Reactions and Synthetic Applications of β-Oxo-sulphoxides. Part VI.[1] A New Synthesis of the Pyrido[4,3-*b*]carbazoles Olivacine and Ellipticine

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The acid-catalysed cyclization of β-oxo-sulphoxides was applied to a synthesis of olivacine and ellipticine. An oxo-sulphoxide derived from methyl *N*-benzylindole-3-propionate was cyclized with trifluoroacetic acid to give a 2-oxo-1.2.3.4-tetrahydrocarbazole derivative. and a side chain was introduced at the carbonyl group. Aromatization and construction of the pyridine ring proceeded efficiently to yield olivacine. In the same way. ellipticine was synthesized from methyl *N*-benzylindole-3-butyrate.

THE synthetic utility of the Pummerer rearrangement [2,3] has remained undeveloped, largely because the rearrangement has been used only for the formation of carbon–heteroatom bonds. Recently, we reported an extension of the Pummerer reaction to the formation of carbon–carbon bonds through acid-catalysed cyclization of β-oxo-sulphoxides, which afforded a new synthesis of condensed aromatic and heteroaromatic compounds such as naphthalene, phenanthrene, carbazole, indole, and benzothiophen derivatives (*e.g.* Scheme 1).[1,4]

The formation of aromatized products such as (3) involves two consecutive acid-catalysed reactions, cyclization of a β-oxo-sulphoxide and aromatization with loss of methanethiol. Since the latter usually requires a stronger acid and/or a higher temperature, either of the two types of product [(2) and (3)] can be selected by appropriate choice of acid and solvent. It was hoped that the introduction of a side chain at the carbonyl

[1] Part V, Y. Oikawa and O. Yonemitsu, *J. Org. Chem.*, 1976, **41**, 1118.

[2] R. Pummerer, *Ber.*, 1909, **42**, 2282; L. Hormer and P. Kaiser, *Annalen*, 1959, **626**, 19.

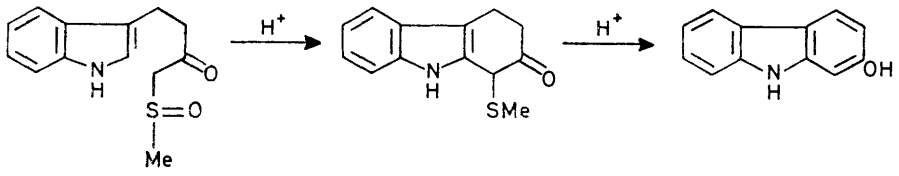
[3] S. Oae, T. Kitao, S. Kawamura, and Y. Kitaoka, *Tetrahedron*, 1963, **19**, 817; C. R. Johnson, J. C. Sharp, and W. G. Phillips, *Tetrahedron Letters*, 1967, 5299; C. R. Johnson and W. G. Phillips, *J. Amer. Chem. Soc.*, 1969, **91**, 682.

[4] Y. Oikawa and O. Yonemitsu, *Tetrahedron*, 1974, **30**, 2653; *Heterocycles*, 1974, **2**, 21.

group in compounds (4) [of type (2)] prior to aromatization [to (6)] would give intermediates (5) appropriate for the synthesis of olivacine (7) and ellipticine (8).

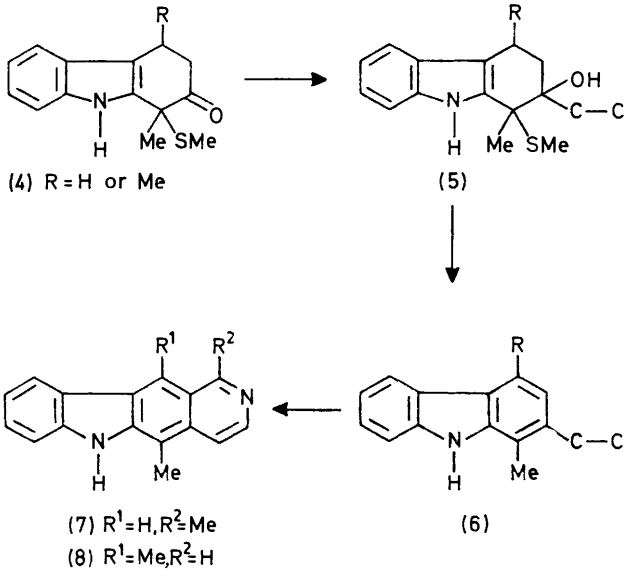
Because of the antitumour activity of the 6*H*-pyrido-[4,3-*b*]carbazole system, many useful methods for the synthesis of either (7) or (8) have been devised.[5] The synthesis reported here is applicable to both olivacine (7) and ellipticine (8).

Olivacine.—The β-oxo-sulphoxide (9), prepared from methyl indole-3-propionate by treatment with sodium methylsulphinylmethanide followed by methylation with methyl iodide, was subjected to the acid-catalysed cyclization. The expected product (10), however, was isolated in only 10% yield,[1] even under optimal reaction conditions.



(1) (2) (3)

SCHEME 1



SCHEME 2

Since alkylation of the NH group of an indole usually results in an improvement of the cyclization,[1] the reaction of 1-benzylindole-3-propionate (11) was studied. Treatment with diethyl sulphoxide in the presence of lithium di-isopropylamide [6] gave an oxo-sulphoxide (12) in 95% yield as a mixture of diastereoisomers (1 : 2.3) which was used directly in the next step. The use of diethyl sulphoxide enabled us to dispense with the methylation step.

Treatment of the sulphoxide (12) with trifluoroacetic acid in boiling benzene resulted in a single cyclization product (13) (43% yield). In acetonitrile–tetrahydrofuran (4 : 1) the yield was improved (51%). The product (13) was identified by mass spectrometry, elemental analysis, and i.r. ($\nu_{max.}$ 1 700 cm^{-1}) and n.m.r. spectra (*C*-methyl signal at δ 1.64; no indole 2-H signal).

In order to introduce efficiently a substituent at the carbonyl position, several reactions were examined. A Reformatsky reaction with ethyl bromoacetate in the presence of zinc gave only an aromatized product (14), identified by comparison with material synthesized from (12) in boiling trifluoroacetic acid.* With the following four reagents: ethyl acetate–lithium amide in liquid ammonia,[7] 2,4,4-trimethyl-Δ^2-oxazoline–butyl-lithium in tetrahydrofuran,[8] ethyl trimethylsilylacetate–lithium di-isopropylamide in tetrahydrofuran,[9] and t-butyl acetate–lithium di-isopropylamide in tetrahydrofuran,[10] the starting material (13) was unchanged; it was apparently unreactive at −78 °C.

t-Butyl lithioacetate [11] reacted with compound (13) in benzene at room temperature to give the expected product (15) in quantitative yield, though the reproducibility was not entirely satisfactory. In the best procedure, compound (13) was treated at room temperature with t-butyl lithioacetate solution previously prepared from t-butyl acetate and butyl-lithium in toluene at −78 °C. Although the product (15) could conceivably have been formed as a diastereoisomeric mixture, only one isomer was in fact observed, that produced by attack from the less-hindered side of the molecule.

* The acid-catalysed aromatization requires usually a stronger acid such as toluene-*p*-sulphonic acid.[1,4] Compound (12), having a methyl substituent at the active methylene group between the carbonyl and sulphinyl groups, however, was easily aromatized to (14) even in trifluoroacetic acid, which is usually too weak to aromatize β-oxo-sulphoxides.

[5] M. Sainsbury, B. Webb, and R. Schinazi, *J.C.S. Perkin I*, 1975, 289; M. Sainsbury and R. F. Schinazi, *J.C.S. Chem. Comm.*, 1975, 540; R. Bessedievre, C. Thal, H. P. Husson, and P. Potier, *ibid.*, p. 90; Y. Langlois, N. Langlois, and P. Potier, *Tetrahedron Letters*, 1975, 955; J. P. Kutney and D. S. Grierson, *Heterocycles*, 1975, **2**, 171; T. Kametani, Y. Ichikawa, T. Suzuki, and K. Fukumoto, *ibid.*, 1975, **3**, 401; M. J. Winchester and F. D. Popp, *J. Heterocyclic Chem.*, 1975, **12**, 547, and references cited therein.

[6] G. Wittig and A. Hesse, *Org. Synth.*, 1970, **50**, 67.

[7] W. R. Dunavant and C. R. Hauser, *Org. Synth.*, Coll. Vol. **5**, 1973, p. 564.

[8] A. I. Meyers and D. L. Temple, jun., *J. Amer. Chem. Soc.*, 1970, **92**, 6644.

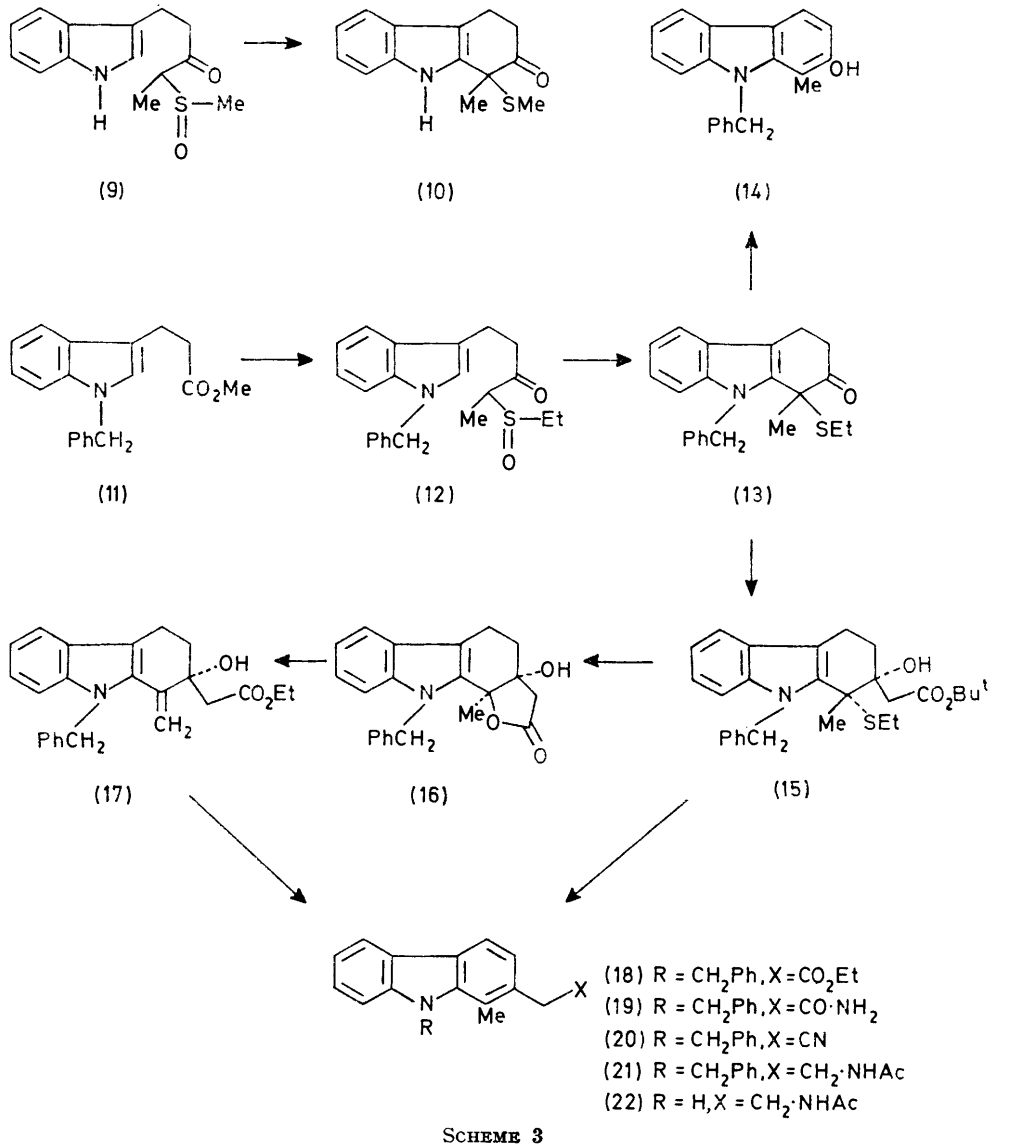
[9] H. Taguchi, K. Shimoji, H. Yamamoto, and H. Nozaki, *Bull. Chem. Soc. Japan*, 1974, **47**, 2529.

[10] M. W. Rathke and A. Lindert, *J. Amer. Chem. Soc.*, 1971, **93**, 2318.

[11] M. W. Rathke and D. F. Sullivan, *J. Amer. Chem. Soc.*, 1973, **95**, 3050.

Through acid-catalysed elimination of ethanethiol and water, compound (15) was expected readily to give an aromatized product. However, when (15) was heated under reflux in ethanol in the presence of toluene-*p*-sulphonic acid, a lactone (16) was isolated quantitatively [$\nu_{max.}$ 3 450 (OH) and 1 770 cm^{-1} (five-membered lactone)]. It is well known that acid-catalysed hydrolysis gave (18) quantitatively. The structure of (18) was easily elucidated spectroscopically (its u.v. spectrum shows the characteristic carbazole chromophore).

The process of aromatization of (15) under the above conditions was examined by t.l.c. Two intermediates, (16) and an exocyclic methylene compound (17), were observed. A relatively rapid conversion of (15) into (16)



SCHEME 3

of t-butyl esters involves alkyl–oxygen fission by an S_N1 mechanism rather than the more usual acyl–oxygen fission.[12] Therefore, compound (15) must have been first converted into an acid, which then underwent intramolecular S_N2 substitution. This mechanistic explanation is in accord with the configurations of (15) and (16). Prolonged heating of (15) at a higher temperature in xylene–ethanol gave the aromatized ester (18) quantitatively. Under the same conditions the lactone (16) also occurred first; disappearance of (15) was complete within 30 min. The second intermediate (17) then appeared as (16) was consumed, and finally all compounds were converted into the product (18). When the reaction was interrupted after 30 min, compounds (16), (17), and (18) were isolated in 70, 25, and 3% yields, respectively. The presence of the exocyclic methylene group in (17) was easily confirmed by distinct signals in the i.r. (890 cm^{-1}) and n.m.r. (5.40 p.p.m.) spectra. The isolated intermediate (17) was also converted into (18). The presence of (17) may indicate that the alkyl–oxygen

[12] R. Breslow, 'Organic Reaction Mechanisms,' Benjamin, New York, 1969, p. 192; M. Bender, *Chem. Rev.*, 1960, **60**, 53.

fission mechanism again acts in the acid-catalysed hydrolysis of the lactone (16) at a higher temperature.

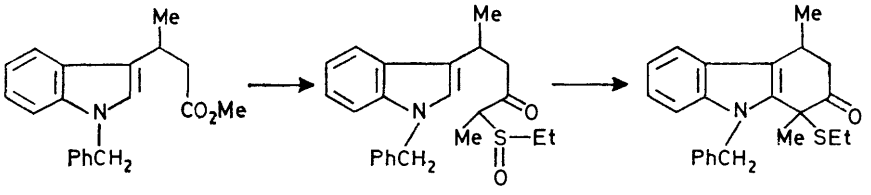
Compound (18) was treated with methanolic ammonia containing sodium methoxide to give an amide (19), which was converted into a nitrile (20) in 95% yield by heating with toluene-*p*-sulphonyl chloride in pyridine. Catalytic reduction of (20) with Raney nickel and acylation with acetic anhydride smoothly gave (21). Debenzylation of (21) was carried out in liquid ammonia with sodium, and the known intermediate (22) [13] was isolated quantitatively.

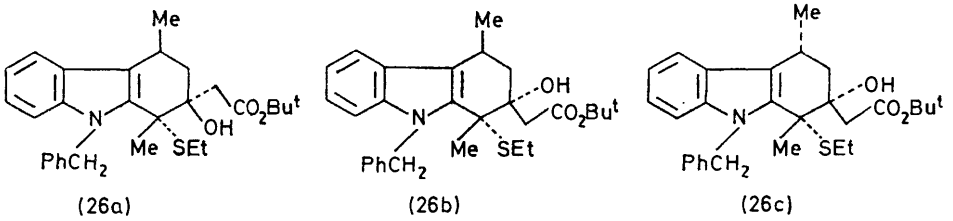
The subsequent steps to olivacine (7) [cyclization with phosphoryl chloride (91%) and dehydrogenation with palladium charcoal (89%)] proceeded smoothly by the established procedures.[13] The overall yield from the starting material (11) was 28%.

Ellipticine.—Ellipticine (8) was synthesized from methyl 1-benzylindole-3-butyrate (23) [1] essentially in the same way as for the synthesis of olivacine (7). Treatment of (23) with the lithium salt of diethyl sulphoxide gave a sulphoxide (24) which was cyclized to (25) (1 : 2 diastereoisomeric mixture) in 53% yield by heating with trifluoroacetic acid. The mixture was converted into (26) in 93% yield by treatment with t-butyl lithioacetate in toluene. Compound (26) was also a mixture of stereoisomers, which was easily separated into three components for structural confirmation. The structures (26a—c) were determined from their n.m.r. spectra.

The mixture (26) was heated with toluene-*p*-sulphonic acid in boiling xylene–ethanol to give a single carbazole derivative (27) in 92% yield. The conversions (27) ⟶ (28) ⟶ (29) ⟶ (30) proceeded efficiently without complication. Compound (30) was already known.[14]

The conversion of (30) into ellipticine (8) was carried out more satisfactorily by a slight modification of the published procedure.[14] Bischler–Napieralski cyclization of (30) with phosphoryl chloride in boiling toluene gave 3,4-dihydro-5,11-dimethyl-6*H*-pyrido[4,3-*b*]carbazole [15] (95%), which was heated with 10% palladium–charcoal to yield ellipticine (8) in 81% yield. The overall yield from the starting material (23) was 23%.





This new synthesis of the 6*H*-pyrido[4,3-*b*]carbazole system, though not a short-cut, may provide easy and efficient routes to various derivatives not synthesized previously.

EXPERIMENTAL

2-(1-*Benzylindol*-3-*yl*)*ethyl* 1-*Ethylsulphinylethyl Ketone* (12).—To a stirred solution of lithium di-isopropylamide in tetrahydrofuran [from a 15% solution of butyl-lithium in hexane (15.5 ml, 36.2 mmol) and di-isopropylamine (3.65 g, 36.2 mmol) in tetrahydrofuran (25 ml) [6]] was added diethyl sulphoxide (3.84 g, 36.2 mmol) in tetrahydrofuran (5 ml) at

[13] J. Schmutz and H. Wittwer, *Helv. Chim. Acta*, 1960, **43**, 793; E. Wenkert and K. G. Dave, *J. Amer. Chem. Soc.*, 1962, **84**, 94.

[14] T. R. Govindachari, S. Rajappa, and V. Sudarsanam, *Indian J. Chem.*, 1963, **1**, 247

[15] J. Schmutz and F. Hunziker, *Helv. Chim. Acta*, 1958, **41**, 288.

−20 to −30 °C. After 30 min, methyl 1-benzylindole-3-propionate (11) [1] (3.79 g, 12 mmol) in tetrahydrofuran (6 ml) was added dropwise at −10 to −20 °C. The mixture was allowed to warm to room temperature, stirred for 1 h, poured into a cold saturated solution of ammonium chloride, and extracted with dichloromethane. The extract was washed with water, dried, and evaporated to leave an oil (12) (4.4 g, 95%) [diastereoisomeric mixture (1 : 2.3)], $\nu_{max.}$ (neat) 1 710 and 1 050 cm^{-1}; *m/e* 289 (*M* − 78) and 220; δ ($CDCl_3$) 1.20 (3 H, t), 1.32 (0.9 H, d, *J* 7 Hz), 1.35 (2.1 H, d, *J* 7 Hz), 2.1—2.9 (3 H, m), 3.03br (3 H, s), 3.68 (0.7 H, q, *J* 7 Hz), 4.10 (0.3 H, q, *J* 7 Hz), 5.20 (2 H, s), 6.9—7.4 (8 H, m), and 7.4—7.7 (1 H, m).

9-Benzyl-1-ethylthio-1,3,4,9-tetrahydro-1-methylcarbazol-2-one (13).—A solution of compound (12) (1.10 g) and trifluoroacetic acid (0.45 g) in acetonitrile–tetrahydrofuran (4 : 1; 31 ml) was heated under reflux for 2.5 h, cooled, neutralized with sodium hydrogen carbonate solution, concentrated *in vacuo*, and extracted with dichloromethane. The extract was dried and evaporated to leave an oil, which was purified by passage in dichloromethane–hexane (1 : 1) through a silica gel column to give the carbazole (13) (0.53 g, 51%). Recrystallization from ethanol gave *needles*, m.p. 167—169° (Found: C, 75.6; H, 6.7; N, 3.95; S, 9.3. $C_{22}H_{23}NOS$ requires C, 75.6; H, 6.65; N, 4.0; S, 9.15%), $\nu_{max.}$ (Nujol) 1 700 cm^{-1}; *m/e* 349 (M^+), 288, and 91 (base peak); δ ($CDCl_3$) 1.12 (3 H, t, *J* 7 Hz), 1.64 (3 H, s), 2.15—3.4 (6 H m), 5.54 (1 H, d, *J* 18 Hz), 6.40 (1 H, d, *J* 18 Hz), 6.8—7.3 (8 H, m), and 7.4—7.6 (1 H, m).

9-Benzyl-1-methyl-9H-carbazol-2-ol (14).—A solution of compound (12) (0.183 g) and trifluoroacetic acid (0.23 g) in acetonitrile (5 ml) was heated under reflux for 2.5 h, cooled, neutralized with sodium hydrogen carbonate solution, and extracted with dichloromethane. The extract was re-extracted with 10% sodium hydroxide solution, and the aqueous layer was acidified with hydrochloric acid to give the *carbazole* (14) (67 mg, 47%). Recrystallization from cyclohexane–ethanol gave pale yellow needles, m.p. 191—195° (Found: C, 83.7; H, 6.45; N, 4.2. $C_{20}H_{17}NO$ requires C, 83.6; H, 5.95; N, 4.9%), $\nu_{max.}$ (Nujol) 3 350, 1 630, 1 605, and 1 590 cm^{-1}; $\lambda_{max.}$ (EtOH) 242, 255infl, and 302 nm; *m/e* 287 (M^+), 196, 167, and 91 (base peak); δ [$CDCl_3$–$(CD_3)_2SO$] 2.45 (3 H, s), 5.72 (2 H, s), and 6.8—8.1 (11 H, m).

t-Butyl 9-Benzyl-1-ethylthio-2,3,4,9-tetrahydro-2-hydoxy-1-methyl-1H-carbazole-2-acetate (15).—(*a*) To a stirred solution of t-butyl acetate (0.58 g, 5 mmol) in toluene (10 ml) a 20% solution of butyl-lithium (5 mmol) in hexane was added dropwise at −78 °C. After 30 min, the solution was allowed to warm to 0 °C, and then compound (13) (0.174 g, 0.5 mmol) in toluene (6 ml) was added dropwise. Stirring was continued for 2 h at room temperature. The mixture was washed with saturated ammonium chloride solution, dried ($MgSO_4$), and evaporated to leave crude (15), which was purified by passage in hexane–dichloromethane (1 : 1) through a silica gel column to give a colourless solid (0.225 g, 97%). Recrystallization from ethanol gave *needles*, m.p. 162—164° (Found: C, 72.3; H, 7.6; N, 3.1; S, 6.7. $C_{28}H_{35}NO_3S$ requires C, 72.25; H, 7.6; N, 3.0; S, 6.85%), $\nu_{max.}$ (Nujol) 3 475 and 1 720 cm^{-1}; *m/e* 465 (M^+), 403, 348, 330, and 287; δ ($CDCl_3$) 1.10 (3 H, t, *J* 8 Hz), 1.52 (12 H, s), 2.1—3.0 (6 H, m), 4.00 (1 H, s), 5.34 (1 H, s), 5.52 (1 H, s), 6.9—7.3 (8 H, m), and 7.4—7.6 (1 H, m).

(*b*) The crude (15) (see above) was triturated in petroleum to give a colourless crystalline powder (86%), which was almost pure.

10-Benzyl-3,3a,4,5,10,10b-hexahydro-3a-hydroxy-10b-methylfuro[2,3-a]*carbazol-2-one* (16).—A solution of compound (15) (30 mg) and toluene-*p*-sulphonic acid monohydrate (50 mg) in ethanol (3 ml) was heated under reflux for 3.5 h, cooled, neutralized with sodium hydrogen carbonate, concentrated, and extracted with dichloromethane. The extract was dried and evaporated to leave an oil which crystallized from ether to give *prisms* (16) (22 mg, 99%), m.p. 199—201° (Found: C, 75.9; H, 6.15; N, 3.9. $C_{22}H_{21}NO_3$ requires C, 76.05; H, 6.1; N, 4.05%), $\nu_{max.}$ (Nujol) 3 450 and 1 770 cm^{-1}; *m/e* 347 (M^+); δ ($CDCl_3$) 1.66 (3 H, s), 2.0—2.4 (3 H, m), 2.52 (1 H, d, *J* 17 Hz), 2.88 (1 H, d, *J* 17 Hz), 2.6—3.2 (2 H, m), 5.40 (1 H, d, *J* 18 Hz), 5.74 (1 H, d, *J* 18 Hz), 6.8—7.3 (8 H, m), and 7.4—7.6 (1 H, m).

Ethyl 9-Benzyl-2,3,4,9-tetrahydro-2-hydroxy-1-methylene-1H-carbazole-2-acetate (17).—A solution of compound (15) (100 mg) and toluene-*p*-sulphonic acid monohydrate (30 mg) in xylene–ethanol (9 : 1) (5 ml) was heated under reflux for 30 min. The solution was cooled, neutralized with sodium hydrogen carbonate solution, dried, and evaporated, and the residue was subjected to layer chromatography on silica gel in dichloromethane–hexane (2 : 1) to give three fractions: (i) the carbazole (18) (2.5 mg, 3%) (see below); (ii) an oil (17) (20 mg, 25%), $\nu_{max.}$ (neat) 3 450, 1 710, and 890 cm^{-1}, $\lambda_{max.}$ (EtOH) 225, 300, 310infl, and 325infl nm, *m/e* 375 (M^+), 360, 357, 342, 330, 288, 270, and 91 (base peak), δ ($CDCl_3$) 1.24 (3 H, t, *J* 8 Hz), 2.1—2.3 (2 H, m), 2.64 (2 H, s), 2.7—3.2 (2 H, m), 4.12 (2 H, q, *J* 8 Hz), 5.04 (1 H, d, *J* 18 Hz), 5.40br (2 H, s), 5.50 (1 H, d, *J* 18 Hz), 6.9—7.4 (8 H, m), and 7.4—7.6 (1 H, m); and (iii) the lactone (16) (52 mg, 70%).

Ethyl 9-Benzyl-1-methyl-9H-carbazole-2-acetate (18).—A solution of compound (15) (2.748 g) and toluene-*p*-sulphonic acid monohydrate (1.60 g) in xylene–ethanol (4 : 1) (125 ml) was heated under reflux (inner temp. 81 °C) for 16 h, then ethanol was distilled off at atmospheric pressure. When the inner temperature reached 115 °C, the distillation was stopped. The residual solution was heated again under reflux for 45 min, cooled, washed with sodium hydrogen carbonate solution, dried, and evaporated *in vacuo*. The residual crude product (18) was decolourized by passage in dichloromethane–hexane (1 : 1) through a silica gel column to give a solid (2.04 g, 98%). Recrystallization from 80% ethanol gave *needles*, m.p. 113—115° (Found: C, 80.4; H, 6.5; N, 3.85. $C_{24}H_{23}NO_2$ requires C, 80.65; H, 6.5; N, 3.9%); $\nu_{max.}$ (Nujol) 1 725 cm^{-1}; *m/e* 357 (M^+, base peak), 284, 193, 192, and 91; $\lambda_{max.}$ (EtOH) 240, 250infl, 263, 285infl, 295, 315infl, 327, and 340 nm; δ ($CDCl_3$) 1.22 (3 H, t, *J* 7 Hz), 2.56 (3 H, s), 3.80 (2 H, s), 4.12 (2 H, q, *J* 7 Hz), 5.70 (2 H, s), 7.0—7.4 (9 H, m), and 7.8—8.1 (2 H, m).

9-Benzyl-1-methyl-9H-carbazole-2-acetonitrile (20).—A solution of compound (18) (0.13 g) in saturated methanolic ammonia (30 ml) containing sodium methoxide (40 mg) was heated at 60—65 °C in a sealed tube for 38 h. The solvent was evaporated off, and the residue was dissolved in dichloromethane, washed with ammonium chloride solution, and dried. Evaporation gave 9-benzyl-1-methyl-9*H*-carbazole-2-acetamide (19), m.p. 197—199.5° (from methanol), which was heated with toluene-*p*-sulphonyl chloride (0.186 g) in pyridine (3 ml) for 3 h. To the solution was added water (0.3 ml), and the mixture was heated at 60 °C for 1 h and cooled. After dilution with benzene, the solution was washed with 2N-hydrochloric acid and sodium chloride solution, dried, and evaporated. The residual solid (0.109 g) was decolourized by passage through a short column of

silica gel in dichloromethane–hexane (1 : 1) to give the *nitrile* (20) (0.107 g, 95%), m.p. 160.5—162.5° (from ethanol) (Found: C, 85.2; H, 5.85; N, 8.9. $C_{22}H_{18}N_2$ requires C, 85.15; H, 5.85; N, 9.05%), $\nu_{max.}$ (Nujol) 2 250, 1 620, 1 595, and 1 580 cm^{-1}; *m/e* 310 (M^+) and 91 (base peak).

N-*Acetyl*-2-(9-*benzyl*-1-*methyl*-9H-*carbazol*-2-*yl*)*ethylamine* (21).—A solution of compound (20) (0.46 g) in methanolic 5% potassium hydroxide (20 ml) and tetrahydrofuran (20 ml) was hydrogenated with Raney nickel (W-7) at atmospheric pressure. After removal of the catalyst, the filtrate was acetylated with acetic anhydride. The solvent was evaporated off, and the residue was extracted with dichloromethane. The extract was washed with water, dried, and evaporated to leave a solid (0.451 g), which was purified by passage in dichloromethane through a silica gel column, to give the amine (21) (0.433 g, 82%). Recrystallization from ether gave *needles*, m.p. 163—165° (Found: C, 80.9; H, 6.75; N, 7.9. $C_{24}H_{24}N_2O$ requires C, 80.85; H, 6.8; N, 7.85%), $\nu_{max.}$ (Nujol) 3 300 and 1 640 cm^{-1}; *m/e* 356 (M^+), 297, 283, and 91.

N-*Acetyl*-2-(1-*methyl*-9H-*carbazol*-2-*yl*)*ethylamine* (22).—To a stirred solution of compound (21) (0.324 g) in liquid ammonia (20 ml) and tetrahydrofuran (16 ml) was added sodium (0.13 g) in small pieces. After 1 h ammonium chloride (0.2 g) was added, the ammonia was allowed to evaporate overnight, and then the tetrahydrofuran was evaporated off *in vacuo*. To the residue was added water (5 ml), and the mixture was extracted with dichloromethane. The extract was washed with water, dried, and evaporated to give a solid (22) (0.24 g, 99%), which was homogeneous on t.l.c. Recrystallization from ether gave prisms, m.p. 159—161° (lit.,[13] 161—163°) (Found: C, 76.75; H, 6.85; N, 10.35. Calc. for $C_{17}H_{18}N_2O$: C, 76.65; H, 6.8; N, 10.5%).

2-(1-*Benzylindol*-3-*yl*)*propyl* 1-*Ethylsulphinylethyl Ketone* (24).—Compound (24) (13.1 g, 96%) was synthesized from ethyl 1-benzylindole-3-butyrate (23) [1] (11.0 g) as described for the preparation of (12), as an oily mixture of diastereoisomers; $\nu_{max.}$ (neat) 1 710 and 1 050 cm^{-1}; *m/e* 303 (M − 78), 234, and 91; δ ($CDCl_3$) 1.1—1.5 (9 H, m), 2.1—2.7 (2 H, m), 3.0br (2 H, t), and 3.4—3.8 (2 H, m).

9-*Benzyl*-1-*ethylthio*-1,3,4,9-*tetrahydro*-1,4-*dimethylcarbazol*-2-*one* (25).—A solution of compound (24) (10.33 g) and trifluoroacetic acid (4.1 g) in acetonitrile–tetrahydrofuran (4 : 1) (286 ml) was heated under reflux for 3 h. Work-up as above gave the carbazole (25) (5.25 g, 53%) as a diastereoisomeric mixture (2 : 1). Recrystallization from ethanol gave *needles*, m.p. 90—95° (Found: C, 75.75; H, 7.0; N, 3.6; S, 8.55. $C_{23}H_{25}NOS$ requires C, 76.0; H, 6.95; N, 3.85; S, 8.8%), $\nu_{max.}$ (Nujol) 1 700 cm^{-1}; *m/e* 363 (M^+), 302, and 91 (base peak); δ ($CDCl_3$) 1.10 (1 H, t, *J* 8 Hz), 1.12 (2 H, t, *J* 8 Hz), 1.28 (2 H, d, *J* 8 Hz), 1.56 (1 H, d, *J* 8 Hz), 1.58 (1 H, s), 1.62 (2 H, s), 2.2—3.8 (5 H, m), 5.50 (1 H, d, *J* 17 Hz), 6.06 (0.67 H, d, *J* 17 Hz), 6.12 (0.33 H, d, *J* 17 Hz), 6.9—7.4 (8 H, m), and 7.5—7.8 (1 H, m).

t-Butyl 9-*Benzyl*-1-*ethylthio*-2,3,4,9-*tetrahydro*-2-*hydroxy*-1,4-*dimethyl*-1H-*carbazole*-2-*acetate* (26).—To a stirred solution of lithium di-isopropylamide [from a 20% solution (1.2 ml) of butyl-lithium in hexane and di-isopropylamine (0.378 g) in toluene (7 ml) [6]] was added t-butyl acetate (0.435 g) in toluene (3 ml) at −78 °C. After 30 min, the solution was allowed to warm to 0 °C, and then compound (25) (91 mg) in toluene (1 ml) was added dropwise. After 5 h, work-up as above gave (26) as an oily mixture of diastereoisomers (0.111 g, 93%), $\nu_{max.}$ (neat) 3 450 and 1 710 cm^{-1}; *m/e* 479 (M^+), 417, 362, 344, 302, and 91 (base peak).

The mixture (100 mg) was separated into its components by layer chromatography on silica gel in dichloromethane–hexane (1 : 1). The first fraction was (26a) (29 mg), δ ($CDCl_3$) 1.03 (3 H, t, *J* 8 Hz), 1.32 (3 H, s), 1.48 (3 H, d, *J* 8 Hz), 1.50 (9 H, s), 2.0—3.5 (7 H, m), 4.12 (1 H, s), 5.48 (1 H, d, *J* 18 Hz), 6.80 (1 H, d, *J* 18 Hz), 6.7—7.2 (8 H, m), and 7.6—7.8 (1 H, m). The second was (26c) (35 mg), δ ($CDCl_3$) 1.12 (3 H, t, *J* 8 Hz), 1.52 (12 H, s), 1.58 (3 H, d, *J* 7 Hz), 1.9—3.2 (7 H, m), 2.18 (1 H, s), 5.52 (1 H, d, *J* 18 Hz), 6.48 (1 H, d, *J* 18 Hz), 6.8—7.3 (8 H, m), and 7.5—7.7 (1 H, m). The third was (26b) (30 mg), δ ($CDCl_3$) 1.12 (3 H, t, *J* 8 Hz), 1.46 (3 H, d, *J* 8 Hz), 1.48 (9 H, s), 1.50 (3 H, s), 2.0—2.6 (4 H, m), 3.0—3.4 (1 H, m), 3.82 (1 H, s), 5.38 (1 H, d, *J* 18 Hz), 5.96 (1 H, d, *J* 18 Hz), 6.9—7.3 (8 H, m), and 7.5—7.7 (1 H, m).

Ethyl 9-*Benzyl*-1,4-*dimethyl*-9H-*carbazole*-2-*acetate* (27).—A solution of compound (26) (3.0 g) and toluene-*p*-sulphonic acid monohydrate (1.7 g) in xylene–ethanol (4 : 1) (134 ml) was heated as described above to yield the product (27) (2.13 g, 92%). Recrystallization from ethanol gave *needles*, m.p. 140—141° (Found: C, 80.85; H, 6.8; N, 3.7. $C_{25}H_{25}NO_2$ requires C, 80.85; H, 6.8; N, 3.75%), $\nu_{max.}$ (Nujol) 1 710 and 1 700 cm^{-1}; *m/e* 371 (M^+, base peak), 298, 206, and 91; $\lambda_{max.}$ (EtOH) 245, 265, 282, 292, 315infl, 327, and 342 nm.

9-*Benzyl*-1,4-*dimethyl*-9H-*carbazole*-2-*acetonitrile* (28).—Compound (27) (1.31 g) was treated with methanolic ammonia (50 ml) containing sodium methoxide (1.18 g) as described above to give an amide (1.34 g), which was treated under reflux with toluene-*p*-sulphonyl chloride (2.06 g) in pyridine (25 ml) for 3 h to yield compound (28) (1.267 g, 88%) as a solid. Recrystallization from ethanol gave *needles*, m.p. 151—153° (Found: C, 85.05; H, 6.25; N, 8.4. $C_{23}H_{20}N_2$ requires C, 85.15; H, 6.2; N, 8.65%), $\nu_{max.}$ (Nujol) 2 250 cm^{-1}; *m/e* 324 (M^+) and 91 (base peak).

N-[2-(9-*Benzyl*-1,4-*dimethyl*-9H-*carbazol*-2-*yl*)*ethyl*]*formamide* (29).—Compound (28) (0.909 g) was hydrogenated over Raney nickel as described above to give an amide, which was formylated with acetic–formic anhydride to yield a solid (29) (0.814 g, 81%). Recrystallization from ethanol gave *needles*, m.p. 189—193° (Found: C, 80.65; H, 6.75; N, 7.65. $C_{24}H_{24}N_2O$ requires C, 80.85; H, 6.8; N, 7.85%), $\nu_{max.}$ (Nujol) 3 250 and 1 660 cm^{-1}; *m/e* 356 (M^+), 311, 298, 207, and 91 (base peak).

N-[2-(1,4-*Dimethyl*-9H-*carbazol*-2-*yl*)*ethyl*]*formamide* (30).—Compound (29) (0.324 g) was debenzylated with sodium (0.13 g) as described above to yield the product (30) (0.236 g, 97%). Recrystallization from ether gave needles, m.p. 189—190° (lit.,[14] 183—185°) (Found: C, 76.6; H, 6.85; N, 10.4. $C_{17}H_{18}N_2O$ requires C, 76.6; H, 6.8; N, 10.5%) $\nu_{max.}$ (Nujol) 3 300, 1 640, and 1 620 cm^{-1}; *m/e* 266 (M^+), 221, and 208 (base peak).

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