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A Synthesis of 8,10-Dimethoxyellipticine via a Diphenylamine

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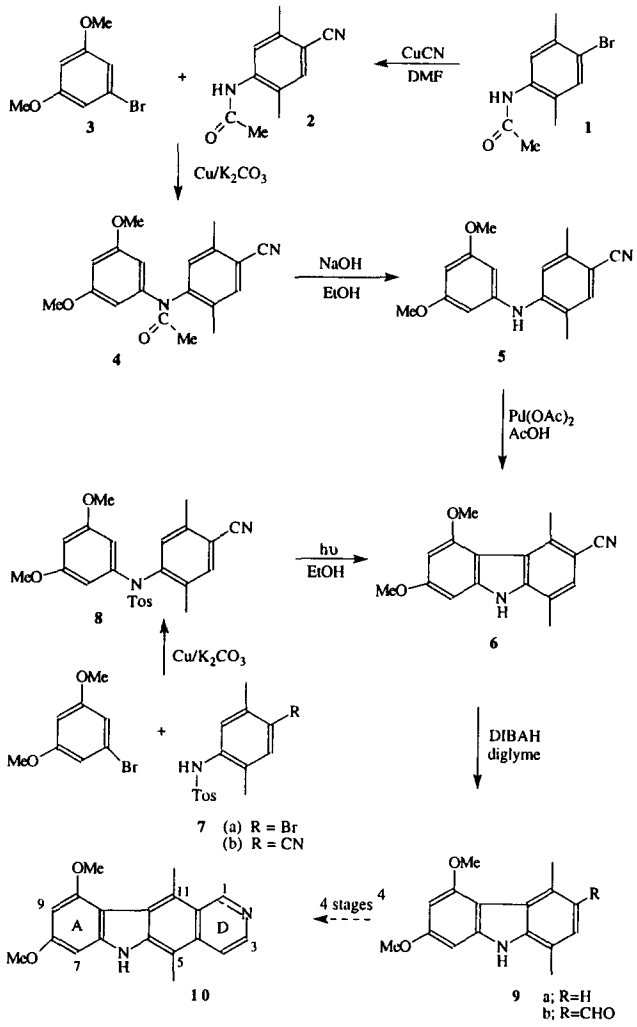
Abstract: 8,10-Dimethoxyellipticine has been synthesised from readily available benzene derivatives via palladium acetate or photochemical cyclisation of intermediate diphenylamine derivatives. The route has advantages over indole based syntheses.

The synthetic route to ellipticine and its derivatives based upon indoles as starting materials has been very successful[1]. In many cases, however, the required indole is expensive or itself obtained only through a lengthy synthesis.

We now describe a total synthesis of a hitherto inaccessible ellipticine - **10** which avoids the need for the appropriate indole as a starting material and also the problem of the lack of regiospecificity in formylation of an indole-derived carbazole of type **9a**. Treatment of the bromide **1**[2] with an excess of copper(I) cyanide in refluxing dimethylformamide gave the nitrile **2**, m.p. 193-195°C, (72%) which on Goldberg condensation with the bromide **3**[3] gave the diphenylamide **4**, m.p. 114-116°C, (72%). Alkaline hydrolysis afforded the diphenylamine **5**, m.p. 135-138°C, (98%) which was cyclised with palladium acetate in acetic acid to the carbazole **6**, m.p. 261-262°C (32%). The yield for this stage has not been optimised. An alternative route to **6**, in lower yield, was via the sulphonamide **7b**, formed via **7a** as for the nitrile **2**, and photolysis of the derived sulphonamide **8**.

The nitrile **6** was reduced with DIBAH in diglyme to the aldehyde **9b**, m.p. 244-245°C, (31%) which was efficiently converted as with previous examples by the sulphonamide modification[4] of the Pomeranz-Fritsch cyclisation route to the required ellipticine **10**. This was purified via its hydrochloride, which on decomposition with aqueous alkali gave the free base as a pale yellow solid which blackened without melting below 300°C., δ_H(d_4-MeOH) 2.70 (3H, s, 5-Me) 3.35 (3H, s, 11-Me) 3.90 (3H, s, OMe) 4.00 (3H, s, OMe) 6.31 (1H, d, J 2Hz, 9-H) 6.61 (1H, d, J 2Hz, 7-H) 7.90 (1H, brs, 4-H) 8.26 (1H, br s, 3-H) and 9.50 (1H, br s, 1-H); λ_{max} (MeOH) 385 (sh, ε 5825) 365.8 (7980) 320 (10870) 296.4 (113440) 239.6 (42,490) nm.

All compounds described gave satisfactory elemental analysis. This route, which depends upon the easy availability of the nitrile **2**, would appear to have application to the relatively simple synthesis of several other ellipticines.



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