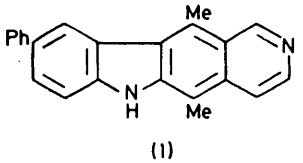
Chemistry of 6*H*-Pyrido[4,3-*b*]carbazoles. Part 7.[1] The Synthesis of 8,9-Benzoellipticine (Benzo[*h*]pyrido[4,3-*b*]carbazole) and Some 5-Alkyl Derivatives of the Pyrido[4,3-*b*]carbazole System

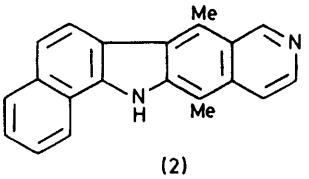
By **Michael Driver, Ian T. Matthews,** and **Malcolm Sainsbury,*** School of Chemistry, University of Bath, Claverton Down, Bath BA2 7AY

Various known procedures have been utilized to synthesize benzo[*h*]pyrido[4,3-*b*]carbazole (8,9-benzoellipticiene) and derivatives of the pyrido[4,3-*b*]carbazole system with extended alkyl substituents attached to position 5. A comparison is made between the various synthetic methods available for the synthesis of ellipticine derivatives of interest as anticancer agents.

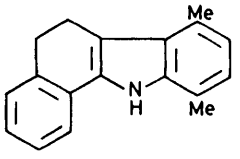
A KEY compound suggested by a Hansch analysis [2] of the 6*H*-pyrido[4,3-*b*]carbazole system is 9-phenylellipticine (1). Some years ago we prepared this derivative [3] and submitted it for anticancer testing. It is inactive, and



(1)



(2)



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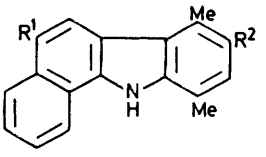
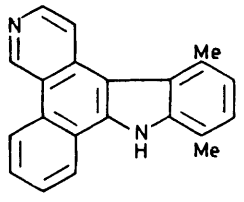


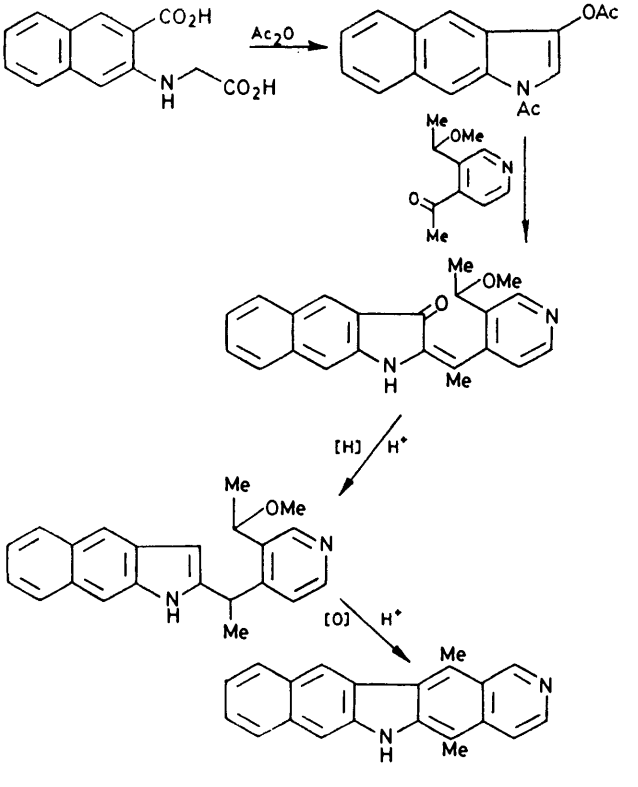
(4) R^1 = H, R^2 = CHO
(5) R^1 = CHO, R^2 = H
(6) R^1 = $CH_2N(SO_2C_6H_4Me\text{-}p)$-$CH_2CH(OMe)_2$, R^2 = H



(7)

at the time we took this result as circumstantial evidence in favour of the hypothesis, now proven,[4] that active ellipticines are intercalated between the base pairs of DNA thus inhibiting cell replication. The ellipticine molecule is planar and arc shaped, ideally suited for intercalation, but bulky substituents attached to the periphery of the tetracycle will obviously reduce or eliminate this property. Nevertheless, the arguments of the Hansch proposals as applied to ellipticines but disregarding steric constraints appear to be valid, and we are still interested in examining the biological effects of extending the conjugation of the parent heterocycle. An obvious step then is to prepare benzo-analogues of ellipticine since these compounds will still retain the planarity of the parent yet have similar electronic and physical properties to those of 9-phenylellipticine.

Our first objective was 7,8-benzoellipticine (2) and we sought to prepare this by a modification of the Cranwell and Saxton approach [5] to ellipticines utilizing some more recent improvements.[6] Accordingly the dihydrocarbazole (3) was synthesized by a Fischer indolization between β-tetralone and 2,5-xylylhydrazine; the dihydrocarbazole was then dehydrogenated by heating over palladium on charcoal in xylene. In line with early work, we expected Vilsmeier formylation of the fully aromatized product to occur at position 8 to give (4), but the only product isolated from such a reaction was the isomer (5). With this compound to hand the *N*-tosylazomethine (6) was formed in an attempt to effect ring closure to the pentacycle (7), but treatment of this compound with acids only served to form highly insoluble deep blue materials of high molecular weight.



(8)

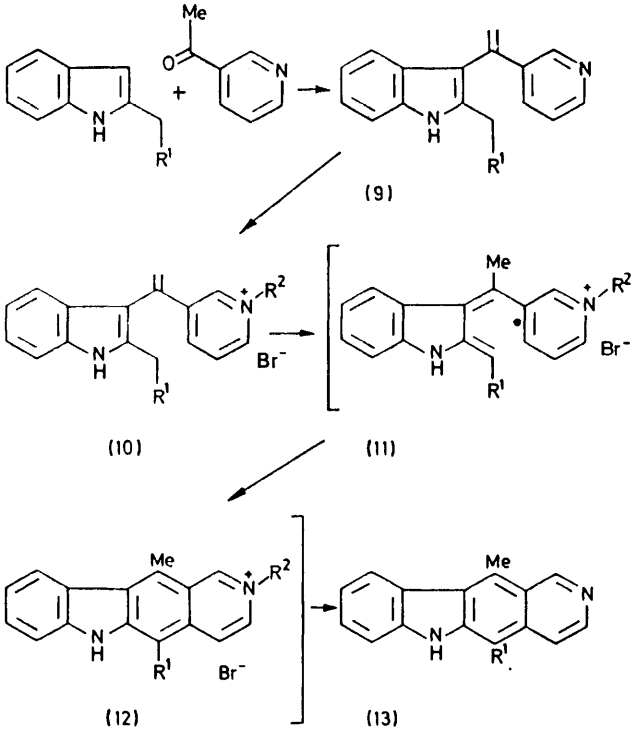
SCHEME 1

The dihydrocarbazole (3) represents an obvious alternative substrate for formylation since now the 5-position is blocked, but a Vilsmeier reaction upon this compound leads to a mixture of monoformylated products which are extremely difficult to separate.

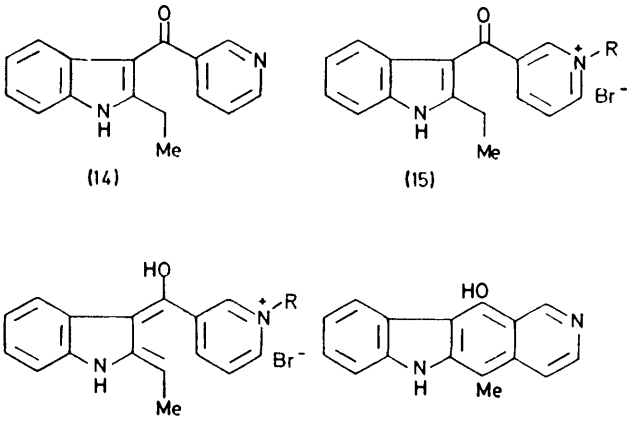
Our attention turned next to the linear benzoellipticine (8) and this we obtained by the route outlined in Scheme 1.[7] This is, of course, simply a modification of the route used by us to prepare 9-phenylellipticine,[3] but in contrast to this early work the yield in the condensation step between the diacetylindoxyl and the 4-acetylpyridine was much lower, and it will be necessary to repeat this sequence in order to acquire sufficient of the benzoellipticine (8) for biological assessment.

It has been shown that the activity of ellipticine against the L1210 murine leukaemia is lost if the methyl groups at C-5 and C-11 are removed, and French workers suggest that the demethyl derivatives are less effective in binding to DNA.[4] As important may be the loss of lipophilicity which aids transport across cell boundaries and in order to provide more information on this point we decided to prepare some structural analogues with extended alkyl chains attached to position 5.

Our first approach was to utilize the synthesis recently announced by Bergman and Carlsson[8] to prepare 5-ethyl-11-methylellipticine (Scheme 2). Accordingly, 2-n-propylindole was condensed with 3-acetylpyridine to afford the vinly compound (9); this was converted into the *N*-n-butyl salt (10) and pyrolysed at 350 °C. On work-up, however, only a trace of the required pyrido-[4,3-*b*]carbazole was isolated. Later we used the technique recommended by Carlsson[9] of warming the tube containing the pyridinium salt in a luminous Bunsen flame, but in our hands the yield of the carbazole (13) was much less than that recorded by them for ellipticine itself.



SCHEME 2 R^1 = Et, R^2 = Bu^n

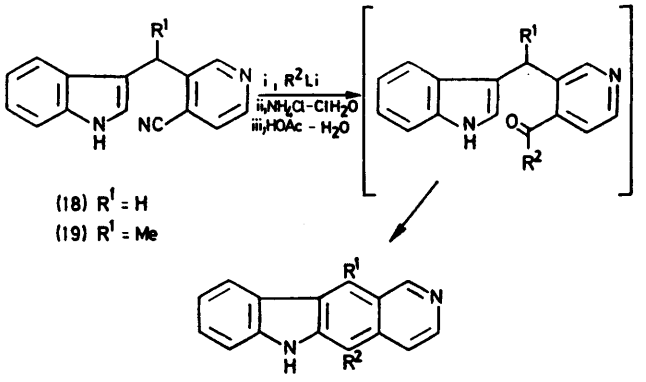


R = Bu^n

The mechanism by which salts of the type (10) are converted into pyrido[4,3-*b*]carbazoles is still debatable, but a likely initial step is the formation of the conjugated tautomer (11) which then cyclizes to the dihydropyridocarbazole (12).[9] The cyclization process should occur either photochemically or thermally but photolysis reactions have so far been unproductive.[9,10] In view of this proposal the carbonyl compound (15) should be a good substrate for the synthesis of 11-hydroxy-5-methyl-6*H*-pyrido[4,3-*b*]carbazole (17) since the ' acidity ' of the methylene protons of the indol-2-yl substituent is enhanced by the presence of the enone unit and thus the formation of the diene tautomer (16) is facilitated. However, pyrolysis of the salt (15) failed to yield the expected product, and attempted photochemical cyclizations with either the salt (15) or the pyridine (14) were also unsuccessful. It has been reported that the methyl protons of 2,3-dimethylindole exchange in the presence of deuterium oxide.[11] Significantly, however, this does not occur with the pyridine (14).

Initially we felt reluctant to use our own route to ellipticines (Scheme 3)[12] to prepare homologues since there is evidence that the cyanide function of the intermediate (19) is sterically hindered. Nevertheless the lack of success just related caused us to carry out some preliminary experiments and we were pleased to find that when the nitrile (18) was treated with n-butyllithium, 5-n-butyl-6*H*-pyrido[4,3-*b*]carbazole (20) was obtained in 87% yield. A similar reaction with the homologue (19) afforded 5-n-butyl-11-methyl-6*H*-pyrido-[4,3-*b*]carbazole (21) also in good yield. The versatility of this approach is supported even further by the fact that phenyl-lithium reacts with the nitrile (18) to give 5-phenyl-6*H*-pyrido[4,3-*b*]carbazole (22) in moderate yield. We now intend to prepare a series of alkylated

derivatives of the pyrido[4,3-*b*]carbazole system by this route in order to complete the pharmacological study referred to earlier in this paper.



(18) R^1 = H
(19) R^1 = Me

(20) R^1 = H, R^2 = Bu^n
(21) R^1 = Me, R^2 = Bu^n
(22) R^1 = H, R^2 = Ph

SCHEME 3

EXPERIMENTAL

U.v. spectra were recorded for solution in 95% aqueous ethanol, and i.r. spectral data refer to Nujol mulls. ^1H N.m.r. spectra were recorded either 60 or 100 MHz with tetramethylsilane as internal standard.

5,6-Dihydro-7,10-dimethyl-11H-benzo[a]*carbazole* (3).—2,5-Xylylhydrazine hydrochloride (35.2 g) was added to 20% hydrochloric acid (500 cm³) and warmed until dissolution was effected. 1-Tetralone (29.2 g) was then introduced in portions over a period of 4 h, during which time the mixture was heated at reflux. On cooling, a brown solid separated. This was collected and triturated with 95% aqueous ethanol. The remaining solid was crystallized from the same solvent affording the *dihydrocarbazole* (3) as plates (37.3 g, 76%), m.p. 165—166 °C; *m/e* 247 (M^+, 100%), 232, and 217; $\nu_{max.}$ 3 430 and 1 610 cm^{-1}; $\lambda_{max.}$ (ε) 255 (24 450) and 347 (6 175) nm; δ ($CDCl_3$) 2.45 (3 H, s, 10-Me), 2.7 (3 H, s, 7-Me), 3.0—3.30 (4 H, m, CH_2CH_2), 6.8 (2 H, 2 × d, *J* 10 Hz, 8- and 9-H), 7.25 (4 H, m, 1-, 2-, 3- and 4-H), and 8.0 br (1 H, s, NH) (Found: C, 87.4; H, 6.8; N, 5.7. $C_{18}H_{16}N$ requires C, 87.4; H, 6.9; N, 5.7%).

7,10-Dimethyl-11H-benzo[a]*carbazole*.—The dihydrocarbazole (3) was dehydrogenated by boiling in xylene solution with 10% palladium–charcoal. After 1—2 h, the catalyst was removed and the filtrate allowed to cool whereupon the product carbazole separated. On a 10-g scale the yield is 98.4%. *7,10-Dimethyl-11H-benzo*[a]*carbazole* has m.p. 161—162 °C; *m/e* 245 (M^+, 100%), 230, and 215; $\nu_{max.}$ 3 440 and 1 515 cm^{-1}; $\lambda_{max.}$ (ε) 255 (23 275), 283 (25 480), and 303 (12 740) nm; δ ($CDCl_3$) 2.55 (3 H, s, 10-Me), 2.83 (3 H, s, 7-Me), 6.98 (2 H, 2 × d, *J* 7 Hz, 8- and 9-H), 7.5 (4 H, 1-, 2-, 3-, and 4-H), 8.0 (2 H, m, 5- and 6-H), and 8.54 br (1 H, s, NH) (Found: C, 88.3; H, 6.1; N, 5.7. $C_{16}H_{15}N$ requires C, 88.1; H, 6.2; N, 5.7%).

7,10-Dimethyl-11H-benzo[a]*carbazole-5-carbaldehyde* (5).—The foregoing benzocarbazole (29.4 g) in *N*-methylformanilide (23 g) was treated with phosphorus trichloride oxide (17 g) in 1,2-dichlorobenzene (60 cm³). The mixture was heated at 100 °C for 3.5 h, then poured into water (200 cm³) containing sodium acetate (46 g) and steam-distilled to remove the solvents. The grey solid residue was extracted with toluene in a Soxhlet apparatus during 10 h and the extract decolourized with charcoal. On cooling the solution afforded green prisms of the *aldehyde* (5) (14.8 g, 45%); m.p. 286—287 °C; *m/e* 273 (M^+, 100%) and 244; $\nu_{max.}$ 3 260 and 2 725 cm^{-1}; $\lambda_{max.}$ (ε) 250 (21 840), 290 (30 849), and 260 (6 279) nm; δ [$(CD_3)_2SO$] 2.7 (3 H, s, 10-Me), 2.9 (3 H, s, 7-Me), 7.1 (2 H, 2 × d, *J* 7 Hz, 8- and 9-H), 7.7 (2 H, m, 2- and 3-H), 8.8 (1 H, s, 6-H), 8.9 (1 H, m, 1-H), 9.5 (1 H, m, 4-H), 10.3 (1 H, s, CHO), and 12.1 br (1 H, s, NH) (Found: C, 83.6; H, 5.55; N, 5.1. $C_{19}H_{15}NO$ requires C, 83.5; H, 5.5; N, 5.1%).

5-[N-(2,2-Dimethoxyethyl)iminomethyl]-7,10-dimethyl-11H-benzo[a]*carbazole*.—The aldehyde (5) (5.46 g) in dimethoxyethylamine (4.2 g) was heated at 100 °C for 3 h. Dry benzene (20 cm³) was then added and the mixture heated for a further 1.5 h in a Dean–Stark apparatus. Evaporation gave a gum which crystallized slowly when triturated with light petroleum (b.p. 60—80 °C) and diethyl ether. Recrystallization from benzene afforded prisms of the title *azomethine*; m.p. 132—134 °C; yield 6.6 g (91%); *m/e* 360 (M^+) and 285 (100%); $\lambda_{max.}$ (ε) 280 (30 960), 295 (27 000), 348 and (18 720); $\nu_{max.}$ 3 330 and 1 620 cm^{-1}; δ ($CDCl_3$) 2.56 (3 H, s, 10-Me), 2.76 (3 H, s, 7-Me), 3.55 (6 H, s, 2 × Me), 3.9 (2 H, d, *J* 6 Hz, CH_2CH), 4.82 (1 H, t, *J* 6 Hz, CH_2CH), 7.04 (2 H, 2 × d, *J* 8 Hz, 8- and 9-H), 7.56 (2 H, m, 2- and 3-H), 8.16 (1 H, m, 1-H), 8.5 (1 H, s, 6-H), 8.9 (1 H, s, CH=N), 9.17 (1 H, m, 4-H), and 10.87 (1 H, s, NH) (Found: C, 76.8; H, 6.8; N, 7.9. $C_{23}H_{24}N_2O_2$ requires C, 76.6; H, 6.7; N, 7.8%).

5-[N-(2,2-Dimethoxyethyl)aminoethyl]-7,10-dimethyl-11H-benzo[a]*carbazole*.—The azomethine (6.86 g) from the previous experiment in ethanol (35 cm³) and tetrahydrofuran (10 cm³) was treated with sodium borohydride (6 g) in portions. After 2 h the solvents were removed and water (15 cm³) was added to the residue. Extraction with chloroform gave crystals of the title *amine* which was recrystallized from light petroleum (b.p. 80—100 °C) to give prisms, m.p. 117—119 °C; yield 5.73 g (85%); *m/e* 362 (M^+) and 258 (100%), $\nu_{max.}$ 3 440 and 3 230 cm^{-1}; δ ($CDCl_3$) 2.45 (3 H, s, 10-Me), 2.7 (3 H, s, 7-Me), 2.90 (2 H, d, *J* 6 Hz, CH_2CH), 2.91 (1 H, s, $NHCH_2$), 3.33 (6 H, s, 2 × OMe), 3.53 (1 H, t, *J* 6 Hz, CH_2CH), 5.21 (2 H, s, $NHCH_2$), 7.00 (2 H, 2 × d, *J* 8 Hz, 8- and 9-H), 7.52 (2 H, m, 2- and 3-H), 8.10—8.35 (3 H, m, 1-, 4-, and 6-H), and 9.30 (1 H, s, NH) (Found: C, 76.2; H, 7.2; N, 7.7. $C_{23}H_{26}N_2O_2$ requires C, 76.2; H, 7.2; N, 7.7%).

5-[N-(2,2-Dimethoxyethyl)-N-(p-tolylsulphonyl)aminomethyl]-7,10-dimethyl-11H-benzo[a]*carbazole* (6).—The amine from the previous experiment (5 g), sodium carbonate (1.5 g), tetrahydrofuran (100 cm³), and water (50 cm³) were stirred while toluene-*p*-sulphonyl chloride (2.6 g) was introduced. After 3 h, the product was precipitated by the addition of water, filtered off, and crystallized from ethyl acetate to give the *sulphonyl compound* (6) as prisms (5 g, 70%); m.p. 165—167 °C; *m/e* 516 (M^+) and 259 (100%) (Found: C, 69.75; H, 6.2; N, 5.4. $C_{30}H_{32}O_4N_2S$ requires C, 69.75; H, 6.2; N, 5.4%).

(E)- and (Z)-2-{1-[3-(1-*Methoxyethyl*)-4-*pyridyl*]*ethylidene*}-1H-*benz*[f]*indol*-3(2H)-*one*.—1-Acetoxy-1-acetyl-1*H*-benz-[*f*]indole (1.2 g) and 4-acetyl-3-(1-methoxyethyl)pyridine (0.81 g) were dissolved in 50% aqueous methanol (12 cm³) which had been previously deoxygenated. The solution was set aside under nitrogen for a week. The mixture was

then poured into 20% acetic acid solution (75 cm^3) previously cooled to 5 °C. After stirring for 10 min the dark blue solid which had formed was collected and washed first with water and then with dichloromethane. The dichloromethane washings were combined, dried, and evaporated to afford a gum which was chromatographed upon neutral alumina, eluting with 10% light petroleum (b.p. 60—80 °C) in ethyl acetate. In this way the title compounds were obtained as a brown amorphous solid (0.63 g, 40.1); *m/e* 344 (M^+), 312 (40%), and 297 (100%); $\nu_{max.}$ 3 120, 1 690, 1 685, and 1 640 cm^{-1}.

The brown residue remaining after washing with dichloromethane was then extracted with dichloromethane and the extracts worked up to afford the (E)-*isomer* only as a pale pink solid (0.03 g, 2.0%); m.p. 197 °C (decomp.); $\lambda_{max.}$ (ε) 210 (1 032), 235 (1 720), 277 (17 544), and 304 (19 264) nm; $\nu_{max.}$ 3 310, 1 690, and 1 640 cm^{-1}; δ [$CDCl_3$ + added $(CD_3)_2SO$] 1.28 and 1.44 (3 H, 2 × d, *J* 7 Hz, CH*Me*), 2.20 and 2.24 (3 H, 2 × s, CMe), 3.13 and 3.24 (3 H, 2 × s, C–OMe), 4.4 (1 H, q, *J* 7 Hz, C*H*Me), 7.0 (1 H, d, *J* 6 Hz, 5′-H), 7.18 (1 H, s, 4-H), 7.24 (1 s, H, d, *J* 8 Hz, 8-H), 7.48 (2 H, 2 × d, *J* 8 Hz, 6- and 7-H), 7.68 (1 H, d, *J* 8 Hz, 5-H), 8.00 (1 H, s, 9-H), 8.46 (1 H, d, *J* 6 Hz, 6′-H), 8.68 (1 H, s, 2′-H), and 8.76 (1 H, s, NH) (primed numbers refer to the pyridyl unit) (Found: C, 76.6; H, 5.7; N, 8.0. $C_{22}H_{20}N_2O_2$ requires C, 76.7; H, 5.85; N, 8.1%).

6H-*Benzo*[h]*pyrido*[4,3-b]*carbazole* (8).—The combined isomers (0.6 g) from the previous experiment were dissolved in 60% aqueous ethanol (50 cm^3) and heated to 45 °C. Excess of sodium borohydride was then added in portions during 30 min. After a further 1 h, the solvent was removed under reduced pressure and the residue extracted with chloroform. The combined extracts were processed to afford a red gum which was dissolved in methanol and the solution saturated with hydrogen chloride gas. Removal of the solvent gave a gum which was triturated with chloroform–2N sodium hydrogen carbonate solution. The chloroform layer was dried and evaporated to yield a further gum. T.l.c. analysis (neutral alumina; dichloromethane) indicated three components one of which fluoresced blue under u.v. light. This component was separated from the other two by column chromatography on neutral alumina and obtained as a yellow oil which separated from diethyl ether as a colourless amorphous solid of indefinite m.p.; yield 0.18 g (28%); *m/e* 330 (M^+) 298 (60%), 283 (100), and 269 (40); $\nu_{max.}$ 3 155 and 1 608 cm^{-1}. Further work-up upon the remaining fractions from the column failed to yield tangible amounts of other compounds, and so the amorphous solid, presumably a mixture of diastereoisomers, was used in the final stage of the reaction. This compound (0.17 g) in 50% hydrobromic acid (25 cm^3) was heated under reflux until no further change was indicated by u.v. spectroscopy. The solution was then cooled to 0 °C, and the solid which formed was collected. The free base was liberated from the salt with aqueous ammonia and dissolved in chloroform. Silica (500 mg) was added and the solvent removed; finally the product was removed from the silica by extraction with hot methanol and ethyl acetate (3 : 1) containing a little ammonia. After evaporation the residue was sublimed at 0.1 mmHg pressure for 3 h, affording 6H-*benzo*[h]*pyrido*[4,3-b]*carbazole* (8) as a yellow solid which crystallized from ethanol as micro-prisms (0.08 g), m.p. 327—329 °C; *m/e* 296 (M^+) and 281 (100%); $\lambda_{max.}$ (ε) 273 (37 900), 309 (30 200), 320 (33 744), and 340 (16 872); δ [$(CH_3)_2SO$] 2.8 (3 H, s, 5-Me), 3.64 (3 H, s, 13-Me), 7.48 (2 H, m, 8- and 9-H), 7.86 (1 H, s, 12-H), 8.12 (3 H, m, 3-, 4-, and 11-H), 8.38 (1 H, m, 10-H), 8.90 (1 H, s, 7-H), 9.68 (1 H, s, 1-H), and 9.72 br (1 H, s, NH) (Found: C, 85.4; H, 5.5; N, 9.65. $C_{21}H_{16}N_2$ requires C, 85.15; H, 5.4; N, 9.5%).

2-*n-Propyl*-3-[1-(3-*pyridyl*)*vinyl*]*indole* (9).—2-n-Propylindole (5 g) and 3-acetylpyridine (3.8 g) in methanol previously saturated with hydrogen bromide were heated at reflux for 3 h. The mixture was then cooled, poured on ice, and neutralized with ammonium hydroxide. The product was extracted into dichloromethane and after drying solvent was removed to give the *vinylindole* (9) which was recrystallized from aqueous ethanol; yield 6.6 g, m.p. 132—133 °C; $\lambda_{max.}$ 249 and 285 nm; $\nu_{max.}$ *ca.* 3 150 and 1 610 cm^{-1}; δ ($CDCl_3$) 8.9 br (1 H, s, NH), 8.7 (1 H, s), 8.5 (1 H, d, (*J* 6 z), 7.6 (1 H, m), 7.2—6.9 (5 H, m), 5.72 (1 H, s), 5.35 (1 H, s), 2.6 (2 H, t, *J* 7 Hz), 1.6 (2 H, sextet), and 0.9 (3 H, t, *J* 7 Hz) (Found: C, 82.3; H, 6.9; N, 10.5. $C_{18}H_{18}N_2$ requires C, 82.4; H, 6.9; N, 10.7%).

Compound (9) when heated with n-butyl bromide gave the salt (10) as a brown glass, $\nu_{max.}$ 3 100, 1 615, and 1 610 cm^{-1}; δ ($CDCl_3$) 10.1 br (1 H, s, NH), 9.28 (1 H, d, *J* 6 Hz), 9.0 (1 H, s), 8.2 (1 H, m), 7.9 (1 H, m), 7.6 (1 H, m), 7.05—6.6 (3 H, m), 6.3 (1 H, s), 5.6 (1 H, s), 2.7 (2 H, m), 1.8 (4 H, m), 1.2 (4 H, m), and 0.9 (6 H, 2 × t, *J* 7 Hz).

5-*Ethyl*-11-*methyl*-6H-*pyrido*[3,4-b]*carbazole* (13).—Portions (*ca.* 5 mg) of the salt (10) were placed in small Pyrex ignition tubes; these were then heated in a luminous Busen flame for 30—60 s. The tubes were crushed in a pestle and mortar and extracted with chloroform. The chloroform extract was boiled with charcoal and the dark resinous product chromatographed on basic alumina, eluting with light petroleum (b.p. 60—80 °C)–chloroform. The major component (0.07 g from 5 g of the salt), $\lambda_{max.}$ 245, 262, 290, and 308 nm, was further purified by sublimation under low pressure to afford the *dialkyl compound* (13) as a yellow solid (0.05 g), m.p. 295 °C (sublimes); $\nu_{max.}$ 3 120, 1 610, and 1 605 cm^{-1}; $\lambda_{max.}$ 240w, 297s, and 308s nm; *m/e* 260 (M^+; 100%), 245, 231, and 230; δ [$CDCl_3$ + $(CD_3)_2SO$] 9.8 (1 H, s), 8.2 (1 H, m), *ca.* 7.4 (5 H, m), 3.05 (2 H, t, *J* 9 Hz), 2.95 (3 H, s), 0.85 (3 H, t, *J* 9 Hz) (Found: C, 83.1; H, 6.3; N, 10.6. $C_{18}H_{16}N_2$ requires C, 83.0; H, 6.2; N, 10.8%).

2-*Ethylindol*-3-*yl Pyridin*-3-*yl Ketone* (14).—2-Ethylindole (40.6 g) in diethyl ether (50 cm^3) was added to ethylmagnesium bromide (from ethyl bromide, 30.5 g) in the same solvent (30 cm^3) maintained at *ca.* 0 °C. After 30 min, nicotinoyl chloride (from nicotinic acid) in benzene (50 cm^3) was introduced and the mixture cooled and stirred for a further 4 h.

Saturated ammonium chloride solution (30 cm^3) was added and the product extracted with dichloromethane (3 × 60 cm^3). Evaporation of the combined, dry extracts gave the crude *ketone* (14) as an orange solid (22 g, 3%). This was recrystallized from aqueous methanol to afford almost colourless prisms; m.p. 199—201 °C; $\lambda_{max.}$ 265 and 325 nm; $\nu_{max.}$ 3 080, 3 065, 3 050, 1 595, and 1 585 cm^{-1}; δ [$(CD_3)_2CO$] 12.0 br (1 H, s), 8.8 (2 H, m), 8.0 (1 H, d of t, *J* 8 and 1.5 Hz), 7.6—7.05 (5 H, m), 2.8 (2 H, q, *J* 7.5 Hz), and 1.15 (3 H, t, *J* 7.5 Hz) (Found: C, 76.6; H, 5.5; N, 11.4. $C_{16}H_{14}N_2O$ requires C, 76.8; H, 5.6; N, 11.2%).

This compound was converted into the corresponding *N*-Bu^n salt (15) by heating with n-butyl bromide. This product was isolated as a brown glass; δ [$(CD_3)_2SO$] 9.4 (2 H, m), 8.85 br (1 H, d, *J* 9 Hz), 8.38 (1 H, m), 7.6 (1 H, d, *J* 8 Hz),

ca. 7.2 (3 H, m), 2.95 (2 H, q, *J* 7.5 Hz), and 1.3 (3 H, t, *J* 7.5 Hz). This product was used directly.

5-n-Butyl-6H-pyrido[4,3-b]*carbazole* (20).— 3-(Indol-3-ylmethyl)pyridine-4-carbonitrile (125 mg) in anhydrous diethyl ether was added dropwise to a solution of n-butyllithium (3 mol. equiv.) in hexane at −100 °C. After stirring for 30 min, ice–water was added followed by 10% ammonium chloride in water. The organic phase was dried and evaporated to afford a gum which was heated with 20% aqueous acetic acid on a steam-bath for 45 min. The solution was then cooled, basified with potassium carbonate, and extracted with chloroform. On work-up the combined extracts afforded the *butyl compound* (20) as a yellow solid which was recrystallized from chloroform as needles (115 mg), m.p. 299—301 °C (decomp., darkens above 270 °C); $\lambda_{max.}$ 275, 285, and 295 nm; $\nu_{max.}$ 3 150, 1 605, and 1 600 cm^{-1}; δ [$CDCl_3$ + $(CD_3)_2SO$] 9.3 br (1 H, s), 8.75 (1 H, s), 8.4—8.1 (2 H, m), 7.9—7.75 (1 H, m), 7.5 (1 H s), 7.4 br (1 H, s), 7.35—7.2 (2 H, m), 3.2 (2 H, m), *ca.* 1.6 (4 H, m), and 0.85 (3 H, t); δ (CF_3CO_2H), 9.35 (1 H, d, *J* 6.5 Hz), 8.66 (1 H, s), *ca.* 8.3 (3 H, m), *ca.* 7.5 (3 H, m), 3.2 (2 H, t, *J* 8 Hz), *ca.* 1.7 (4 H, m), and 1.05 (3 H, t, *J* 7 Hz) (Found: C, 83.0; H, 6.4; N, 10.1. $C_{19}H_{18}N_2$ requires C, 83.2; H, 6.6; N, 10.2%).

5-n-Butyl-11-methyl-6H-pyrido[4,3-b]*carbazole* (21).—This was prepared from 3-[1-(indol-3-yl)ethyl]pyridine-4-carbonitrile using a similar procedure to that described in the previous experiment. The *dialkyl compound* (21) was obtained in 78% yield as yellow prisms, m.p. 285—287 °C (sublimes); $\lambda_{max.}$ 277, 286, and 295 nm; $\nu_{max.}$ 3 150, 1 605, and 1 600 cm^{-1}; δ (CF_3CO_2H) 9.6 (1 H, d, *J* 6.5 Hz), *ca.* 8.4 (3 H, m), 7.6—7.3 (3 H, m), 3.2 (2 H, t, *J* 8 Hz), 3.16 (3 H, s), *ca.* 1.8 (4 H, m), and 1.1 (3 H, t, *J* 8 Hz) (Found: C, 83.2; H, 6.9; N, 9.6. $C_{20}H_{20}N_2$ requires C, 83.3; H, 7.0; N, 9.7%).

5-Phenyl-6H-pyrido[4,3-b]*carbazole* (22).—This was prepared from 3-(indol-3-yl)methyl pyridine-4-carbonitrile by the action of phenyl-lithium, the reaction being carried out at −10 °C. The *phenyl compound* (22), obtained by a similar work-up procedure to that used for (20), was recrystallized from ethanol as yellow prisms; m.p. 289—290 °C (rapid heating); it sublimes at 280—285 °C; yield 20%; $\lambda_{max.}$ 226, 265 (infl.) 276, 285, 293, and 310 nm; $\nu_{max.}$ 3 150, 1 605, and 1 600 cm^{-1}; δ [$(CD_3)_2SO$] 9.5 br (1 H, s), 9.15 (1 H, s), 8.8 (2 H, m), 8.3—7.5 (7 H, m), and 7.25 (3 H, m); *m/e* 294 (M^+; 100%) and 147 (12%) (Found: C, 85.6; H, 4.8; N, 9.3. $C_{21}H_{14}N_2$ requires C, 85.7; H, 4.8; N, 9.5%).

The authors gratefully acknowledge financial support from the Cancer Research Campaign.

[8/2151 *Received*, 14*th December*, 1978]

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