A New Synthesis of Ellipticine

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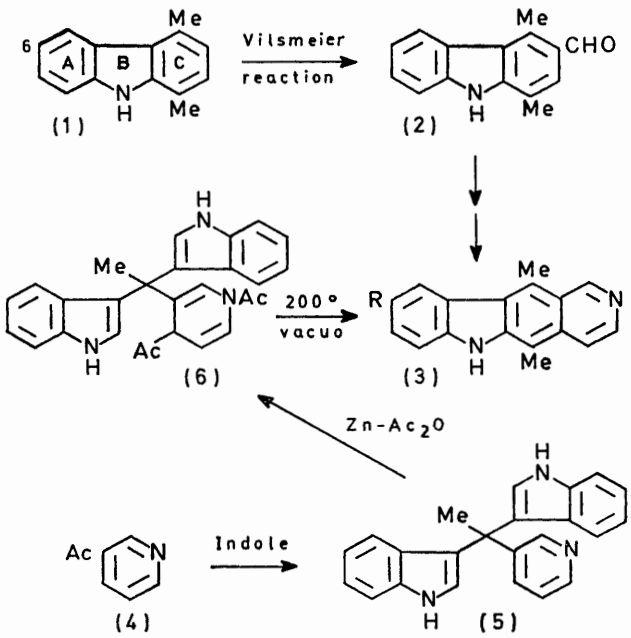
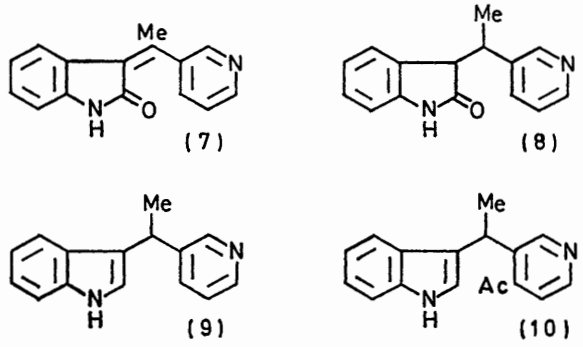
The tumour-inhibiting alkaloid ellipticine has been synthesized from indolin-3-one and 4-acetyl-3-(1-methoxyethyl)pyridine in 4 steps. This potentially versatile synthesis was accomplished in an overall yield of 31% (based on indolin-3-one).

THE alkaloids ellipticine (3; R = H) and 9-methoxyellipticine (3; R = OMe), which are commonly found in plants of the genera *Ochrosia* [1] or *Aspidosperma* [2] (Apocynaceae), have stimulated much interest because of their antitumour and antileukemic activity.[3] Although several syntheses of ellipticine have been described these are either very lengthy, or else the overall yield is poor. The hitherto most useful approach [4] suffers from the disadvantage that in the initial step it is necessary to convert 1,4-dimethylcarbazole (1) into the 3-formyl derivative (2). Since, however, the 6-position of the carbazole is also susceptible to electrophilic attack, problems due to isomers result. These difficulties are increased if electron-donating substituents are present in ring A other than at C-6. Woodward's synthesis [5]



of ellipticine from indole and 3-acetylpyridine (4) is extremely simple, but unfortunately the pyrolysis of (6) proceeds in only 2% yield. Nevertheless, the use of indoles or indole derivatives as starting materials is very attractive, since this would permit access to many ellipticine derivatives which are available only with difficulty by conventional methods, and initially we sought to adapt Woodward's scheme in the hope of increasing substantially the overall yield.

3-Acetylpyridine was reacted with indolin-2-one in the presence of pyrrolidine to yield the unsaturated amide (7), or its geometric isomer, and this was reduced with sodium borohydride in aqueous methanol to the dihydro-derivative (8). We expected that (8) could be

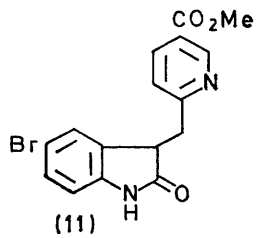


converted into the indole (9) and this in turn treated with zinc and acetic anhydride to give, after oxidation, the acetylpyridine (10). Cyclization of (10) to a dihydroellipticine should then be straightforward.

Confusion exists in the chemical literature concerning the action of lithium aluminium hydride upon indolin-2-one and its 3-alkyl derivatives; some authors claim [6] that reduction to the corresponding indoline may be achieved, whereas others [7] indicate that the reduction either does not proceed at all or else only with extreme difficulty. We support the latter point of view, since reaction of the indolinone (8) with lithium aluminium hydride under a variety of conditions did not lead to significant reduction. Julia and his co-workers [8] have shown that the indolinone (11) may be reduced with diborane to the indoline (12), but we were unable to achieve reduction of the indolinone (8) under the same conditions. The reason for our failure is not clear and although other reagents, *e.g.* phosphorus penta-

[1] K. N. Kilminster, M. Sainsbury, and B. Webb, *Phytochemistry*, 1972, **11**, 389, and references cited therein.
[2] G. Büchi, D. W. Mayo, and F. A. Hochstein, *Tetrahedron*, 1961, **15**, 167.
[3] G. H. Svoboda, G. A. Poore, and M. L. Montfort, *J. Pharm. Sci.*, 1968, **57**, 1720; J. Le Men, M. Hayat, G. Mathé, J. C. Guillon, E. Chenu, M. Humblot, and Y. Masson, *European Clinical and Biol. Research*, 1970, **15**, 534.
[4] P. A. Cranwell and J. E. Saxton, *J. Chem. Soc.*, 1962, 3842; see also K. Dalton, S. Demerac, B. C. Elmes, J. W. Loder, J. M. Swan, and T. Teitei, *Austral. J. Chem.*, 1967, **20**, 2715.
[5] R. B. Woodward, G. A. Iacobucci, and F. A. Hochstein, *J. Amer. Chem. Soc.*, 1959, **81**, 4434.
[6] P. A. S. Smith and T. Yu, *J. Amer. Chem. Soc.*, 1952, **74**, 1096.
[7] P. L. Julian and H. C. Printy, *J. Amer. Chem. Soc.*, 1949, **71**, 3206; C. B. Hudson and A. V. Robertson, *Austral. J. Chem.*, 1967, **20**, 1699.
[8] M. Julia, F. Le Goffic, J. Igolen, and M. Baillarge, *Tetrahedron Letters*, 1969, 1569.

sulphide [9] and sodium in propanol,[10] have been used to reduce indolin-2-ones, we decided, after a brief study, to abandon this approach and to examine a route based upon indolin-3-one where problems due to the inertness of the carbonyl group are avoided.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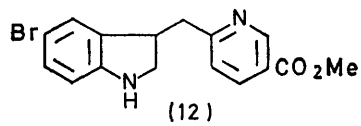
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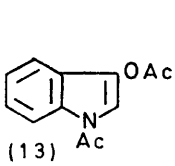
While indolin-3-one is very unstable in air, forming indigotin, the molecule may be handled conveniently as its 1,3-diacetyl derivative (13) and condensed with 4-acetyl-3-ethylpyridine (15; R = H) in the presence of aqueous alkali to give the unsaturated ketone (16; R = H). Attempts to cyclize this material to ellipticine failed, but we were able to show that reduction with sodium borohydride followed by acidification of the product (18; R = H) afforded the indole (19; R = H) in good yield. Consequently, we expected that if a suitable function were introduced into the α-position of the ethyl side-chain of (19; R = H)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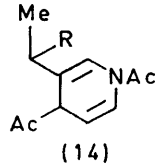
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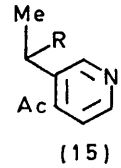
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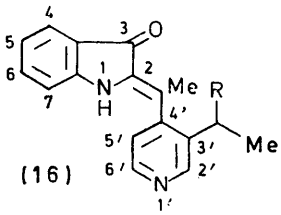
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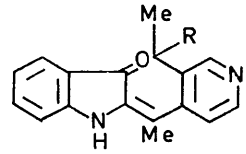
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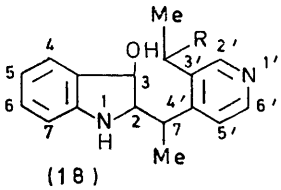
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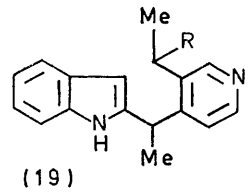
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cyclization and oxidation to ellipticine would follow easily.[11]

Thus, the diacetyldihydropyridine (14; R = OMe) was prepared and oxidized to the acetylpyridine (15; R = OMe); * this material was condensed with 1-acetylindol-3-yl acetate (13) affording a mixture of two geometric isomers (16; R = OMe) and (17; R = OMe).† Reduction of either isomer with sodium borohydride, followed by acidification, gave the indole (19; R = OMe). This material was heated under reflux with aqueous hydrogen bromide, then neutralized, and the product absorbed onto silica gel. After standing for 6—7 h, the silica was removed and repeatedly extracted with chloroform to yield ellipticine 40%.

This new synthesis offers a rapid and efficient route to ellipticine and should provide access to a wide range of derivatives not available previously.

EXPERIMENTAL

U.v. spectra were recorded for solutions in 95% aqueous ethanol, i.r. data refer to Nujol mulls unless otherwise stated: ^{1}H n.m.r. spectra were recorded either at 60 or 100 MHz for deuteriochloroform solutions with tetramethylsilane as an internal standard.

1-Acetylindol-3-yl Acetate (13).—This compound was prepared from anthranilic acid by the published method.[13]

1,4-Diacetyl-3-ethyl-1,4-dihydropyridine (14; R = H).—3-Ethylpyridine (23 g) [14] was dissolved in acetic anhydride (250 ml) and cooled to 0°; zinc dust (25 g) was added portionwise to the stirred solution during 3 h, maintaining the temperature at 0°. The mixture was stirred for a further 4 h at 0—5°, and left to warm to room temperature overnight. The zinc and zinc acetate were removed by filtration, and the acetic anhydride evaporated under reduced pressure at 40—45°.

The residual yellow oil was distilled affording starting material (10 g, b.p. 40° at 0·15 mmHg) and the dihydropyridine (14; R = H) (18 g), b.p. 126—128° at 0·1 mmHg (88%, based on 11·5 g of 3-ethylpyridine),‡ M^+, 193 (v weak), 149, and 136 (*P*), $\nu_{max.}$ 1708 (Ac), 1670 (NAc), and 1630 cm^{-1} (C=C), $\lambda_{max.}$ 260 nm, δ 1·05 (3H, t, *J* 6·5 Hz, CH_2*Me*), 2·0 (2H, q, *J* 6·5 Hz, *CH*$_2$Me), 2·15 (3H, s, Ac), 2·25 (3H, s, AcN), 3·75 (1H, d, *J* 5·0 Hz, 4-H), 5·0 (1H, m, 5-H), 6·70 (1H, m, 6-H), and 7·20 p.p.m. (1H, m, 1-H). This compound rapidly decomposed on standing and consequently satisfactory analytical figures were not obtained.

4-Acetyl-3-ethylpyridine (15; R = H).—The diacetyl compound (14; R = H) (10 g) in glacial acetic acid (100 ml) was treated dropwise with chromium trioxide (2 g) in water (20 ml) during 15 min. The mixture was stirred for 1 h at room temperature. Propan-2-ol (20 ml) was added and stirring continued for a further 15 min. The solvents were removed at 35° under reduced pressure, leaving

* 3-(1-Acetoxyethyl)pyridine was also prepared but it was not possible to convert this into the ester (15; R = OAc).

† A discussion of the stereochemical phenomena encountered in this work is given in ref. 12.

‡ 50% of starting material is recovered from this reaction which is considered to proceed by a disproportionation mechanism.[15]

[9] H. Plieninger and G. Werst, *Angew. Chem.*, 1958, **70**, 272; S. Sugasawa, *J. Pharm. Soc.* (*Japan*), 1938, **58**, 139.

[10] G. Tacconi, S. Pietra, and M. Zaglio, *Farmaco* (*Pavia*) *Ed. Scientifica*, 1965, **20**, 470.

[11] See, for example, F. E. Ziegler, E. B. Spitzner, and C. K. Wilkins, *J. Org. Chem.*, 1971, **36**, 1759.

[12] K. N. Kilminster and M. Sainsbury, *J.C.S. Perkin I*, in the press.

[13] D. Raileanu, O. Constantinescu-Simon, E. Mosanu, and C. Nenitzescu, *Rev. roumaine chim.*, 1967, **12**, 105.

[14] T. I. Fand and C. F. Lutomski, *J. Amer. Chem. Soc.*, 1949, **71**, 2931.

[15] J. P. Wibaut and J. F. Arens, *Rec. trav. chim.*, 1941, **60**, 119.

a dark green gum. This was extracted with saturated sodium hydrogen carbonate solution and ether. The ether extract was separated, washed with sodium hydrogen carbonate solution, and re-extracted with N-hydrochloric acid. The acid phase was washed with ether, made basic with solid sodium hydrogen carbonate, and the product was re-extracted into ether. The ethereal solution was dried ($MgSO_4$) and the solvent was removed under reduced pressure to yield *4-acetyl-3-ethylpyridine*, an oil (6·3 g, 81%), M^+, 149 and 134 (*P*), $\nu_{max.}$ 1690 (Ac) cm^{-1}, $\lambda_{max.}$ (ε) 225 (3800) and 278 (2100) nm, δ 1·20 (3H, t, *J* 7 Hz, *Me*CH_2), 2·58 (3H, s, Ac), 2·80 (2H, q, *J* 7 Hz, *CH_2*Me), 7·3 (1H, d, *J* 5 Hz, 5-H), 8·55 (1H, d, *J* 5 Hz, 6-*H*), and 8·60 p.p.m. (1H, s, 2-H) (Found: C, 72·5; H, 7·4. $C_9H_{11}NO$ requires C, 72·45; H, 7·4%).

3-(1-Chloroethyl)pyridine.—1-(3-Pyridyl)ethanol (20 g) (from a sodium borohydride reduction of 3-acetylpyridine) was dissolved in dry benzene (50 ml) and thionyl chloride (20 ml) was added dropwise, maintaining the temperature at 5—10°. The mixture was evaporated under reduced pressure to give a brown gum, which was taken up in cold water and washed with ether. The aqueous solution was made basic with solid sodium hydrogen carbonate and extracted with ether. The ethereal solution was washed, dried ($MgSO_4$), and evaporated under reduced pressure to yield the chlorinated compound as a mobile unstable brown liquid (22 g, 96%), $\nu_{max.}$ 650 cm^{-1}.

3-(1-Methoxyethyl)pyridine.— 3-(1-Chloroethyl)pyridine (22 g) was added to dry methanol (150 ml) containing sodium (5 g). The mixture was heated under reflux for 5 h. The precipitated NaCl was removed by filtration and the methanol was evaporated under reduced pressure to yield a dark brown mobile liquid. This was distilled to give *3-(1-methoxyethyl)pyridine* (16·5 g, 78%), b.p. 57° at 4 mmHg, M^+, 137 and 106 (*P*), $\nu_{max.}$ 1100 (OMe) and 2800 cm^{-1}, $\lambda_{max.}$ (ε) 255 (2110), 261 (2210), and 268 (1930) nm, δ 1·40 (3H, d, *J* 6·5 Hz, CH*Me*), 3·20 (3H, s, OMe), 4·33 (1H, q, *J* 6·5 Hz, *CH*Me), 7·15—7·40 (1H, m, 5-H), 7·55—7·80 (1H, m, 4-H), and 8·50—8·61 p.p.m. (2H, m, 2- and 6-H) (Found: C, 70·0; H, 8·1. $C_6H_{11}NO$ requires C, 70·0; H, 8·0%).

4-Acetyl-3-(1-methoxyethyl)pyridine (15; R = OMe).—3-(1-Methoxyethyl)pyridine (16 g) was dissolved in acetic anhydride (250 ml) and the temperature of the stirred solution was reduced to 0°. Zinc dust (19 g) was added portionwise to the solution (3 h), maintaining the temperature at 0° during the addition and then for a further 4 h. The mixture was stirred at room temperature for 2 days. The zinc and zinc acetate were removed by filtration and the acetic anhydride was evaporated at 40° *in vacuo* to yield a viscous orange oil. When the oil was heated under reflux with methanol (200 ml) (*a*) for 5 h, a mixture of starting material and the 1,4-diacetyl-1,4-dihydro-3-(1-methoxyethyl)pyridine (14; R = Me) was obtained, $\nu_{max.}$ 1710 (Ac), 1670 (AcN), and 1630 cm^{-1} (C=C), $\lambda_{max.}$ 260 nm (*b*) for 4 days, a mixture of starting material, a small amount of (14; R = OMe) and the required 4-acetyl-3-(1-methoxyethyl)pyridine (15; R = OMe) was obtained. From the latter reaction, the methanol was removed and the residue was dissolved in chloroform and extracted with 2N-HCl. The aqueous fractions were made basic with sodium hydrogen carbonate and re-extracted with chloroform. Evaporation of the dried extracts gave an oil which was distilled to yield starting material (7 g), b.p. 50° at 2 mmHg, and *product* (15; R = OMe) (6·5 g, 63%), b.p. 86—90° at 0·1 mmHg, $\nu_{max.}$ 1700 (Ac) cm^{-1}, δ 8·92 (1H, s, 2-H), 8·7 (1H, d, *J* 5 Hz, 6-H), 7·4 (1H, d, *J* 5 Hz, 5-H), 3·3 (3H, s, OMe), 2·6 (3H, s, Ac), 4·78 (1H, q, *J* 6 Hz, Me*CH*), and 1·5 p.p.m. (3H, d, *J* 6 Hz, *Me*CH) (Found: C, 67·1; H, 7·3; N, 7·8. $C_{10}H_{13}NO_2$ requires C, 67·0; H, 7·3; N, 7·8%).

(Z)-2-[1-(3-Ethyl-4-pyridyl)ethylidene]indolin-3-one (16; R = H).—4-Acetyl-3-ethylpyridine (3 g) in 50% aqueous methanol (50 ml) containing potassium hydroxide (10 g) was added to the acetate (13) (4·3 g) in a nitrogen-purged flask. The vessel was tightly stoppered and left for 3 days at room temperature. Filtration under nitrogen then afforded the *ketone* (16; R = H) (4·2 g, 80%), orange rods, m.p. 205—210° (decomp.), M^+, 264 and 235 (*P*), $\nu_{max.}$ 1680 (CO), 1630 (C=C), and 3100 cm^{-1} (NH), $\lambda_{max.}$ (ε) 239 (16,900), 263 (26,200), 297 (13,400), and 470 (7700) nm, δ 8·2 (1H, s, 2′-H), 8·2 (1H, d, *J* 6 Hz, 6′-H), 7·0 (1H, d, *J* 6 Hz, 5′-H), 7·84 (1H, bs, NH), 7·66 (1H, m, 4-H), 7·36 (1H, m, 7-H), 6·9—6·5 (2H, m, 5- and 6-H_2), 2·56 (3H, s, CMe), 2·52 (2H, q, *J* 7 Hz, *CH_2*Me), and 1·16 p.p.m. (3H, q, *J* 7 Hz, CH*Me*) (Found: C, 77·0; H, 6·1; N, 10·6. $C_{17}H_{16}N_2O$ requires: C, 77·3; H, 5·9; N, 10·4%).

2-{1-[3-(1-Methoxyethyl)-4-pyridyl]ethylidene}indolin-3-one (17; R = OMe).—This reaction was carried out as for the indolinone (16; R = H) and yielded a mixture of orange *rods* (16; R = OMe), m.p. 181—182°, and green *needles* (17; R = OMe), m.p. 180—181°. The total yield (2·3 g) was 80%, M^+, 294 and 235 (*P*), $\nu_{max.}$ (green needles) 1690 (CO), 1635 (C=C), and 3120 cm^{-1} (NH), $\nu_{max.}$ (orange rods) 1685 (CO), 1630 (C=C), and 3180 cm^{-1} (NH), $\lambda_{max.}$ (ε) 238 (17,000), 262 (24,200), 295 (11,250), and 470 (7800) nm. The n.m.r. spectra are interpreted in the following paper [12] [Found: C, 73·4; H, 6·1; N, 9·4 (orange); C, 73·4; H, 6·15; N, 9·45 (green). $C_{18}H_{18}N_2O_2$ requires C, 73·5; H, 6·2; N, 9·5%].

2-[1-(3-Ethyl-4-pyridyl)ethyl]indolin-3-ol (18; R = H).—The indolinone (16; R = H) (500 mg) in 70% aqueous ethanol (40 ml) was warmed to 70° and treated with sodium borohydride. After 0·5 h the solvent was evaporated and the residue was partitioned between chloroform and water. Removal of the chloroform gave a sticky solid (490 mg, 96%) which crystallized from methanol as *needles*, m.p. 185—186°, M^+, 268 and 135 (*P*), $\nu_{max.}$ 3285 (NH), 3110 (OH), and 1025 cm^{-1} (C–O–), $\lambda_{max.}$ (ε) 245 (7850) and 300 (1865) nm, δ (Me_2SO) 8·35 (1H, d, *J* 5 Hz, 6′-H), 8·30 (1H, s, 2′-H), 7·3 (1H, d, *J* 5 Hz, 5′-H), 7·2—6·35 (4H m, 4-, 5-, 6-, and 7-H_4), 5·45 (1H, d, *J* 6 Hz, OH), 5·25 (1H, d, *J* 4 Hz, NH), 4·85 (1H, t, *J* 6 Hz, C*H*·OH), 3·70 (1H, m, NH·C*H*), 3·25 (2H, q, *J* 7 Hz, MeC*H*), 2·65 [2H, q, finely coupled *J* 7 Hz (2 Hz), C*H_2*Me], 1·3 (3H, d, *J* 7 Hz, *Me*CH), and 1·10 p.p.m. (3H, t, *J* 7 Hz, *Me*CH_2) (Found: C, 75·9; H, 7·5; N, 10·6. $C_{17}H_{20}N_2O$ requires C, 76·1; H, 7·5; N, 10·4%).

2-{1-[3-(1-Methoxyethyl)-4-pyridyl]ethyl}indolin-3-ol (18; R = OMe).—Reduction of the enone (16; R = OMe) or (17; R = OMe) with sodium borohydride as described for the previous compound gave the title compound as an amorphous solid which was used directly.

2-[1-(3-Ethyl-4-pyridyl)ethyl]indole (19; R = H).—The alcohol (18; R = H) (100 mg) in dry methanol (50 ml) was saturated with hydrogen chloride. After 30 min, the solution was treated with an excess of potassium hydroxide pellets and the precipitated sodium chloride was removed by filtration. Evaporation gave a gum which was dissolved in chloroform and washed with brine to yield,

after removal of chloroform, a yellow oil. Continued extraction of the oil with hot light petroleum (b.p. 60—80°) followed by concentration of the extracts afforded cubes of the *indole* (19; R = H) (84%), m.p. 126—127° M^+, 250 and 235 (*P*), $\nu_{max.}$ 1620 (C=C), 1598, 3100, and 3040 cm^{-1} (NH), $\lambda_{max.}$ (ε) 270 (11,000), 283 (10,350), and 291 (9200) nm, δ 8·70 (1H, bs, NH), 8·26 (1H, s, 2′-H), 8·20 (1H, d, *J* 6 Hz, 6′-H), 6·96 (1H, d, *J* 6 Hz, 5′-H), 7·5—6·8 (4H, m, 4-, 5-, 6-, and 7-H_4), 6·4 (1H, bs, 3-H), 4·46 (1H, q, *J* 7 Hz, 7′-H), 2·70 (2H, q, *J* 7 Hz, CH_2Me), 1·66 (3H, d, *J* 7 Hz, CH*Me*), and 1·2 p.p.m. (3H, t, *J* 7 Hz, CH_2*Me*) (Found: C, 81·9; H, 7·1; N, 11·2. $C_{17}H_{18}N$ requires C, 81·6; H, 7·3; N, 11·2%).

2-{1-[3-(1-*Methoxyethyl*)-4-*pyridyl*]*ethyl*}*indole* (19; R = OMe).—The alcohol (18; R = OMe) was treated as in the previous experiment to yield the *methoxyindole* (19; R = OMe) (95%), plates, m.p. 165—166° (from aqueous ethanol), M^+, 280 and 233 (*P*), $\nu_{max.}$ 1620 (C=C), 1600, and 3140 cm^{-1} (NH), $\lambda_{max.}$ (ε) 269 (11,850), 283 (10,700), and 291 (9300) nm n.m.r.[12] (Found: C, 77·1; H, 7·3; N, 9·9. $C_{18}H_{20}N_2O$ requires C, 77·1; H, 7·2; N, 10·0%).

1-(3-*Pyridyl*)*ethyl Acetate*.—1-(3-Pyridyl)ethanol (50 g) in benzene (200 ml) was treated with acetyl chloride (50 ml) with vigorous stirring. After 30 min, the solvents were evaporated and the residue was dissolved in water and washed thoroughly with benzene. The aqueous phase was made basic with solid sodium hydrogen carbonate and extracted with ether. The combined ether extracts were washed with brine and then evaporated to give the crude *ester*, which was purified by distillation to yield an oil (57·5 g, 85%), b.p. 62° at 0·08 mmHg, $\nu_{max.}$ 1730 (OAc) and 1235 cm^{-1} (CO), $\lambda_{max.}$ (ε) 256, 262, and 270 nm, δ 8·7—8·5 (2H, m, 2- and 6-H_2), 7·8—7·55 (1H, m, 4-H), 7·35—7·10 (1H, m, 5-H), 5·90 (1H, q, *J* 6·5 Hz, C*H*Me), 2·05 (3H, s, OAc), and 1·55 p.p.m. (3H, d, *J* 6·5 Hz, CH*Me*) (Found: C, 65·35; H, 6·6. $C_9H_{11}NO_2$ requires C, 65·45; H, 6·7%).

Reaction of 1-(3-*Pyridyl*)*ethyl Acetate with Zinc Dust and Acetic Anhydride*.—1-(3-Pyridyl)ethanol (25 g) was treated with zinc dust and acetic anhydride as previously described. Removal of the acetic anhydride yielded a thick orange gum, the i.r. spectrum of which indicates that it is a dimeric structure.[15] Several attempts were made to carry out the disproportionation reaction but these failed.

Attempted Cyclizations on the Methoxy-indole (19; R = OMe).—The following reagents were tried: polyphosphoric acid, polyphosphoric ester, boron trifluoride–acetic anhydride,[16] sodium di-isopropylamide,[17] and sodium–potassium alloy.[18] All these attempts failed to yield ellipticine or its derivatives, giving only starting material or complex mixtures.

Ellipticine (3; R = H).—The indole (19; R = OMe) (400 mg) was dissolved in water containing hydrogen bromide 60% and heated under reflux until no further change was observed in the u.v. spectrum (4 h). The orange solution was made basic with ammonia and extracted with chloroform. The chloroform extracts were left over silica gel (10 g) for 6—7 h. The silica was then removed and repeatedly extracted with boiling chloroform. Evaporation gave a residue which crystallized when triturated with ether to yield pure ellipticine (140 mg, 40%), m.p. and mixed m.p. 309—312° (lit.,[4] 309—313°) (Found: C, 83·0; H, 5·6; N, 11·2. Calc. for $C_{17}H_{14}N_2$: C, 82·9; H, 5·7; N, 11·4%).

3-[1-(3-*Pyridyl*)*ethylidene*]*indolin-2-one* (7).—3-Acetylpyridine (12·1 g) and indolin-2-one (13·3 g) were heated under reflux in benzene (250 ml) and pyrrolidine (7·1 g) for 6 h in a flask equipped with a Dean–Stark trap. The dark red solution was evaporated to low bulk and left to cool, whereupon the *indolinone* (7) (19 g, 81%) crystallized and was collected as orange needles, m.p. 164—165°, M^+, 236 (*P*), $\nu_{max.}$ 1695 (CO·NH), 1630 (C=C), and 3200 cm^{-1} (NH), $\lambda_{max.}$ (ε) 220sh (10,400), 257 (12,800), and 305 (5300) nm, δ 2·8 (3H, s, MeC=C), 6·6—7·75 (6H, m), 8·55—8·75 (2H, m, 2′- and 6′-H_2), and 9·95 p.p.m. (1H, s, NH) (Found: C, 76·2; H, 5·2; N, 11·65. $C_{15}H_{15}N_2O$ requires C, 76·25; H, 5·1; N, 11·85%).

Reduction of the Indolinone (7) *with Sodium Borohydride*.—The foregoing unsaturated amide (2 g) in 50% aqueous ethanol (50 ml) was heated to reflux and treated with sodium borohydride (2 g). The pale yellow solution was evaporated to dryness, water was added, and the whole was extracted with $CHCl_3$. The extract was washed with brine, dried. and evaporated to give a pale yellow gum (2 g). This could not be purified, although the physical characteristics are in accord with a mixture of diastereomers of the 3-[1-(3-pyridyl)ethyl]indolin-2-one (8), M^+, 238 (*P*), $\nu_{max.}$ 1715 (CO·NH) and 3160 cm^{-1} (NH), $\lambda_{max.}$ (ε) 255 (9500) and 261sh nm (8400), δ 1·3—1·35 (3H, 2 × d, *J* 7 Hz, *Me*CH), 3·0—3·3 (2H m, CO·C*H*·C*H*Me·), 6·7—7·5 (6H, m), 8·0—8·3 (2H, m, 2′- and 6′-H_2), and 9·50 p.p.m. (1H, s, NH). This material was then used directly.

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