which was treated with trimethylsilyl

† All compounds gave satisfactory elemental analyses and spectral data.

‡ Although 1-acetylidolin-3-ones are enolizable ketones which rarely react with nucleophiles,<sup>10</sup> (3), for which enolization is remarkably hindered by its 2-methoxy group reacts smoothly with (4).

iodide in the presence of hexamethyldisilazane (HMDS) to provide the desired 3-buta-1,3-dienylindole (6) in 80% yield. On heating (6), an electrocyclic reaction occurred leading to intermediate (7) from which methanol was spontaneously liberated to give the 3-hydroxycarbazole (9) and its silylate (8) in 13% and 53% yields, respectively, of which the latter was treated with tetrabutylammonium fluoride (TBAF) to afford (9) in 81% yield. Methylation of (9) with dimethyl sulphate and sodium hydroxide at room temperature followed by standard deacetylation gave hyellazole (1) in 72% yield. This synthetic carbazole derivative was spectroscopically identical with natural hyellazole.<sup>1</sup>

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