New General Approach to the Synthesis of Yuehchukene Analogues. Stereoselective Synthesis of 9,10-Dihydro-7α,9-didemethylyuehchukene. X-Ray Molecular Structure of 6β-(Indol-3'-yl)-7β-methyl-5-phenylsulphonyl-5,6,6aβ,7,8,9,10,10aβ-octahydroindeno[2,1-*b*]indole

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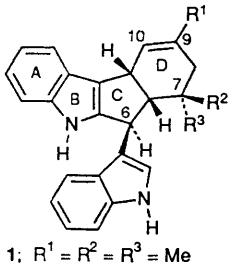
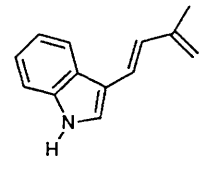
A versatile synthetic strategy for the syntheses of the yuehchukene analogues 6β-(indol-3'-yl)-7β-methyl-5,6,6aβ,7,8,9,10,10aβ-octahydroindeno[2,1-*b*]indole and 7β-methyl-6β-(2'-methylindol-3'-yl)-5,6,6aβ,7,8,9,10,10aβ-octahydroindeno[2,1-*b*]indole is described. The key reactions involve trapping of the vinyllithium derivative 6-methylcyclohex-1-enyllithium, generated from the trisylhydrazone of 2-methylcyclohexanone, with indole-2-carbaldehyde, and Nazarov cyclization of the α,β-unsaturated 2-acylindole 6-methylcyclohex-1-enyl *N*-phenylsulphonylindol-2-yl ketone.

The structure of yuehchukene (YCK), **1** isolated from the root of Murraya paniculata (L.) Jack was determined on the basis of careful spectral analysis [1] and confirmed by X-ray crystallography.[2] Owing to its significant anti-implantation activity in rats,[3] YCK is regarded as a potential antifertility agent and has attracted synthetic studies.[4–8]

Since our first synthesis of YCK by intramolecular Diels–Alder cyclization of dehydroprenylindole **3**,[4] we have looked into a more general synthetic route which would provide access to YCK analogues for our structure–activity relationship study. In our preliminary structure–activity study,[9] it was shown that the C-9, C-10 double bond does not exert any effect in the biological activity of YCK. We regard the tetracyclic unit **4** is the essential structural unit of YCK to retain its activity. Therefore efforts were directed toward the acquisition of intermediates such as compounds **5**.



1; $R^1 = R^2 = R^3 = Me$
2; $R^1 = Me$, $R^2 = R^3 = H$



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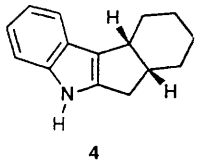

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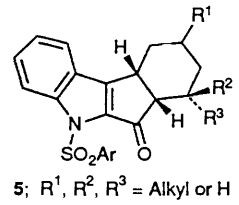


5; R^1, R^2, R^3 = Alkyl or H

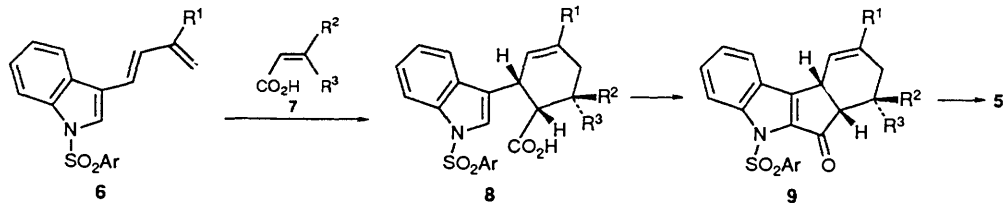
At the beginning of the work, compounds **5** were envisaged to be derived from the intramolecular Diels–Alder reaction of the diene **6** with substituted acrylic acid **7**, followed by intermolecular acylation of the product **8** and hydrogenation of the tetracycle **9** (Scheme 1).

Indeed, this route has successfully provided the 7,7-dinor-YCK analogue **2**.[5] However, when this strategy was extended to the synthesis of 7-mono- or 7,7-di-substituted YCK analogues, the necessary Diels–Alder reaction of the diene **6** with β-mono- or β,β-di-substituted acrylic acids did not proceed well.[10] Therefore we began an investigation into an alternative route to the synthesis of this key intermediate **5**.

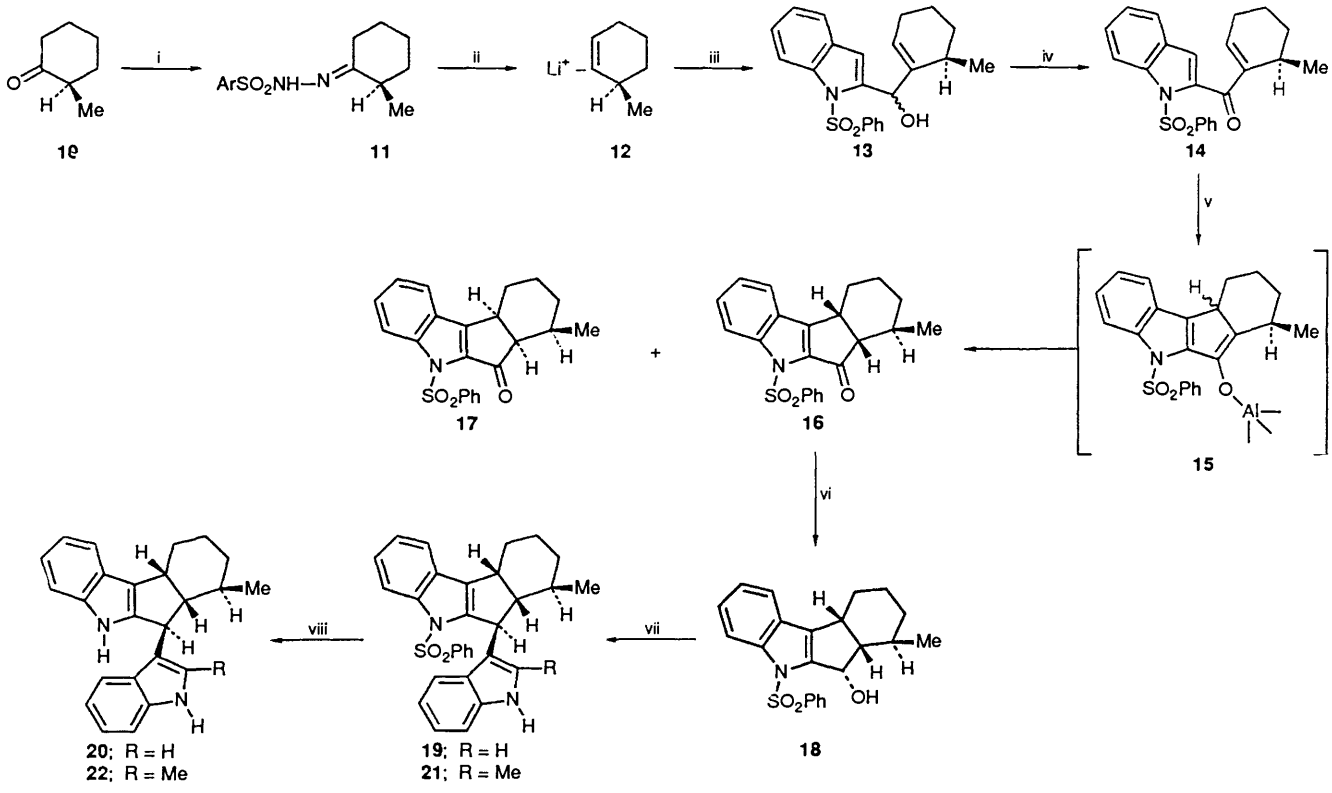
It is well established that reaction of tosylhydrazones with excess of an alkyllithium provides a ready method for the generation of vinyllithium derivatives and the latter can be trapped by various electrophilic reagents.[11,12] Therefore we envisaged that reaction of *tert*-butyllithium with a tosylhydrazone, such as **11**, might afford the vinyl anion such as **12**, which can then be trapped by an indole-2-carbaldehyde derivative to give the allylic alcohol **13**. Oxidation of the alcohol **13** would readily give the divinyl ketone **14**, which on treatment with a Lewis acid would undergo Nazarov cyclization [13,14] to form the target tetracyclic intermediate **16**. Initial study of this approach showed it to be viable.[15] In this account we report the stereoselective synthesis of YCK analogues **20** and **22** by this strategy (Scheme 2).

The starting material for the present synthesis is 2-methylcyclohexanone **10** which can be readily converted into its triisopropylphenylsulphonylhydrazone (trisylhydrazone) derivative **11**.[16,17] The requisite vinyllithium intermediate **12** was prepared by treatment of the trisylhydrazone **11** with 2 mol equiv. of *tert*-butyllithium at −80 °C, followed by warming to 0 °C. Subsequent trapping of intermediate **12** with *N*-phenylsulphonylindole-2-carbaldehyde at −80 °C afforded the allylic alcohol **13** which consisted of a 1:1 epimeric mixture differing in configuration at C-6 as determined by ^1H NMR integration. As the chiral centre at C-6 would be destroyed in the next oxidation step, the epimeric alcohol mixture was not separated. Oxidation (MnO_2) of epimeric alcohols **13** afforded a single ketone **14**.

The next objective in our synthetic strategy involved the Nazarov cyclization of ketone **14** into the tetracyclic ketone. The Nazarov reaction proceeds *via* initial kinetically controlled electrocyclization of the divinyl ketone to form enolates **15**, followed by reversible protonation. Although four possible stereoisomeric cyclization products were possible, owing to the introduction of two new chiral centres at C-10a and C-6a, the two isomers involving a *trans*-fused hydroindanone system should be excluded as they are thermodynamically unfavourable. Further, it has been shown [18] that, based on conformational analysis, in Nazarov cyclization of divinyl ketones such as **14** the pathway leading to the product **16** should be energetically more favourable than that leading to the alternative *cis*-product **17**; thus the major product expected should be **16**. Indeed when compound **14** was subjected to Nazarov cyclization conditions by treatment with



Scheme 1



Scheme 2 *Reagents and conditions:* i, Trisylhydrazine, MeOH, HCl; ii, Bu'Li, THF, −70 °C to 0 °C; iii, *N*-phenylsulphonylindole-2-carbaldehyde, THF; iv, MnO_2, PhH, room temp.; v, $AlCl_3$, PhH, room temp. 20 h; vi, $LiAlH_4$, THF; vii, BF_3·Et_2O, 0 °C, indole (**18** ⟶ **19**); 2-methylindole (**18** ⟶ **21**); viii, Na_2HPO_4, Na–Hg, MeOH

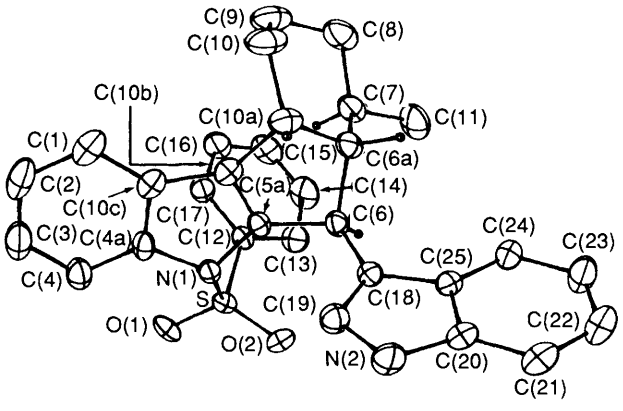


Fig. 1 ORTEP drawing for compound **19** with atom-numbering scheme. Ellipsoids are drawn at 30% probability level. For clarity most hydrogen atoms are omitted.

$AlCl_3$ in refluxing chloroform, two cyclization products, in the ratio 3:1, were isolated. Both exhibited very similar spectroscopic data. The major product was assigned the structure **16** and the minor one structure **17**. This assignment was supported by ^1H NMR analysis that showed 6a-H for **16** and **17** appearing as a double doublet at δ 2.16 ($J_{6a,10a}$ 6.1, $J_{6a,7}$ 8.3 Hz) and δ 3.03 ($J_{6a,10a}$ 6.1, $J_{6a,7}$ 6.1 Hz), respectively. These coupling constants were in agreement with the values derived from structures generated by molecular mechanics calculations.[19]

The major ketone **16** was then reduced with lithium aluminium hydride to give stereoselectively the 6α-alcohol **18**, which on condensation with indole in diethyl ether in the presence of BF_3·Et_2O afforded compound **19**. To ascertain the stereochemistry of the product **19** at C-6, C-6a, C-10a and C-7, an X-ray crystallographic analysis was carried out. The crystal structure of compound **19** (Fig. 1) obtained showed that rings C and D were *cis*-fused, and that the C-7 methyl and C-6 indolyl groups were also *cis* with respect to the ring-junction protons. Therefore our earlier stereochemical assignment for compound **16** was confirmed.

Finally, removal of the *N*-phenylsulphonyl group with sodium amalgam in methanol with disodium hydrogen phosphate buffer[20] afforded the title YCK analogue **20**.

Similarly, condensation of the 6α-alcohol **18** with 2-methylindole followed by *N*-deprotection of the intermediate **21** afforded the YCK analogue **22**.

Experimental

M.p.s were measured on a Reichert Kofler-block apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer 577 spectrophotometer and were calibrated with polystyrene.

NMR spectra were recorded on a JEOL FX-90Q spectrometer for solutions in deuteriochloroform unless otherwise stated, with tetramethylsilane as internal standard. *J*-Values are given in Hz. Mass spectra were recorded on Hitachi RMS-4 and VG 70–70F high-resolution mass spectrometers. UV spectra were recorded on a Shimadzu UV 240 spectrophotometer. TLC was performed using Merck pre-coated silica gel F-254 plates (thickness 0.25 mm). Flash chromatography was carried out with Kieselgel 60 (Merck) as the stationary phase.[21] Analytical HPLC was performed on a Beckmann Model 331 HPLC System with Model 163 variable-wavelength UV–VIS detector. Organic extracts were dried over anhydrous sodium sulphate and evaporated at aspirator pressure on a rotary evaporator. Light petroleum refers to the fraction boiling in the range 40–60 °C and was redistilled before use. All reactions requiring anhydrous conditions were conducted in oven-dried apparatus at 120 °C and under a static atmosphere of dry nitrogen. New compounds whose elemental compositions were established through accurate mass determination were shown to be homogeneous by spectroscopic and chromatographic methods. All compounds described are racemic.

2-Methylcyclohexanone 2,4,6-Triisopropylphenylsulphonylhydrazone **11**.—To a solution of 2-methylcyclohexanone (1.0 g, 8.9 mmol) and triisopropylphenylsulphonylhydrazine (2.6 g, 8.9 mmol) in anhydrous methanol (9 cm^3) was added conc. HCl (0.09 cm^3). The resulting solution was stirred at room temp. overnight and was then kept at 0 °C for 24 h. The hydrazone **11** that separated out was recrystallized from methanol (2.96 g, 85%), m.p. 108–109 °C; ν_{max}(Nujol)/cm^{-1} 3250, 1588, 1330, 1190, 1018, 815 and 690; δ_H(90 MHz) 1.26 (21 H, d, *J* 6.6, 7 × Me), 1.3–2.0 (6 H, m, 3-, 4- and 5-H_2), 2.0–2.26 (3 H, m, 2-H and 6-H_2), 2.95 (1 H, septet, *J* 6.6), 4.19 (2 H, septet, *J* 6.6) and 7.16 (2 H, s, ArH); δ_C(22.5 MHz) 15.98 (q), 23.59 (q), 24.51 (t), 24.86 (q), 26.08 (t), 26.13 (t), 29.76 (d), 34.15 (d), 35.50 (t), 39.08 (d), 123.45 (d), 131.80 (s), 151.33 (s), 152.84 (s) and 161.76 (s); *m/z* 392 (M^+).

(6-Methylcyclohex-1-enyl)(1′-phenylsulphonylindol-2′-yl)methanol **13**.—To a solution of the trisylhydrazone **11** (1.37 g, 3.25 mmol) in anhydrous tetrahydrofuran (THF) (21 cm^3) at −70 °C was added *tert*-butyllithium (1.7 mol dm^{-3}; 5 cm^3). The resulting deep red solution was warmed to room temp. During this period nitrogen was evolved. When nitrogen ceased to evolve, the resulting yellow solution was cooled to −70 °C, treated with a solution of indole-2-carbaldehyde[22] (1.1 g, 3.85 mmol) in anhydrous THF (10 cm^3) and the mixture was allowed to warm to ambient temp. overnight. The solution was then poured into saturated aq. ammonium chloride. Usual work-up and column chromatography afforded a mixture of the *epimeric alcohols* **13** as a viscous liquid (Found: M^+, 381.1402. $C_{22}H_{23}NO_3S$ requires M, 381.1397) (0.98 g, 74%). A small sample was subjected to column chromatography separation on silica gel and was eluted with diethyl ether–light petroleum (1:1). The major alcohol **13a** had m.p. 112 °C (from CH_2Cl_2), ν_{max}(neat)/cm^{-1} 3530, 3420, 1450, 1370, 1180, 760, 730 and 690; δ_H(90 MHz) 0.88 (3 H, d, *J* 7.0, Me), 1.60 (4 H, m, 4- and 5-H_2), 2.14 (3 H, m, 3-H_2 and 6-H), 3.05 (1 H, br s, OH), 5.71 (1 H, br s, *H*COH), 6.03 (1 H, t, *J* 1.8, 2-H), 6.60 (1 H, s, 3′-H) and 7.11–8.19 (9 H, m, ArH); δ_C(22.5 MHz) 18.85 (t), 19.61 (q), 25.24 (t), 30.33 (d), 30.82 (t), 66.90 (d), 110.73 (d), 114.68 (d), 121.24 (d), 123.62 (d), 123.73 (d), 124.92 (s), 126.38 (d), 128.93 (d), 129.25 (d), 133.81 (d), 137.54 (s), 139.06 (s), 141.17 (s) and 143.26 (s); *m/z* 381 (M^+), 363, 240, 222 and 144.

The minor alcohol **13b** had δ_H(90 MHz) 0.93 (3 H, d, *J* 7.0, Me), 1.20–3.08 (6 H, m, 3-, 4- and 5-H_2), 2.40 (1 H, m, 6-H) 3.12 (1 H, br s, OH), 5.51 (1 H, br s, *H*COH), 5.79 (1 H, t, *J* 1.8, 2-H), 6.71 (1 H, s, 3′-H) and 7.09–8.20 (9 H, m, ArH); δ_C(22.5 MHz) 19.12 (t), 19.77 (q), 25.35 (t), 30.55 (d), 31.37 (t), 69.29 (d), 111.27 (d), 114.63 (d), 120.97 (d), 123.62 (d), 124.60 (s), 126.01 (d), 126.33 (d), 126.98 (d), 129.04 (d), 133.65 (d), 137.49 (s), 138.79 (s), 142.10 (s) and 143.45 (s).

6-Methylcyclohex-1-enyl 1′-Phenylsulphonylindol-2′-yl Ketone **14**.—A mixture of active manganese dioxide[23] (20 g) and the epimeric alcohols **13** (2.00 g, 5.25 mmol) in benzene (300 cm^3) was stirred at room temp. for 12 h. Usual work-up and purification of the crude product by column chromatography and elution with diethyl ether–light petroleum (1:4) afforded the *ketone* **14** (Found: M^+, 379.1246. $C_{22}H_{21}NO_3S$ requires M, 379.1241) as a gum (1.35 g, 68%); ν_{max}(neat)/cm^{-1} 1640, 1606, 1530, 1450, 1375, 1185, 755, 730 and 690; δ_H(90 MHz) 11.8 (3 H, d, *J* 7, Me), 1.69 (4 H, m, 4- and 5-H_2), 2.23 (2 H, m, 3-H_2), 3.00 (1 H, m, 16-H), 6.76 (1 H, s, 3′-H), 6.80 (1 H, t, *J* 3.7, 2-H), 7.17–7.57 (6 H, m, ArH) and 8.03–8.14 (3 H, m, ArH); δ_C(22.5 MHz) 17.55 (t), 19.58 (q), 26.60 (t), 26.98 (d), 29.52 (t), 114.25 (d), 114.79 (d), 122.05 (d), 124.00 (d), 126.20 (d), 127.52 (d), 128.66 (s), 128.96 (d), 133.81 (d), 137.00 (s), 138.33 (s), 145.16 (s), 146.27 (d) and 189.01 (s).

7β-Methyl-6-oxo-5-phenylsulphonyl-5,6,6aβ,7,8,9,10,10aβ-octahydroindeno[2,1-b]indole **16** *and its 7-Epimer* **17**.—A mixture of the ketone **14** (2.0 g, 5.28 mmol) and $AlCl_3$ (0.67 g, 5.28 mmol) in anhydrous benzene (50 cm^3) was stirred at room temp. for 20 h, after which water (50 cm^3) was added, and the resulting mixture was extracted with diethyl ether. Usual work-up and purification by column chromatography on elution with diethyl ether–light petroleum (1:4) gave a stereoisomeric mixture of *ketones* **16** and **17** (1.5 g, 73%) (**16** 66%, **17** 34%) as a gum (Found: C, 69.7; H, 5.7. $C_{22}H_{21}NO_3S$ requires C, 69.7; H, 5.6%). Fractional recrystallization from diethyl ether–light petroleum gave pure compound **16**, m.p. 122–124 °C; ν_{max}(Nujol)/cm^{-1} 1695, 1380, 1190, 760, 730 and 690; δ_H(90 MHz) 1.22 (3 H, d, *J* 6.3, Me), 1.57–2.20 (7 H, m, 7-H and 8-, 9- and 10-H_2), 2.61 (1 H, dd, *J* 8.3, 6.1, 6a-H), 3.40 (1 H, m, 10a-H), 7.23–7.70 (6 H, m, ArH) and 8.11–8.39 (3 H, m, ArH); δ_C(22.5 MHz) 20.13 (t), 20.88 (q), 28.09 (t), 29.77 (d), 30.96 (t), 33.07 (d), 59.59 (d), 115.85 (d), 121.75 (d), 123.92 (d), 124.87 (s), 127.55 (d), 128.85 (d), 129.12 (d), 133.86 (d), 139.04 (s), 143.45 (s), 155.29 (s) and 192.10 (s); *m/z* 379 (M^+), 324, 238, 210, 196 and 77.

7β-Methyl-5-phenylsulphonyl-5,6,6aβ,7,8,9,10,10aβ-octahydroindeno[2,1-b]indol-6α-ol **18**.—A mixture of ketone **16** (0.98 g, 2.6 mmol) and lithium aluminium hydride (0.15 g, 3.9 mmol) in anhydrous THF (20 cm^3) was stirred at 0 °C for 1 h. Usual work-up recrystallization of the crude product gave the *alcohol* **18** (0.89 g, 90%) (Found: C, 69.4; H, 5.9. $C_{22}H_{23}NO_3S$ requires C, 69.3; H, 6.1%), m.p. 124–125 °C; ν_{max}(Nujol)/cm^{-1} 3560, 1360, 1180, 750 and 730; δ_H(90 MHz) 1.14 (3 H, d, *J* 6.6, Me), 1.32–2.61 (7 H, m, 7-H and 8-, 9- and 10-H_2), 2.50 (1 H, ddd, *J* 6.6, 6.6, 6.6, 6a-H), 2.85 (1 H, br s, OH), 2.95 (1 H, m, 10a-H), 5.41 (1 H, d, *J* 6.6, 6-H) and 7.15–8.01 (9 H, m, ArH); δ_C(22.5 MHz) 20.07 (t), 21.59 (q), 26.27 (d), 28.96 (t), 29.52 (t), 35.51 (d), 54.24 (d), 70.83 (d), 114.41 (d), 120.08 (d), 123.49 (3), 124.54 (d), 126.36 (s), 126.68 (d), 129.23 (d), 133.73 (d), 138.47 (s), 139.93 (s) and 143.97 (s).

6β-(Indol-3′-yl)-7β-methyl-5-phenylsulphonyl-5,6,6aβ,7,8,9,-10,10aβ-octahydroindeno[2,1-b]indole **19**.—To a solution of the alcohol **18** (200 mg, 0.52 mmol) and indole (61 mg, 0.52 mol) in anhydrous diethyl ether (10 cm^3) at 0 °C was added boron trifluoride–diethyl ether (0.076 cm^3, 0.162 mmol). The resulting solution was stirred for 0.5 h. Work-up and purification of the crude product by flash chromatography and elution with diethyl ether–light petroleum (1:2) gave *compound*

19 as a solid (207 mg, 83%). Recrystallization from diethyl ether–light petroleum gave cubic crystals (Found: C, 74.8; H, 5.9. $C_{30}H_{28}N_2O_2S$ requires C, 75.0; H, 5.9%), m.p. 205–206 °C; ν_{max}(Nujol)/cm^{-1} 3420, 1360, 1175, 1110, 755, 750 and 730; δ_H(90 MHz; [$^2H_6$]benzene) 0.80–1.80 (7 H, m, 7-H and 8-, 9- and 10-H_2), 1.28 (3 H, br s, Me), 2.24 (1 H, m, 6a-H), 3.52 (1 H, m, 10a-H), 4.75 (1 H, s, 6-H), 6.23 (2 H, d, *J* 1.3, 2′-H), 6.90–7.80 (12 H, m, ArH) and 8.12 (1 H, br s, NH); δ_C(22.5 MHz; [$^2H_6$]benzene) 22.16 (q), 26.87 (t), 33.42 (d), 33.94 (t), 37.35 (d), 44.18 (d), 59.92 (d), 111.43 (d), 115.42 (d), 116.50 (s), 119.37 (d), 119.51 (d), 119.83 (d), 121.94 (d), 122.11 (d), 123.73 (d), 123.84 (d), 126.74 (d), 127.31 (s), 127.79 (s), 128.53 (d), 132.89 (d), 137.11 (s), 139.55 (s), 141.23 (s) and 146.92 (s); *m*/*z* 480 (M^+), 339, 222, 130 and 77.

6β-(*Indol-3′-yl*)-7β-*methyl*-5,6,6aβ,7,8,9,10,10aβ-*octahydroindeno*[2,1-b]*indole* **20**.—To a solution of the sulphonamide **19** (163 mg, 0.34 mmol) in a mixture of anhydrous diethyl ether (2.6 cm^3) and anhydrous methanol (5.4 cm^3) was added disodium hydrogen phosphate (2.6 g), followed by sodium amalgam (5%; 2.6 g). The mixture was stirred at room temp. until all the solid sodium amalgam became liquid mercury, after which water and diethyl ether were added to the reaction mixture. The liquid was decanted and washed successively with water and brine, dried over anhydrous sodium sulphate, and concentrated. The residue was purified by flash chromatography [diethyl ether–light petroleum (1:2)] to give the *YCK analogue* **20** (75 mg, 65%) as a solid (Found: M^+, 340.1934. $C_{24}H_{24}N_2$ requires M, 340.1939), m.p. 118 °C; ν_{max}(Nujol)/cm^{-1} 3400 and 750; δ_C(90 MHz; [$^2H_6$]benzene) 1.04 (3 H, d, *J* 6.7, Me), 0.66–1.80 (7 H, m, 7-H and 8-, 9- and 10-H_2), 2.40 (1 H, m, 6a-H), 3.42 (1 H, m, 10a-H), 4.21 (1 H, d, *J* 5.0, 6-H), 6.10 (1 H, d, *J* 2.2, 2′-H) and 6.38–7.72 (8 H, m, ArH); δ_C(22.5 MHz; [$^2H_6$]benzene) 20.78 (t), 21.89 (q), 29.09 (t), 31.94 (d), 36.62 (d), 41.47 (d), 60.35 (d), 111.52 (d), 112.03 (d), 117.34 (s), 118.88 (d), 119.59 (d), 119.91 (d), 120.83 (d), 121.86 (d), 122.32 (d), 122.95 (s), 125.38 (s), 127.55 (s), 137.17 (s), 141.04 (s) and 145.27 (s).

7β-*Methyl*-6β-(2′-*methylindol*-3′-*yl*)-*phenylsulphonyl*--5,6,6aβ,7,8,9,10,10aβ-*octahydroindeno*[2,1-b]*indole* **21**.—Following the procedure as for the preparation of compound **19**, *compound* **21** (205 mg, 80%) was obtained, from the alcohol **18** (200 mg, 0.52 mmol) and 2-methylindole (68 mg, 0.52 mol), as a solid, m.p. 102–103 °C (Found: C, 75.1; H, 5.9. $C_{31}H_{30}N_2O_2S$ requires C, 75.3; H, 6.1%); ν_{max}(Nujol)/cm^{-1} 3400, 1370, 1175, 750 and 730; δ_H(90 MHz; [$^2H_6$]benzene) 0.50–1.80 (7 H, m, 7-H) and 8-, 9- and 10-H_2), 1.04 (3 H, d, *J* 5.9, 7-Me), 2.01 (3 H, s, 2′-Me), 2.08 (1 H, m, 6a-H), 3.62 (1 H, m, 10a-H), 4.80 1 H, s, 6-H), 6.29–7.53 (13 H, m, ArH) and 8.33–8.43 (1 H, br s, NH); δ_C(22.5 MHz; [$^2H_6$]benzene) 12.84 (q), 22.51 (t), 23.02 (q), 28.01 (t), 33.89 (t), 34.08 (d), 39.30 (d), 44.94 (d), 61.81 (d), 111.16 (d), 113.47 (s), 116.12 (d), 120.05 (d), 120.35 (d), 120.70 (d), 121.70 (d), 124.44 (d), 124.73 (d), 126.71 (d), 127.39 (d), 128.12 (s), 129.15 (d), 129.56 (s), 132.07 (s), 133.35 (s), 136.49 (s), 140.53 (s), 142.02 (s) and 146.57 (s); *m*/*z* 494 (M^+), 475, 353, 222, 140, 130 and 77.

7β-*Methyl*-6β-(2′-*Methylindol*-3′-*yl*)-5,6,6aβ,7,8,9,10,10aβ-*octahydroindeno*[2,1-b]*indole* **22**.—Following the same procedure as in the preparation of compound **20**, dephenylsulphonylation of compound **21** (168 mg) afforded *compound* **22** (84 mg, 70%) as a solid (Found: M^+, 354.2083. $C_{25}H_{26}N_2$ requires M, 354.2096), m.p. 123 °C; ν_{max}(Nujol)/cm^{-1} 3400 and 750; δ_H(90 MHz; [$^2H_6$]benzene) 0.911 (3 H, d, *J* 6.8, 7-Me), 1.02–1.54 (7 H, m, 7-H and 8-, 9- and 10-H_2), 1.88 (3 H, s, 2′-Me), 2.70 (1 H, m, 6a-H), 3.25 (1 H, m, 10a-H), 4.30 (1 H, d, *J* 7.7, 6-H), 6.50 (1 H, br s, NH) and 6.50–7.76 (9 H, m, NH and ArH); δ_C(22.5 MHz; [$^2H_6$]benzene) 11.62 (q), 19.88 (t), 21.37 (q), 29.90 (t), 30.42 (t), 30.80 (d), 36.16 (d), 40.22 (d), 60.11 (d), 110.46 (d), 111.98 (d), 118.94 (d), 119.34 (d), 119.91 (d), 120.81 (d), 121.38 (d), 124.11 (s), 125.28 (s), 127.61 (s), 128.31 (d), 128.69 (s), 131.13 (s), 135.95 (s), 140.93 (s) and 144.45 (s).

Table 1 Fractional co-ordinates for the non-hydrogen atoms in compound **19**

Atom	*x*	*y*	*z*
S	0.526 05(6)	0.238 92(6)	0.459 27(5)
O(1)	0.473 4(2)	0.341 5(2)	0.452 4(1)
O(2)	0.509 2(2)	0.157 8(2)	0.517 8(1)
N(1)	0.656 4(2)	0.264 6(2)	0.491 0(2)
N(2)	0.849 5(2)	0.063 2(2)	0.749 3(2)
C(1)	0.862 3(3)	0.420 8(3)	0.438 4(2)
C(2)	0.827 6(3)	0.527 2(3)	0.441 4(2)
C(3)	0.733 5(3)	0.550 8(3)	0.458 1(2)
C(4)	0.668 9(3)	0.469 2(3)	0.473 5(2)
C(4a)	0.702 6(2)	0.362 7(2)	0.470 6(2)
C(5a)	0.725 8(2)	0.180 0(2)	0.481 9(2)
C(6a)	0.813 3(2)	0.027 7(3)	0.451 4(2)
C(6)	0.732 5(2)	0.060 5(2)	0.502 2(2)
C(7)	0.753 5(3)	−0.007 0(3)	0.354 7(2)
C(8)	0.824 9(3)	−0.003 9(3)	0.295 1(2)
C(9)	0.870 2(3)	0.109 1(4)	0.293 6(2)
C(10)	0.941 6(3)	0.138 7(4)	0.385 5(2)
C(10a)	0.885 4(2)	0.129 2(3)	0.457 8(2)
C(10b)	0.808 7(2)	0.219 6(3)	0.460 2(2)
C(10c)	0.798 7(2)	0.337 0(3)	0.454 1(2)
C(11)	0.702 8(4)	−0.118 8(3)	0.352 1(3)
C(12)	0.501 4(2)	0.182 5(2)	0.352 3(2)
C(13)	0.451 1(3)	0.082 8(3)	0.334 8(2)
C(14)	0.428 7(3)	0.040 7(3)	0.248 8(3)
C(15)	0.458 4(3)	0.096 1(3)	0.185 0(3)
C(16)	0.510 6(3)	0.193 1(3)	0.203 7(2)
C(17)	0.531 6(3)	0.238 1(3)	0.287 7(2)
C(18)	0.776 0(2)	0.039 8(2)	0.601 5(2)
C(19)	0.807 0(3)	0.114 5(3)	0.667 9(2)
C(20)	0.846 3(2)	−0.047 5(3)	0.735 4(2)
C(21)	0.882 0(3)	−0.131 6(3)	0.795 9(2)
C(22)	0.868 3(3)	−0.235 6(3)	0.762 9(2)
C(23)	0.819 8(3)	−0.256 5(3)	0.672 2(2)
C(24)	0.785 1(2)	−0.172 0(3)	0.612 5(2)
C(25)	0.799 3(2)	−0.065 7(3)	0.643 6(2)

Crystal Structure Determination of Compound **19**.—*Crystal data.* $C_{30}H_{28}N_2O_2S$, prisms, M = 480.63. Monoclinic, space group $P2_1/n$ (a non-standard form of $P2_1/c$, No. 14), a = 13.173(2), b = 12.283(2), c = 15.698(1) Å, β = 107.67(1)°, V = 2420(1) Å^3, Z = 4, D_c = 1.319 g cm^{-3}, μ(Mo-Kα) = 1.56 cm^{-1}. Crystal size: 0.11 × 0.18 × 0.25 mm. Intensity data were collected on an Enraf–Nonius CAD4 diffractometer with graphite-monochromated Mo-Kα radiation (λ 0.710 73 Å) using the ω–2θ scanning technique with a variable scan width of 0.60 + 0.34 tanθ. Reflections within the (h, k, $\pm l$) quadrants extending to 2θ = 46° were measured. A total of 3130 independent reflections were obtained of which 2034 with $|F_o| > 3\sigma|F_o|$ were considered to be observed and were used in subsequent calculations.

Solution and refinement. The structure was solved by direct methods with MULTAN 82[24] from which all the non-hydrogen atoms were located. Positions of the hydrogen atoms were revealed in difference maps at a later stage; however, only those bonded to C(6), C(6a), C(10a) and the methyl carbon atom C(11) were taken from the difference map and all others were generated geometrically (C–H = 0.95 Å). The refinement was by full-matrix least squares; all the non-hydrogen atoms were refined anisotropically while the hydrogen atoms with assigned isotropic temperature factors were not refined but were allowed to ride on their parent atoms. Atomic scattering factors were obtained from ref. 25. Calculations were carried out on a MicroVax II computer using the Structure Determination

Table 2 Selected torsion angles (°)

H(6)–C(6)–C(6a)–H(6a)	82.2(3)
H(6)–C(6)–C(6a)–C(7)	−30.4(3)
H(6)–C(6)–C(6a)–C(10a)	−153.5(2)
H(6a)–C(6a)–C(10a)–H(10a)	−44.6(4)
H(6a)–C(6a)–C(10a)–C(10)	82.6(4)
H(6a)–C(6a)–C(10a)–C(10b)	−151.2(3)

Package (SDP).[26] The final R-values were: $R = 0.037$ and $R_w = 0.047$, where $w = 4F_o^2/[\sigma^2(F_o^2) + (0.04\ F_o^2)^2]$. In the final difference map the residual electron densities were between −0.30 and 0.19 e Å^{-3}. Fractional atomic co-ordinates are given in Table 1, and selected torsion angles in Table 2.*

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* *Supplementary material* (see Instructions for Authors, section 5.6.3, January issue): Tables of hydrogen-atom parameters, thermal parameters, bond lengths and bond angles are available on request from the Cambridge Crystallographic Data Centre.

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