

The Reaction of Indoles with Dimethyl Acetylenedicarboxylate

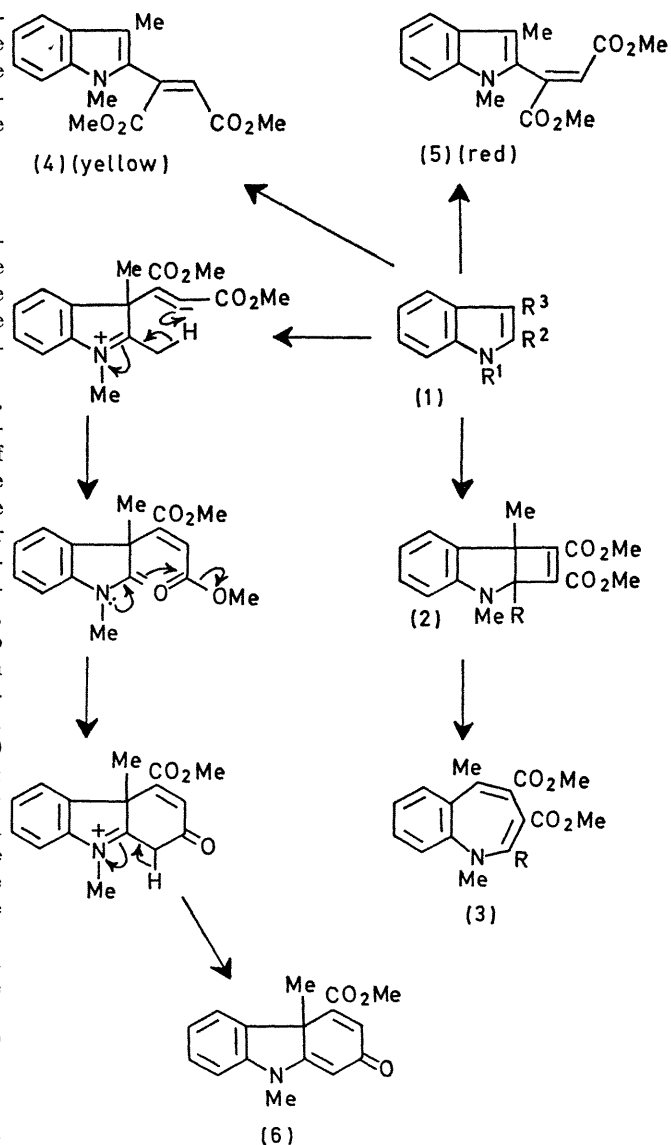
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Summary 1,3-Dimethylindole reacts with dimethylacetylenedicarboxylate in the presence of $\text{BF}_3\text{-Et}_2\text{O}$ to give the benzazepine (**3**; $\text{R} = \text{H}$), the maleate (**4**), and the fumarate (**5**); 1,2,3-trimethylindole under similar conditions reacted to give the benzazepine (**3**, $\text{R} = \text{Me}$) and the dienone (**6**).

THE reaction of indoles with acetylenic esters has been extensively investigated,¹ and although ring expansion of the enol ether (**1**; $\text{R}^1 = \text{R}^3 = \text{H}$, $\text{R}^2 = \text{OEt}$) and recently the enamine (**1**; $\text{R}^1 = \text{COMe}$, $\text{R}^2 = \text{H}$, $\text{R}^3 = \text{piperidino}$) have been described,^{2,3} no mention of the ring expansion of non-activated indoles appears to have been recorded.

No reaction of 1,3-dimethylindole (**1**; $\text{R}^1 = \text{R}^2 = \text{Me}$, $\text{R}^3 = \text{H}$), with dimethylacetylenedicarboxylate (dmad) occurred under a variety of conditions, but in the presence of $\text{BF}_3\text{-Et}_2\text{O}$ rapid reaction took place at room temperature to give a 3-component mixture (t.l.c.). On heating, one component disappeared to be replaced by a more polar product, which may be reasonably interpreted as the formation of a ring-expanded product by thermal decomposition of an intermediate cyclobutene adduct (**2**; $\text{R} = \text{H}$), no other changes being observed. However, attempts to isolate the cyclobutene were unsuccessful. Dry-column chromatography separated the product of thermal decomposition (10%) as pale yellow cubes, m.p. $87\text{--}89^\circ$, τ (CDCl_3) 7.72 (s, 3H, C-Me), 6.93 (s, 3H, N-Me), 6.29 (s, 3H, O-Me), 6.39 (s, 3H, O-Me), and 2.6–3.3 (m, 5H); λ_{max} (EtOH) 245 ($\log \epsilon$ 4.2), 282 (3.85), and 312 (3.7) nm; and ν_{max} 1700 and 1720 cm^{-1} . In particular, the higher field N-Me (6.93), compared with the values (τ ca. 6.3) for the alternative structures (**4**) and (**5**), the u.v. data and the derivation of the compound under thermal conditions are compatible with the ring-expanded structure (**3**; $\text{R} = \text{H}$). The mixture (20%) remaining after separation of compound (**3**) was separated by fractional crystallisation into the yellow maleate (**4**): τ 7.68 (s, 3H, C-Me), 6.32 (s, 3H, N-Me), 6.14 and 6.15 (each s, 3H, OMe), 3.88 (s, 1H), and 2.3–2.9 (m, 4H); λ_{max} (EtOH) 226 ($\log \epsilon$ 4.5), 260 (3.8), 277 (3.75), and 340 (3.95) nm; and the red fumarate (**5**): τ 7.85 (s, 3H, C-Me), 6.44, 6.42, 6.22 (each s, 3H, O-Me and N-Me), and 2.3–2.9 (m, 5H); λ_{max} (EtOH) 227 ($\log \epsilon$ 4.55) and 295 (3.8) nm.



SCHEME

In order to prevent 2-substitution and facilitate the ring-expansion the analogous reaction between 1,2,3-trimethylindole (**1**; $R^1 = R^2 = R^3 = \text{Me}$) and dmad was investigated. The $\text{BF}_3\text{-Et}_2\text{O}$ catalysed addition gave a mixture from which two products could be separated by column chromatography. The less polar product (30%) had ν_{max} 1700 and 1720 cm^{-1} ; λ_{max} (EtOH) 245 ($\log \epsilon$ 4.1) 283 (3.6), and 306 (3.5) nm; and τ (CDCl_3) 7.67 (s, 3H, C-Me), 7.55 (s, 3H, C-Me), 6.92 (s, 3H, N-Me), 6.41 and 6.29 (each s, 3H, OMe), and 2.6—3.1 (m, 4H), compatible with the benzazepine structure (**3**; $R = \text{Me}$). The other product (25%) had a parent ion of 269 consistent with the

loss of methanol from a 1:1 adduct, and showed ν_{max} 1720, 1640, and 1580 cm^{-1} ; λ_{max} (EtOH) 238 ($\log \epsilon$ 4.4), 278 (4.0), 324 (3.55), and 422 (3.8) nm; and τ (CDCl_3) 8.15 (s, 3H, C-Me), 6.75 (s, 3H, N-Me), 6.1 (s, 3H, O-Me), 4.33 (d, 1H, $J_{1,3}$ 1.5 Hz), 3.11 (d, 1H, $J_{1,3}$ 1.5 Hz), 2.6—3.2 (m, 3H), and 2.0—2.2 (m, 1H). The loss of the 2-methyl signal, and the coupling constants of the doublets at τ 3.11 and 4.33⁴ are compatible with the dienone structure (**6**), which could arise as indicated (Scheme). Satisfactory analyses have been obtained for all compounds mentioned.

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