Synthesis of (6*S*,6a*S*,7*R*,10*S*,10a*R*)-6-(Indol-3-yl)-7,11,11-trimethyl-5,6,6a,7,8,9,10,10a-octahydro-7,10-methanoindeno[2,1-*b*]indole and its Enantiomer: Absolute Configuration of Active Yuehchukene

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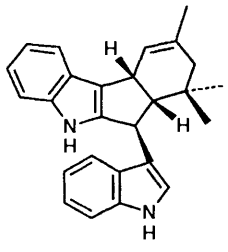
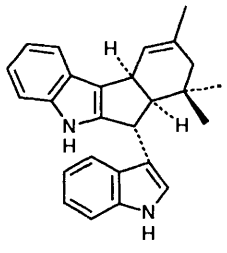
Efficient synthesis of the title compound and its *R*-enantiomer from readily available (1*S*)-(−)-camphor or (1*R*)-(+)-camphor, respectively, is described. Stable conformations of the title compounds and yuehchukene were compared by employment of the MM2 force field for energy calculation and minimization. Since yuehchukene occurs in Nature in racemic form, a bioassay study of enantiomerically pure *S*- and *R*-enantiomer of the title compound would provide an indication as to which enantiomer of yuehchukene is responsible for its activity. Results of the study led to the conclusion that the enantiomer of yuehchukene which is biologically active should possess the *R*-absolute configuration at C-6.

(±)-Yuehchukene (YCK) [(*R*)-**1** and (*S*)-**1**] is a dimeric indole natural alkaloid first isolated from *Murraya paniculata*[1] and later from other *Murraya* species.[2,3] Owing to its anti-implantation biological activity,[4] there is considerable interest in the synthesis of YCK and related structural analogues.[5–9] In our initial structure–activity relationship study,[10] it was shown that a number of analogues exhibit similar activity as YCK in various degrees. Both naturally occurring and synthetic YCK and all the synthetic analogues studied so far are in racemic form. It is reasonable to assume that only one of the enantiomers is responsible for the biological activity. It is therefore important to identify the active enantiomer so that the biological activity can be at least doubled for the same dose. Attempts to resolve racemic YCK into its enantiomers by chiral column chromatographic separation or derivatization with chiral resolving agents such as camphor-10-sulphonic acid were unsuccessful. Concurrently we carried out an investigation into enantioselective synthesis of YCK and its analogues.

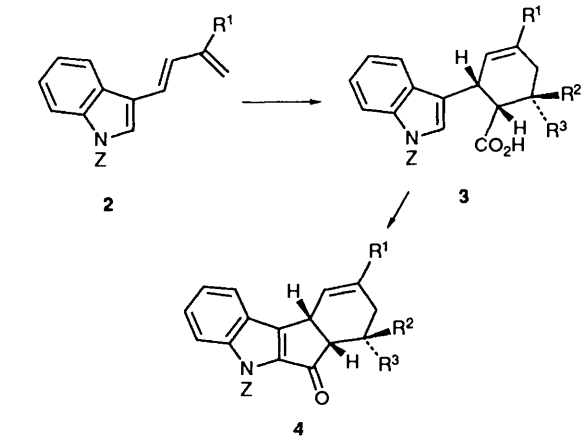


(*S*)-**1**

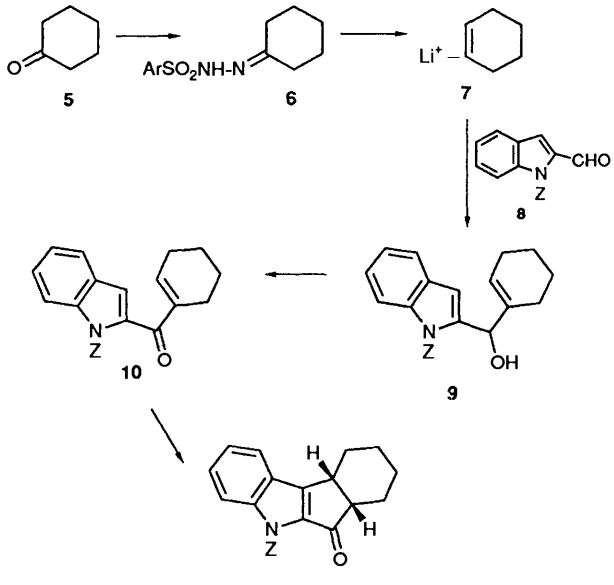


(*R*)-**1**

In our earlier investigation into a general route to YCK analogues, the strategy involved the synthesis of the tetracyclic ketone **4** as the key synthetic intermediate.[11] The method we have developed to obtain ketone **4** involves intermolecular Diels–Alder reaction of the diene **2**, followed by intramolecular acylation of the acid **3** (Scheme 1). This intermediate **4** has been successfully transformed into YCK analogues. Recently, our laboratory group has developed an alternative synthetic route to another key intermediate tetracyclic ketone[12] **11** in which the key steps involve trapping of the vinyllithium derivative **7**, obtained from the corresponding ketone **5** *via* arylhydrazone **6**, with indole-2-carbaldehyde **8** to give the alcohol **9**, and subsequent Nazarov cyclization of the divinyl ketone **10** (Scheme 2); and we have successfully synthesized a YCK analogue.[13]



Scheme 1



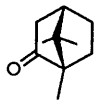
Scheme 2

It became obvious that if an enantiomerically pure ketone is employed to generate the vinyllithium derivative, then the eventual YCK analogue obtained by this stereoselective syn-

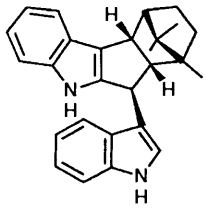
Table 1 Energies and C-5a–C-6–C-3′–C-2′, dihedral angles of MM2-calculated conformations for YCK and camphor-YCK

	Yuehchukene		Camphor-YCK	
Stable conformer	Dihedral angle	Energy kJ/mol^{-1}	Dihedral angle	Energy kJ/mol^{-1}
i	19.3	219.20	28.6	309.80
ii	93.2	219.36	83.4	310.00
iii	210.5	219.39	224.5	307.12

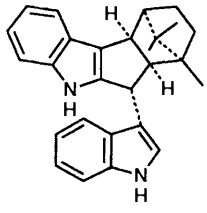
thetic strategy would also be enantiomerically pure. Among the naturally occurring chirons, (1*S*)-(−)-camphor **12** is an attractive candidate for the present purpose, and would lead to analogue (*S*)-**13**, (*S*)-camphor-YCK. Likewise, commercially available enantiomerically pure (1*R*)-(+)-camphor would afford (*R*)-**13**, (*R*)-camphor-YCK. The present paper describes a stereoselective synthesis of these two enantiomerically pure YCK analogues.



12



(*S*)-**13**



(*R*)-**13**

From an examination of Dreiding molecular models, camphor-YCK and YCK are very close in their geometry. YCK consists of a rather rigid tetracyclic unit in which the A, B and C rings are coplanar and the D ring is slightly bent away from the general plane. Camphor-YCK possesses similar geometry except that the D ring is now replaced by a bicyclo[2.2.1]-heptane system. The indole moiety at C-6 in both YCK and camphor-YCK is generally free to rotate about the C-6,C-3′ bond. The relative orientation of the free indole at C-6 with respect to the general plane of the tetracyclic unit can be specified by the dihedral angle defined by C-5a–C-6–C-3′–C-2′.

To ascertain that camphor-YCK and YCK are structurally similar, and hence that camphor-YCK would exhibit similar biological activity, we also examined their molecular models by molecular mechanic calculations[14] employing the MM2 force field[15] for energy calculation and minimization.

The results of MM2 calculations revealed, indeed, that YCK and camphor-YCK are closely related, and that they possess three conformational-energy minima, corresponding to three different C-5a–C-6–C-3′–C-2′ dihedral angles (Table 1). It is pertinent to note that while the three minima of YCK are of identical energy (219.3 ± 0.1 kJ mol^{-1}), camphor-YCK has a global minimum (conformer iii). The stereoscopic graphic representations of the MM2-calculated geometries for YCK and camphor-YCK are shown in Figs. 1 and 2, respectively.

Commercially available (1*S*)-(−)-camphor **12** (99% pure; $[\alpha]_D$ −43°) was converted into its 2,4,6-triisopropylphenyl-sulphonylhydrazone (trisylhydrazone) derivative[16,17] **14** (Scheme 3). Treatment of compound **14** with *t*-butyllithium in tetrahydrofuran (THF) generated the vinyllithium derivative

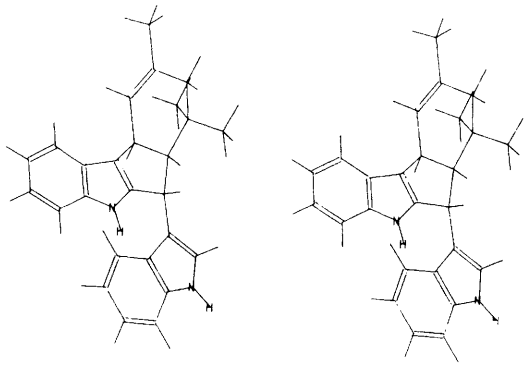


Fig. 1 Stereoscopic graphic representation of the MM2-calculated geometry of YCK (confomer iii)

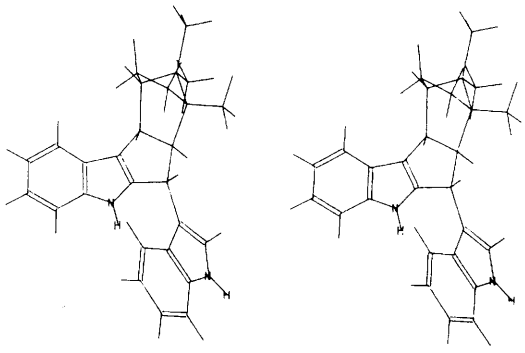
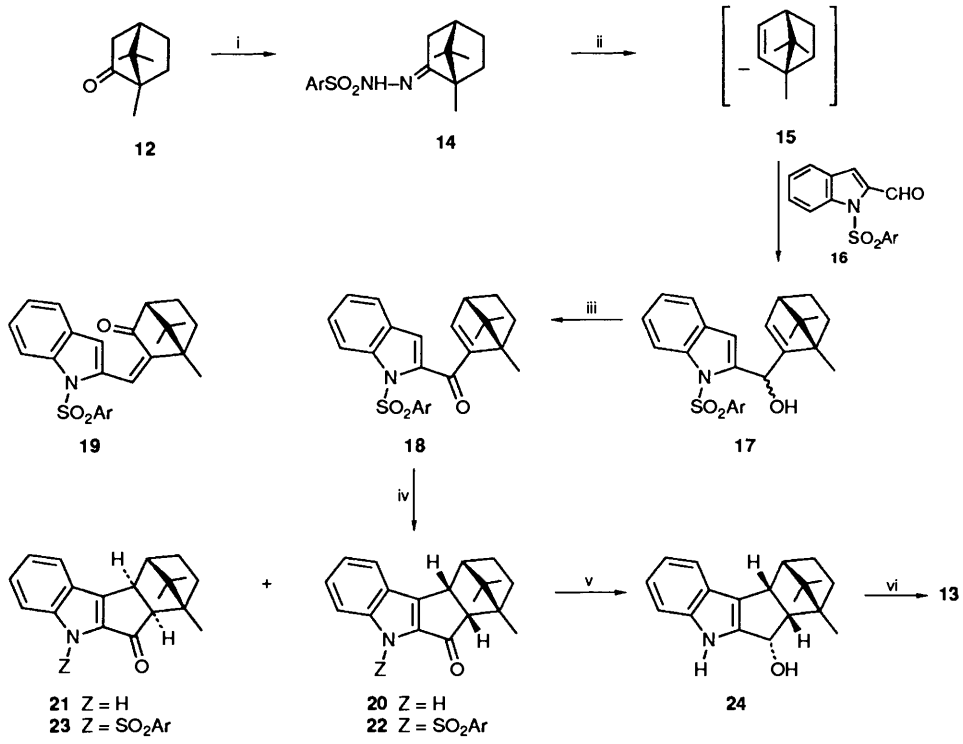


Fig. 2 Stereoscopic graphic representation of the MM2-calculated geometry of camphor-YCK (conformer iii)

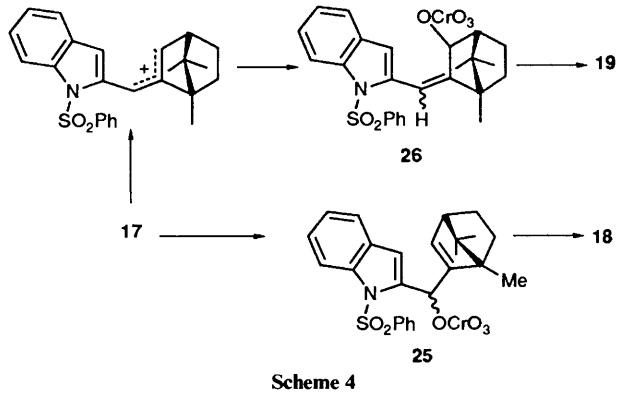
15, which was trapped by indole-2-carbaldehyde **16**[18] to give the allylic alcohol **17**, epimeric (1:1) at C-6. The ^{1}H NMR exhibited six methyl singlets and two singlets at δ 6.73 and 6.66 for 3′-H. As this chiral centre at C-6 was to be destroyed in the next oxidation step, the epimeric alcohols were not separated.

An attempt to oxidize compound **17** with pyridinium chlorochromate (PCC)[19] in CH_2Cl_2 afforded the rearranged ketone **19**, which was probably formed from initial solvolysis of alcohol **17** (Scheme 4) followed by preferred formation of the chromate ester **26** over its isomer **25** due to steric hindrance of the *N*-phenylsulphonyl group and angular methyl group. To suppress this undesirable solvolysis, the oxidation was carried out with sodium acetate buffer whereby the desired ketone **18** was obtained together with its isomer **19** in an equal amount. On the other hand, when the alcohol **17** was oxidized with active MnO_2[20] in benzene, compound **18** was obtained as the sole product in 78% yield.

The next objective in our synthetic strategy involved cyclization of the divinyl ketone **18** into tetracyclic ketone by Nazarov cyclization.[21,22] For this purpose, a number of different Lewis acids were employed. Ketone **18** with $AlCl_3$ in refluxing benzene gave very complicated products. Treatment of ketone **18** in the presence of an excess of BF_3·Et_2O in refluxing toluene afforded two tetracyclic products, **20** and **21** in the ratio 10:1 with concomitant removal of the *N*-phenylsulphonyl group. The stereochemistry of the products were determined by NMR spectroscopy. The coupling constants of 6.56 Hz between 6a-H (δ 3.16) and 10a-H (δ 3.85) and 4.6 Hz between 10a-H and 10-H (δ 2.17) established the stereochemistry of the major compound to be the *endo*-cyclized product **20**. The isomeric, minor, *exo*-product **21** exhibited a coupling constant of 5.3 Hz between 6a-H (δ 2.90) and 10a-H (δ 3.34), and no coupling between 10a-H and 10-H (δ 2.17). It is interesting to note that when cyclization of compound **18** was conducted in the presence of conc. HCl in *p*-dioxane, the *N*-phenylsulphonyl



Scheme 3 *Reagents and conditions:* i, Trisylhydrazine, HCl, MeCN; ii, Bu^{t}Li, THF, −70 ⟶ 0 °C; iii, MnO_2, room temp., 12 h; iv, BF_3·Et_2O, toluene, reflux, 15 h (**18** ⟶ **20**, **21**); conc. HCl, dioxane, reflux, 43 h (**18** ⟶ **22**, **23**); v, DIBAH, THF, 0 °C; vi, BF_3·Et_2O, indole, THF, 0 °C



Scheme 4

group remained intact and the ratio of the *endo*-product **22** to the *exo*-product **23** reversed to 2:5.

Stereoselective reduction of ketone **20** with diisobutylaluminium hydride (DIBAH)[23] in THF furnished the alcohol **24**, bearing the alcohol function in the α-orientation. The coupling constant of 9.0 Hz between 6-H and 6a-H established the stereochemistry as presented. It is pertinent to point out that compound **24** was extremely labile and had to be used for subsequent reaction immediately.

Treatment of the alcohol **24** with indole in BF_3·Et_2O afforded the title compound (*S*)-**13**. The stereochemistry at C-6 was established by NMR spectroscopy which showed a coupling constant of 1.0 Hz between 6-H (δ 4.41) and 6a-H (δ 3.14). This value is in agreement with the value (2.3 Hz) generated from a molecular mechanics calculation.

Compound (*S*)-**13** prepared from (1*S*)-(−)-camphor exhibited $[\alpha]_D$ −40.8°. The enantiomer of (*R*)-**13** prepared from (1*R*)-(+)-camphor showed $[\alpha]_D$ +40.5°.

Analogues (*R*)-**13** and (*S*)-**13** thus prepared were separately tested in three models of bioassay. Results indicated that only (*R*)-**13** was active and equipotent with YCK in anti-implantation activity tests.[24] Since we have shown that the geometry of camphor-YCK is closely related to YCK, it is therefore reasonable to conclude that the absolute configuration of the active YCK should be as represented by structure (*R*)-**1**. Details of other aspects in the biological activity studies on the title compound will be reported elsewhere.

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[25] was carried out with Kieselgel 60 (Merck) as the stationary phase. 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 apparatus dried in an oven 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.

(1S)-*Camphor 2,4,6-Triisopropylphenylsulphonylhydrazone* **14**.—To a solution of (1*S*)-(−)-camphor (4.6 g, 30 mmol) and 2,4,6-triisopropylphenylsulphonylhydrazine (10 g, 33 mmol) in acetonitrile (30 cm^3) was added conc. HCl (3 cm^3). The resulting solution was stirred at room temp. for 12 h and was then kept at 0 °C for another 12 h. The crude hydrazone **14** separated out

and was redissolved in chloroform, and the solution was filtered. The filtrate was washed with saturated aq. sodium hydrogen carbonate, dried, and concentrated to give the hydrazone **14** as a solid (8.9 g, 70%), m.p. 195–197 °C (lit.,[16] 197–199 °C); ν_{max}(Nujol)/cm^{-1} 3240, 1175 and 680; δ_H(90 MHz) 0.60 (3 H, s), 0.86 (6 H, s), 1.25 (6 H, d, *J* 6.8), 1.27 (12 H, d, *J* 6.6), 1.60–2.21 (7 H, m), 2.91 (1 H, septet, *J* 6.8), 4.25 (2 H, septet, *J* 6.8) and 7.16 (2 H, s); *m/z* 432 (M^+).

(1′-*Phenylsulphonylindol-2′-yl*)[(1S,4S)-1,7,7-*trimethylbicyclo*[2.2.1]*hept-2-en-2-yl*]*methanol* **17**.—To a solution of the trisylhydrazone **14** (8.6 g, 20 mmol) in anhydrous THF (60 cm^3) at −70 °C was added *t*-butyllithium (1.7 mol dm^{-3}; 27.3 cm^3, 47 mmol). The resulting solution was allowed to warm up to room temp. During this period, nitrogen was evolved. When nitrogen ceased to evolve, the solution was cooled to −70 °C, treated with a solution of 1-phenylsulphonylindole-2-carbaldehyde[18] (7.7 g, 20 mmol) in anhydrous THF (90 cm^3), and was allowed to warm to room temp. overnight. The solution was poured into saturated aq. ammonium chloride. The usual work-up and column chromatography of the crude product afforded a 1:1 epimeric mixture of the alcohol **17** as a solid, m.p. 123.5–124.5 °C; ν_{max}(KBr/cm^{-1}) 3540, 3430, 1450, 1370, 1090 and 755; δ_H(90 MHz) 0.74–0.98 (9 H, 6 s, Me), 1.06–1.84 (4 H, m, 5- and 6-H_2), 2.30 (1 H, m, 4-H), 2.88 (1 H, m, OH), 5.91 (2 H, m, 3-H and *H*COH), 6.66 and 6.74 (1 H, s, 3′-H) and 7.07–8.16 (9 H, s, ArH) (Found: M^+, 421.1723. $C_{25}H_{27}NO_3S$ requires M, 421.1714).

1′-(*Phenylsulphonyl*)*indol-2′-yl* (1S,4S)-1,7,7-*Trimethylbicyclo*[2.2.1]*hept-2-en-2-yl Ketone* **18**.—A mixture of active manganese dioxide (30 g) and the alcohol **17** (3.0 g) in benzene was stirred at room temp. for 12 h. Work-up and purification of the crude product by column chromatography on silica gel eluted with diethyl ether–light petroleum (1:4) afforded the ketone **18** (2.3 g, 78%) as a solid, m.p. 136 °C; ν_{max}(KBr)/cm^{-1} 1640, 1180, 760 and 730; λ_{max}(EtOH)/nm 293; δ_H(90 MHz; [$^2H_6$]benzene) 0.67 (3 H, s, Me), 0.96 (3 H, s, Me), 1.63 (3 H, s, Me), 0.70–2.00 (4 H, m, 5- and 6-H_2), 2.14 (1 H, t, *J* 3.2, 4-H), 6.36 (1 H, d, *J* 3.2, 3-H), 6.48 (1 H, s, 3′-H), 6.71–7.27 (6 H, m, ArH) and 8.04–8.29 (3 H, m, ArH); δ_C(22.5 MHz; [$^2H_6$]benzene) 11.84 (q, Me), 19.01 (q, Me), 19.8 (q, Me), 25.08 (t), 31.34 (t), 53.23 (d, C-4), 54.99 (s, C-7), 56.88 (s, C-7), 113.55 (d), 115.47 (d), 122.27 (d), 124.19 (d), 126.25 (d), 127.79 (d), 128.80 (d), 129.45 (s), 133.43 (d), 137.52 (s), 138.87 (s), 139.74 (s), 150.41 (s), 152.04 (d), 185.27 (s, C=O) (Found: M^+, 419.1552. $C_{25}H_{25}NO_3S$ requires M, 419.1557).

(1R,4S)-4,7,7-*Trimethyl*-3-{[1′-*phenylsulphonyl*)*indol-2′-yl*]*methylene*}*bicyclo*[2.2.1]*heptan-2-one* **19**.—A mixture of ketone **17** (0.5 g, 1.20 mmol) in dichloromethane (6 cm^3) containing PCC (0.38 g, 1.78 mmol) was stirred at room temp. for 2 h. The resulting black gum was extracted with diethyl ether. The combined extracts were filtered through a pad of silica gel. Removal of the solvent and purification of the residue by column chromatography on elution with diethyl ether–light petroleum (3:7) afforded the ketone **19** (0.45 g, 90%) as a yellow solid, m.p. 127–128 °C; ν_{max}(Nujol)/cm^{-1} 1720, 1610, 1350 and 900; λ_{max}(EtOH)/nm 330; δ_H(90 MHz) 0.90 (3 H, s, Me), 0.99 (3 H, s, Me), 1.25 (3 H, s, Me), 1.45–2.05 (4 H, m, 5- and 6-H_2), 2.27 (1 H, br s, 1-H) and 7.14–8.23 (11 H, m, ArH); δ_C(22.5 MHz) 12.57 (q, Me), 17.71 (q, Me), 20.37 (q, Me), 22.51 (t, C-5 or -6), 34.45 (t, C-6 or -5), 46.02 (s, C-4 or -7), 53.55 (s, C-7 or -4), 60.46 (d, C-1), 115.25 (d), 116.96 (d), 119.05 (d), 121.73 (d), 124.17 (d), 125.76 (d), 126.22 (d), 128.85 (d), 130.02 (s), 133.51 (d), 134.65 (s), 137.76 (s), 138.49 (s), 146.29 (s) and 204.42 (s, C=O); *m/z* 419 (M^+) (Found: C, 71.8; H, 6.1; N, 3.2. Calc. for $C_{25}H_{25}NO_3S$: C, 71.6; H, 6.0; N, 3.3%).

(6aR,7R,10S,10aR)-7,11,11-*Trimethyl*-6-*oxo*-5,6,6a,7,8,9,10,10a-*octahydro*-7,10-*methanoindeno*[2,1-b]*indole* **20** *and* (6aS,7R,10S,10aS)-*Isomer* **21**.—A solution of the ketone **18** (27 g, 63.6 mmol) in anhydrous toluene (125 cm^3) and BF_3·Et_2O (125 cm^3) was heated under reflux for 15 h. The resulting solution was poured into water (1.5 dm^3), and extracted with dichloromethane. The extract was washed with saturated aq. sodium hydrogen carbonate, dried, and concentrated. The residue was purified by column chromatography on silica gel and eluted with diethyl ether–light petroleum (1:2) to give compound **20** as a solid (6.3 g, 55%), m.p. 208–209 °C (from diethyl ether–light petroleum); $[\alpha]_D$ −58.3° (*c* 0.28, $CHCl_3$); ν_{max}(KBr)/cm^{-1} 3200, 1645, 1620, 1330 and 750; δ_H(90 MHz) 0.95 (3 H, s, Me), 1.14 (3 H, s, Me), 1.20 (3 H, s, Me), 0.50–1.60 (4 H, m, 8- and 9-H_2), 2.17 (1 H, dd, $J_{10.10a}$ 4.6, $J_{9.10}$ 3.0, 10-H), 3.16 (1 H, d, $J_{6a.10a}$ 6.56, 6a-H), 3.85 (1 H, dd, $J_{6a.10a}$ 6.56, $J_{10.10a}$ 4.6, 10a-H), 7.03–7.64 (4 H, m, ArH) and 10.48 (1 H, br s, NH); δ_C(22.5 MHz) 15.22 (q, Me), 18.64 (q, Me), 20.40 (q, Me), 23.08 (t), 30.99 (t), 40.66 (d, C-10), 47.65 (d, C-6a or -10a), 50.11 (s, C-7 or -11), 53.63 (s, C-11 or -7), 64.52 (d, C-10a or -6a), 113.93 (d), 120.54 (d), 121.54 (d), 123.84 (s), 127.17 (d), 139.90 (s), 144.13 (s), 147.81 (s) and 197.95 (s, C=O); *m/z* 279 (M^+) (Found: C, 81.6; H, 7.6; N, 5.1. Calc. for $C_{19}H_{21}NO$: C, 81.7; H, 7.6; N, 5.0%).

The enantiomer of compound **20** prepared from (1*R*)-(+)-camphor, showed $[\alpha]_D$ +58.9° (*c* 0.35, $CHCl_3$).

Further elution afforded the isomeric ketone **21** as a solid, m.p. 212.5–213.5 °C; ν_{max}(Nujol)/cm^{-1} 3200, 1645, 1325, 1159 and 748; δ_H(90 MHz) 0.30 (3 H, s, Me), 0.78 (3 H, s, Me), 1.27 (3 H, s, Me), 0.5–1.6 (4 H, m, 8- and 9-H_2), 2.14 (1 H, br s, 10-H), 2.90 (1 H, d, *J* 5.3, 6a-H), 3.34 (1 H, d, *J* 5.3, 10a-H), 7.03–7.64 (4 H, m, ArH) and 10.22 (1 H, br s, NH); δ_C(22.5 MHz) 12.35 (q), 20.04 (q), 23.05 (q), 29.30 (t), 38.41 (t), 44.45 (d), 47.67 (d), 47.86 (s), 50.73 (s), 66.69 (d), 113.89 (d), 120.45 (d), 121.51 (d), 123.27 (s), 126.95 (d), 140.58 (s), 144.07 (s), 150.01 (s) and 197.16 (s) (Found: M^+, 279.1617. $C_{19}H_{21}NO$ requires M, 279.1622).

(6aR,7R,10S,10aR)-7,11,11-*Trimethyl*-6-*oxo*-5-*phenylsulphonyl*-5,6,6a,7,8,9,10,10a-*octahydro*-7,10-*methanoindeno*[2,1-b]*indole* **22** *and* (6aS, 7R, 10S, 10aS)-*Isomer* **23**.—A solution of compound **18** (0.24 g, 0.57 mmol) in dioxane (12 cm^3) and conc. hydrochloric acid (12 cm^3) was heated under reflux for 43 h. The resulting solution was poured into ice–water, neutralized with saturated aq. sodium hydrogen carbonate, and extracted with diethyl ether. Column chromatography of the crude product on silica gel and elution with light petroleum afforded, first, compound **22** (48 mg, 20%) as a solid, m.p. 226–227 °C; ν_{max}(Nujol)/cm^{-1} 1691, 1379, 1188, 1122, 1088 and 744; δ_H(90 MHz) 0.92 (3 H, s, Me), 1.07 (3 H, s, Me), 1.13 (3 H, s, Me), 2.13 (1 H, dd, $J_{10.10a}$ 6.0, $J_{9.10}$ 4.4, 10-H), 0.5–1.6 (4 H, m, 8- and 9-H_2), 3.07 (1 H, d, $J_{6a.10a}$ 6.0, 6a-H), 3.68 (1 H, dd, $J_{10.10a}$ 6.0, $J_{6a.10a}$ 6.0, 10a-H) and 7.20–8.44 (9 H, m, ArH); δ_C(22.5 MHz) 14.97 (q), 18.46 (q), 20.06 (q), 23.04 (t), 30.57 (t), 39.29 (d), 47.23 (d), 50.48 (s), 53.33 (s), 62.24 (d), 115.84 (d), 121.61 (d), 124.08 (d), 125.16 (s), 127.33 (d), 129.11 (d), 129.30 (d), 133.91 (d), 138.81 (s), 143.31 (s), 155.31 (s) and 192.90 (s); *m/z* 419 (M^+); $[\alpha]_D$ +13.30° (*c* 0.263, $CHCl_3$).

Further elution afforded the isomeric ketone **23** as a solid (120 mg, 50%); ν_{max}(Nujol)/cm^{-1} 1685, 1180, 755 and 740; δ_H(90 MHz) 0.11 (3 H, s, Me), 0.72 (3 H, s, Me), 1.16 (3 H, s, Me), 0.6–2.2 (5 H, m, 8- and 9-H_2, and 10-H), 2.84 (1 H, d, $J_{6a.10a}$ 5.8, 6a-H), 3.14 (1 H, d, $J_{6a.10a}$ 5.8, 10a-H) and 7.25–8.42 (9 H, m, ArH); δ_C(22.5 MHz) 47.00 (q), 47.10 (q), 47.20 (q), 51.11 (s), 66.39 (d), 115.87 (d), 121.62 (d), 123.97 (d), 124.78 (s), 127.44 (d), 128.99 (d), 133.89 (d), 139.17 (s), 139.90 (s), 143.34 (s), 156.88 (s) and 191.91 (s); *m/z* 419 (M^+) (Found: C, 71.7; H, 5.9; N, 3.5. Calc. for $C_{25}H_{25}NO_3S$: C, 71.6; H, 6.0; N, 3.4%).

(6S,6aS,7R,10S,10aR)-6-(*Indol*-3-*yl*)-7,11,11-*trimethyl*-5,6,6a,7,8,9,10,10a-*octahydro*-7,10-*methanoindeno*[2,1-b]*indole*. (S)-*Camphor-YCK* (S)-**13**.—DIBAH (1 mol dm^{-3}; 1 cm^3, 1.0 mmol) was added dropwise to a solution of ketone **20** (140 mg, 0.5 mmol) in anhydrous THF (3 cm^3) at 0 °C. After the resulting solution had been stirred for 30 min, water (10 cm^3) was added and the mixture was extracted with diethyl ether. Removal of solvent under reduced pressure afforded the alcohol **24**, which was used immediately in the subsequent reaction without further purification.

To a solution of compound **24** and indole (59 mg, 0.5 mmol) in diethyl ether (10 cm^3) at 0 °C was added BF_3-Et_2O (0.076 cm^3, 0.62 mmol). The resulting solution was stirred at 0 °C for 30 min. Work-up and purification of the crude product by flash chromatography on silica gel and elution with diethyl ether–light petroleum (1:2) afforded (*S*)-camphor-YCK (*S*)-**13** (82 mg, 43%) as a pale yellow solid, m.p. 132–132.5 °C; ν_{max}(Nujol)/cm^{-1} 3400, 1662, 1456, 1094, 1011 and 741; δ_H(90 MHz; [$^2H_6$]benzene) 0.89 (3 H, s, Me), 0.91 (3 H, s, Me), 1.00 (3 H, s, Me), 0.50–1.70 (4 H, m, 8- and 9-H_2), 2.05 (1 H, dd, $J_{10.10a}$ 2.0, $J_{9.10}$ 2.0, 10-H), 3.14 (1 H, dd, $J_{6.6a}$ 1.0, $J_{6a.10a}$ 9.0, 6a-H), 3.96 (1 H, ddd, $J_{6a.10a}$ 9.0, $J_{6.10a}$ 1.0, $J_{10.10a}$ 2.0, 10a-H), 4.41 (1 H, dd, $J_{6.6a}$ 1.0, $J_{6.10a}$ 1.0, 6-H), 6.29 (1 H, d, *J* 2.2, 2′-H), 6.55 (1 H, br s, NH) and 6.60–7.59 (8 H, m, ArH); δ_C (22.5 MHz; [$^2H_6$]benzene) 16.04 (q, Me), 18.61 (q, Me), 20.88 (q, Me), 23.73 (t), 29.55 (t), 36.05 (d, C-6), 43.47 (d, C-10a), 48.40 (d, C-10), 49.05 (s, C-7 or -11), 51.46 (s, C-11 or -7), 66.44 (d, C-6a), 111.38 (d), 112.00 (d), 119.18 (d), 119.43 (d), 120.02 (d), 121.29 (d), 121.46 (d), 122.40 (d), 125.76 (s), 127.39 (s), 127.58 (s), 128.34 (d), 130.48 (s), 137.19 (s), 141.93 (s) and 145.67 (s) (Found: 380.2245. $C_{27}H_{28}N_2$ requires M, 380.2252); $[\alpha]_D$ −40.8° (*c* 0.27, $CHCl_3$).

(*R*)-Camphor-YCK (*R*)-**13** showed $[\alpha]_D$ +40.5° (*c* 0.285, $CHCl_3$).

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