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CONVERSION OF DIINDOLYL METHANES TO 3-VINYLINDOLES. A SIMPLE SYNTHESIS OF THE INDOLE ALKALOID OLIVACINE.

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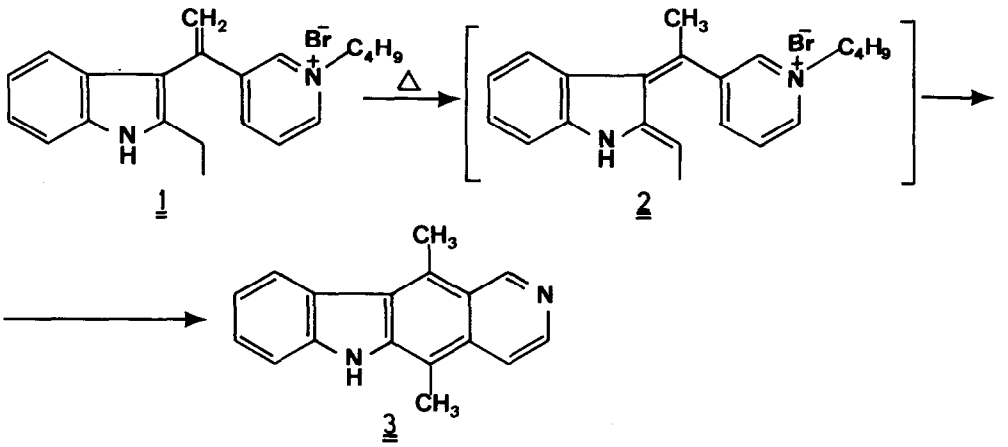
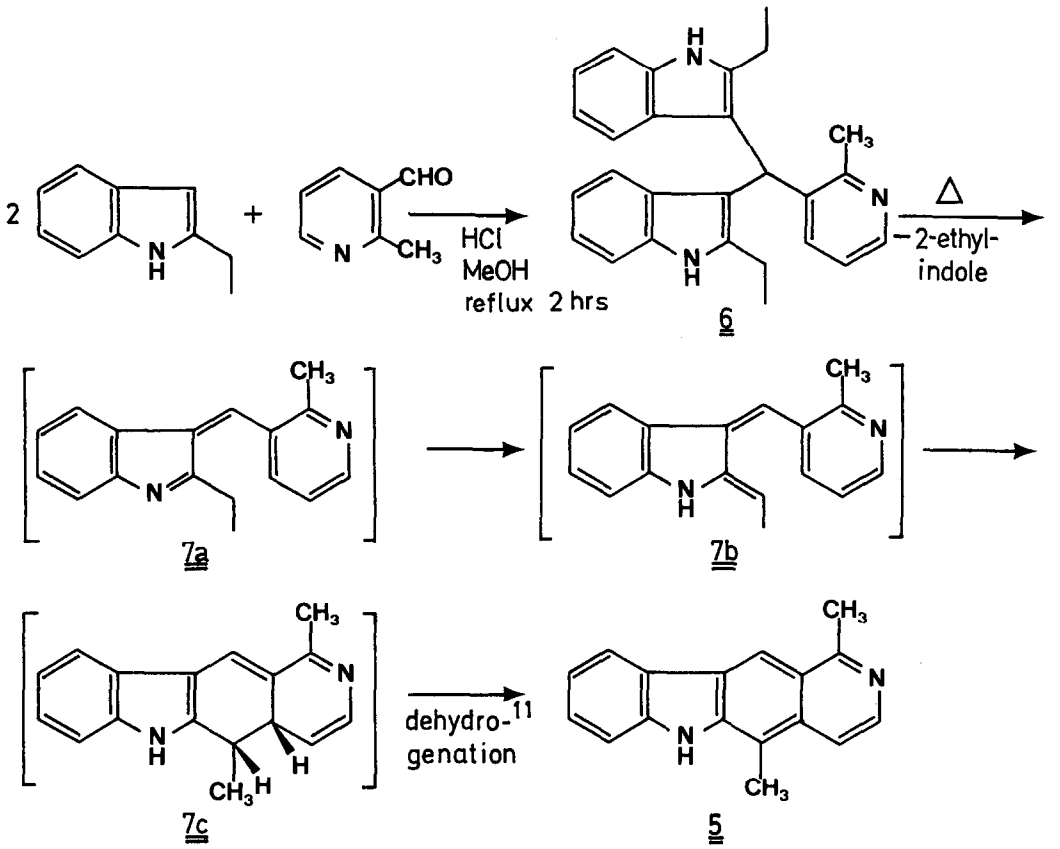
We have recently[1] developed a convenient synthesis of the anti-cancer active indole alkaloid ellipticine (3) (based on thermolysis of the readily available compound 1).

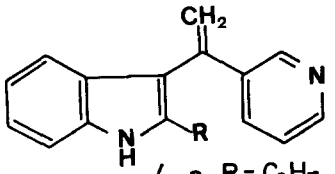


1 2 3

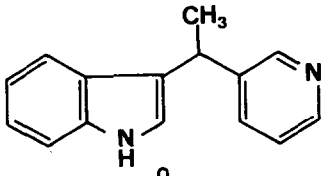
Compound 1 is prepared by condensation of 2-ethylindole with 3-acetylpyridine (yielding compound 4a)[2] followed by quaternization with butyl bromide. We now wanted to apply a similar approach to the synthesis of the likewise anti-cancer active alkaloid olivacine (5), starting with 2-ethylindole and 2-methyl-3-formylpyridine.[3] As expected, the condensation could not be stopped at the 1:1 stage, but proceeded further yielding the 2:1 condensation product (6), which, however, on thermolysis under reduced pressure split off 2-ethylindole yielding olivacine directly. The synthesis, which is much simpler than those previously reported[4-10] for the synthesis of olivacine, is summarized below.



In a related experiment it was found that thermolysis of the known[13] 2:1 condensation product (8) of indole and 3-acetylpyridine readily gave the new 3-vinylindole, 1-(3-indolyl)-1-(3-pyridyl)ethylene (4b)[14] in good yield (86 %). Catalytic hydrogenation of 4b gave the known[15] compound (9), which has been used as the crucial intermediate in an interesting synthesis of ellipticine[15]. We believe that the attractiveness of this synthesis has now increased.



4 a R = C_2H_5
b R = H



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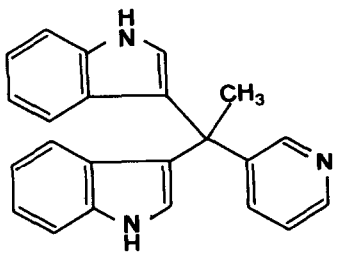

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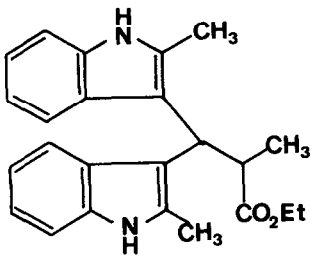

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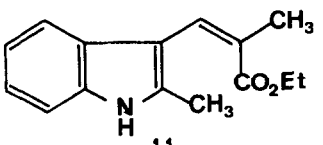

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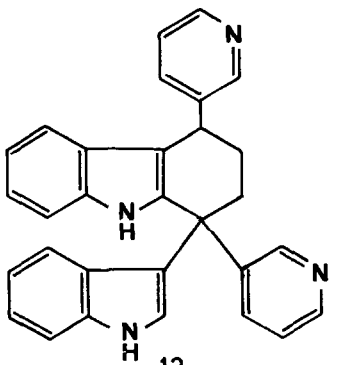

12

Thermolysis of 10 (cf the preceding paper) similarly gave 2-methylindole and 11. The principle of thermolytic cleavage of bisindoles seems to be rather general for the preparation of indolenines (in situ) and 3-vinylindoles, provided that the vinyl group is conjugated with an aromatic ring or a carbonyl group. Nonconjugated 3-vinylindoles should be expected to give oligomeric products (e.g. dimers) (cf ref 16 and 17). In this connection it might be added that a Diels-Alder dimer of 4b (12) was formed as a minor product in some preparations of 4b. The mass spectrum[18] of 12 showed a diagnostic M-28 peak due to the expulsion of C_2H_4 in a retro-Diels-Alder reaction, which is characteristic[19] for 2,3-unsubstituted 1,2,3,4-tetrahydrocarbazoles.

REFERENCES AND NOTES

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