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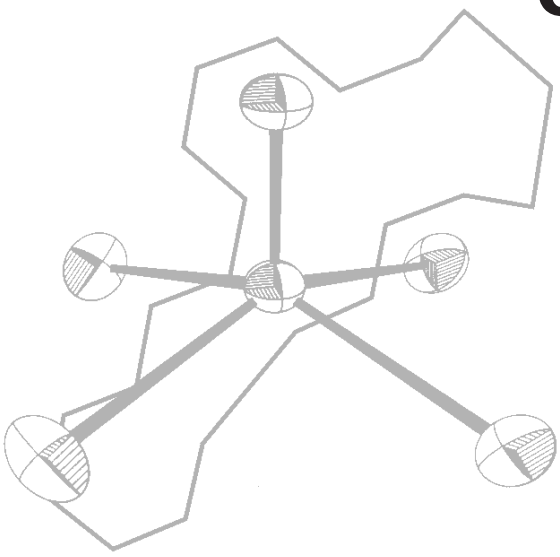

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Total Synthesis of (±)-Iso-*trans*-trikentrin B

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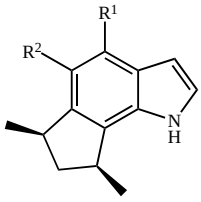
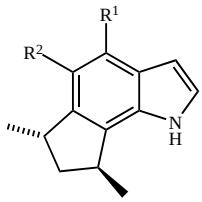
The synthesis of the title compound, a member of a family of cyclopent[*g*]indoles isolated from a marine sponge, is described. Most of the synthetic sequence was developed starting from the more readily available *cis*-1,3-dimethylindan. An X-ray crystal structure of the indanol (24), the precursor of *trans*-1,3-dimethylindan, confirmed its relative stereochemistry.

The trikentrins (1)–(5) are a family of novel cyclopent[*g*]indoles, isolated from the marine sponge *Trikentrion flabelliforme*, which exhibit growth inhibitory activity against Gram-positive bacteria.[1] Since the first reported total synthesis by us of (±)-*cis*- and *trans*-trikentrin A, (1) and (3) respectively,[2,3] other groups have published syntheses of racemic (1)[4–6] and (3)[4,6] as well as syntheses of (±)-*cis*-trikentrin B (2),[5,7] (±)-*trans*-trikentrin B (4)[5] and (±)-iso-*trans*-trikentrin B (5).[5] The absolute stereochemistry of the trikentrins was established by enantioselective syntheses of either the natural product or its enantiomer.[5,8–11] These syntheses have utilized a variety of approaches to fabricate the tricyclic ring system, including aryl radical cyclization,[2,3] intramolecular Diels–Alder reactions,[6,7] and acid-catalysed indole cyclization.[5] We now report a synthesis of (±)-iso-*trans*-trikentrin B (5) which follows the same basic methodology that we used previously for the elaboration of the cyclopent[*g*]indole system.[2,3]

Results and Discussion

Because *cis*-1,3-dimethylindan (6a) could be prepared more readily than the *trans*-isomer (6b), by using procedures developed previously,[3] exploratory reaction steps leading to the target compound (5) were first carried out with (6a) as the starting material.





	R^1	R^2
(1)	Et	H
(2)	H	(*E*)-but-1-enyl

	R^1	R^2
(3)	Et	H
(4)	H	(*E*)-but-1-enyl
(5)	(*E*)-but-1-enyl	H

Friedel–Crafts acylation of (6a) with butyryl chloride/aluminium chloride gave a single regioisomer (7a) in 82% yield, whose structure was verified by n.m.r. and mass spectrometry. Sodium borohydride reduction of ketone (7a) gave in high yield the benzylic alcohol (8a) as a mixture of diastereomers, which was converted into its methoxymethyl ether (9a). All attempts to formylate (9a) directly were unsuccessful. Attempted *ortho*-directed metalation[12] of (9a), with a variety of alkyllithium reagents of increasing basicity followed by quenching with methan(D)ol, showed no deuterium incorporation in the recovered starting material (9a), as evidenced by g.c.–m.s. analysis of the reaction product. When the same series of reactions was performed on the alcohol (8a), with 2 equiv. of alkyllithium, a high incorporation of one deuterium atom was observed, but only when t-butyllithium was used. Replacement of methan(D)ol with dimethylformamide as the quenching agent gave a product mixture which contained some starting material (8a) together with the lactol (10) as the major product and the hydroxy aldehyde (11a) in minor amounts. Although (9a) could be readily separated from (10) and (11a), the free aldehyde itself could not be isolated. N.m.r. studies of the equilibrium concentrations of the interconverting aldehyde (11a) and lactol (10) showed that, under all conditions of pH and solvent used, the lactol form predominated. It was not surprising, therefore, that no aldehyde derivates (acetal, thioacetal) could be formed from (10), nor was any identifiable product given on attempted condensation with ethyl azidoacetate. The formation of the lactol, together with the presence of two aromatic singlets in its ^{1}H n.m.r. spectrum, did nevertheless confirm that proton abstraction had occurred exclusively from the 6-position of (8a).

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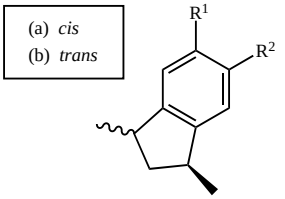
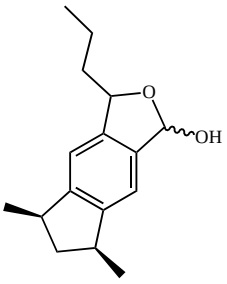


	R^1	R^2
(6)	H	H
(7)	COPr	H
(8)	CH(OH)Pr	H
(9)	$CH(OCH_2OMe)Pr$	H
(11)	CH(OH)Pr	CHO
(12)	CH(OH)Pr	Br
(13)	$CH(OCH_2OMe)Pr$	Br
(14)	$CH(OCH_2OMe)Pr$	CHO
(15)	$CH(OCH_2OMe)Pr$	$CH{=}C(N_3)CO_2Et$

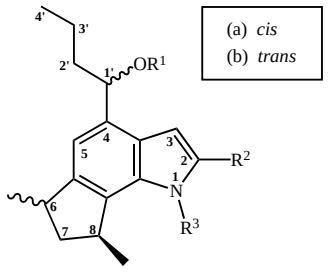


(10)

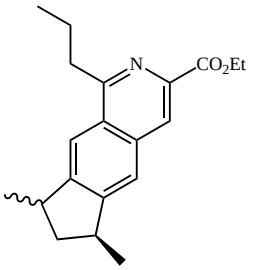
To overcome the undesirable intermediacy of the lactol, the aldehyde functionality was replaced by a bromine atom. A number of brominating agents were used to quench the aryllithium from (8a), with carbon tetrabromide giving the cleanest product and best yields of the 6-bromo compound (12a). Protection of the benzylic hydroxy group of (12a) as its methoxymethyl ether gave (13a), which was treated with butyllithium followed by dimethylformamide to afford the aldehyde (14a) in 81% yield. The regiochemistry of (14a) was confirmed by its n.m.r. and mass spectra.

Elaboration of the pyrrole ring onto the indan ring followed the procedure developed by Moody[13] and used by us for the synthesis of (1) and (3).[2,3] The aldehyde (14a) was condensed with ethyl azidoacetate to give the unstable azidocinnamate (15a). The nitrene generated by heating (15a) can undergo either electrocyclization to give the required indole ester (16a) or insertion into the adjacent benzylic position of the alkoxybutyl side chain to give the unwanted isoquinoline (17a).[13] Thermolysis of (15a) in refluxing benzene provided the indole (16a) and isoquinoline (17a) in approximately equal amounts with an overall yield of >95%. When the thermolysis was carried out in refluxing toluene, the overall yield was lower but the isolated yield of the indole (16a) increased considerably (60–80%).

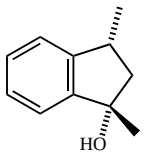
In our earlier synthesis of (1) and (3), the ethoxycarbonyl group on the indole ring was removed by base hydrolysis to give the acid, followed by decarboxylation by flash vacuum pyrolysis.[2,3] The equipment required for the latter reaction was no longer available to us and therefore decarboxylation of the acid (18a), from basic hydrolysis of (16a), was attempted by using copper/quinoline at high temperature.[14] Less than 10% of the desired product (19a) was recovered from the reaction mixture, the rest being decomposition products. We therefore explored the alternative procedure used by Moody[13,15] of rhodium-catalysed decarbonylation of the indole-2-carbaldehyde derived from the ethyl ester (16a). Direct reduction of (16a) to the carbaldehyde (21a) by using diisobutylaluminium hydride was unsuccessful and instead gave the corresponding alcohol (20a) in about 90% yield. Oxidation of (20a) with manganese dioxide[16] provided the aldehyde (21a). Decarbonylation of (21a) was carried out with a catalytic amount of bis(triphenylphosphine)(carbonyl)rhodium(I) chloride and 1,3-bis(diphenylphosphino)propane in refluxing mesitylene,[13,15] giving (19a) in yields of 60–70%.



	R^1	R^2	R^3
(16)	CH_2OMe	CO_2Et	H
(18)	CH_2OMe	CO_2H	H
(19)	CH_2OMe	H	H
(20)	CH_2OMe	CH_2OH	H
(21)	CH_2OMe	CHO	H
(22)	CH_2OMe	H	COMe
(23)	H	H	COMe



(17)



(24)

The final step in the model reaction sequence with the *cis*-analogue was the introduction of the (*E*) double bond in the C_4 side chain of (19a). It was necessary to leave this until late in the synthesis because of the lability of the resultant 'styryl' system. Natsume[9,10] had shown that elimination of the C_4 side chain benzylic alcohol from an *N*-protected precursor of *cis*- and *trans*-trikentrin B, (2) and (4), could be carried out in high yield by using a catalytic amount of *p*-toluenesulfonic acid in refluxing benzene. These conditions were applied to the methoxymethyl ether (19a) in the expectation that deprotection of the benzylic alcohol and subsequent dehydration would occur in a one-pot reaction. In the event, no identifiable products could be isolated. Since Natsume had used an *N*-benzenesulfonate in the dehydration reaction, we attempted to form the *N*-benzenesulfonate derivative of (19a). This was unsuccessful probably due to steric hindrance. It was possible, however, to form an *N*-acetyl derivative (22a) with acetic anhydride. The methoxymethyl protecting group was then removed from (22a) with dimethylboron bromide[17] and the resulting benzylic alcohol (23a) treated with *p*-toluenesulfonic acid in benzene. Only starting material and no olefinic products could be identified in the reaction mixture. By this stage, the synthesis of (±)-iso-*trans*-trikentrin B (5) was well underway and further developmental studies using the model *cis*-isomer were put aside.

The starting compound for the synthesis of (5), *trans*-1,3-dimethylindan (6b), had previously been prepared by reduction of *cis*-1,3-dimethylindan-1-ol (24)

with W7 Raney nickel.[3] The indanol (24) could be isolated and purified as a crystalline compound from the mixture (*c.* 1 : 1) of the *cis*- and *trans*-isomers formed from an aryl radical intramolecular cyclization of 2-(2-bromophenyl)pent-4-en-2-ol.[3] We have obtained an X-ray crystal structure of (24) (Fig. 1) which confirms the *trans*-relationship of the two methyl groups. A more direct and stereoselective route to the *cis*-indanol (24) involved treatment of 3-methylindan-1-one with methylmagnesium iodide; this gave a product that contained predominantly the *cis*-isomer.[18] 3-Methylindan-1-one was prepared in *c.* 80% yield in a one-pot reaction of benzene and but-2-enoic acid, by using a modification of the method of Koelsch *et al.*[19]

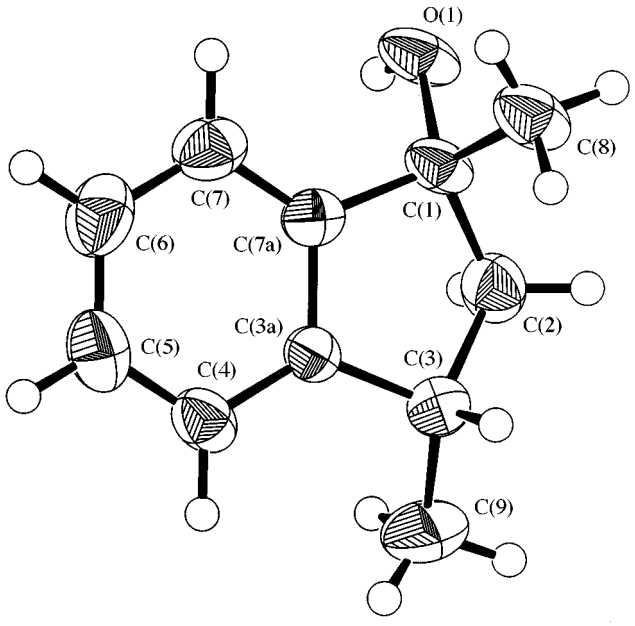


Fig. 1. ORTEP projection of (24) derived from X-ray crystallographic data.

Stereoselective hydrogenolysis[20] of the *cis*-indanol (24) by using Raney nickel to give *trans*-1,3-dimethylindan (6b), that is, with retention of configuration, proved to be a capricious reaction which was very dependent on the method of preparation of the reagent. In many cases, the major reduction product was the *cis*-isomer (6a). The optimum conditions for the production of (6b) were the use of freshly prepared, slightly alkaline Raney nickel (pH of washings between 7·5 and 8·5) and distilled, degassed ethanol as solvent.

By following the above procedures developed with the *cis*-isomer, *trans*-1,3-dimethylindan (6b) was converted into the ketone (7b), which was reduced to a diastereomeric mixture of benzylic alcohols (8b). Metalation of (8b) followed by treatment with carbon tetrabromide gave (12b) which was protected as the methoxymethyl ether (13b). The aryllithium generated from (13b) was quenched with dimethylformamide to give the aldehyde (14b). Annelation of (14b) to the cyclopent[*g*]indole ring system of (16b), via thermolysis of the azidocinnamate (15b), proceeded satisfactorily. Less than 10% of a minor component was present in the reaction product and this, from ^{1}H n.m.r. spectroscopy of the crude mixture, was identified as the alternative isoquinoline cyclization product (17b). The n.m.r. and mass spectra of the major component were consistent with its assigned structure (16b).

Reduction of the indole ester (16b) gave the alcohol (20b) which was oxidized to the aldehyde (21b) with manganese dioxide and then decarbonylated to provide the indole (19b). It was from this point that the model synthesis with the *cis*-isomer had encountered difficulties, in attempting to introduce the (*E*) double bond into the C_4 side chain of (19a). Since *p*-toluenesulfonic acid catalysed elimination of water from the benzylic alcohol (23a) was unsuccessful, we proposed replacing the methoxymethyl ether protecting group of (19b) with a good leaving group that could be eliminated under mild conditions. To carry this out, the ether (19b) was treated with dimethylboron bromide followed by triethylamine, under conditions which had been shown to remove the methoxymethyl protecting group in the *cis*-compound (22a). Somewhat surprisingly, the only identifiable component isolated from the reaction mixture in 63% yield was racemic iso-*trans*-trikentrin B (5). The elimination of the benzylic ether during the reaction could have been triggered by removal of the proton on nitrogen by triethylamine in the intermediate complex formed after addition of dimethylboron bromide. This pathway was not available to the *cis*-compound (22a) which is *N*-acetylated. The n.m.r. and mass spectrometric data obtained for the synthetic product were comparable with the partial data available for natural iso-*trans*-trikentrin B (5)[1] (which was isolated as an inseparable mixture with *cis*-trikentrin B (2)) and matched those reported by Natsume for (±)-iso-*trans*-trikentrin B (5) synthesized by an alternative route.[5]

Experimental

Melting points were determined on a Reichert hot-stage apparatus and are uncorrected. Microanalyses were carried out by the Australian National University Microanalytical Service. Low-resolution electron-impact mass spectra and high-resolution accurate mass measurements were recorded on either a VG Micromass 7070F or a VG ZAB-2SEQ mass spectrometer. The molecular ion (M^+), if present, significant high-mass ions and the more intense low-mass ions are reported. Chemical-ionization mass spectra were measured on the VG Micromass 7070F mass spectrometer, employing ammonia as the reagent gas. Infrared spectra were recorded on a Perkin–Elmer 683 or Perkin–Elmer 1800 (Fourier transform) spectrophotometer as films (neat) or dichloromethane (CH_2Cl_2) solutions. The following abbreviations were adopted to indicate the intensity and to describe the shape of the band: s (strong), m (medium), w (weak) and br (broad). ^{1}H n.m.r. spectra were recorded on either a Varian Gemini-300 (300 MHz), a Varian VXR-300 (300 MHz) or a Varian VXR-500 (500 MHz) spectrometer. Unless otherwise stated spectra were recorded at 300 MHz by using $CDCl_3$ as solvent and tetramethylsilane as the internal reference. The chemical shifts of diastereomers are in parentheses. ^{13}C n.m.r.

spectra were recorded on a Varian Gemini-300 (75·5 MHz) or a Varian VXR-300 (75·4 MHz) spectrometer. The solvent signal was used as the internal reference (76·9 ppm for chloroform) and the signals are quoted as δ values (ppm downfield from tetramethylsilane). The chemical shifts of diastereomers are in parentheses. Two-dimensional n.m.r. experiments were carried out on a Varian VXR-300 spectrometer by using standard Varian pulse sequences. Ultraviolet–visible spectra were recorded on a Shimadzu model UV-160 or a Cary 1E spectrophotometer. Where necessary, solvents and reagents were purified and dried according to procedures of Perrin and Armarego.[21] Flash chromatography[22] was carried out with 230–400 mesh silica gel. For thin-layer chromatography, 0·25-mm Merck silica gel F_{254} plates were used for analytical purposes. Thin-layer chromatograms were visualized under ultraviolet light or by spraying with 13% vanillin in sulfuric acid, followed by heating at *c.* 200°C.

*1-(*cis*-1′,3′-Dimethylindan-5′-yl)butan-1-one (7a)*

Butyryl chloride (4·58 ml, 44·1 mmol) in dry dichloromethane (20 ml) was added dropwise to a vigorously stirred suspension of aluminium trichloride (5·88 g, 44·1 mmol) in dry dichloromethane (20 ml) under argon. The mixture was stirred for 50 min and was then cooled to 0°C. A solution of *cis*-1,3-dimethylindan (6a) (4·30 g, 29·4 mmol), prepared by the method of MacLeod and Monahan,[3] in dry dichloromethane (10 ml) was added dropwise at a rate sufficient to maintain the reaction temperature at *c.* 2°C. The reaction mixture turned orange and, after the addition was complete, the mixture was allowed to warm to room temperature. After being stirred for 1·5 h, the mixture was poured onto ice (100 g). Dichloromethane (50 ml) was added to the iced reaction mixture with stirring. The organic layer was separated and the aqueous layer was reextracted with dichloromethane (3×40 ml). The combined organic fractions were washed with saturated sodium hydrogen carbonate solution (3×30 ml) and dried ($MgSO_4$). The dichloromethane and residual butyryl chloride were removed by distillation which gave an oil. The oil was chromatographed on silica (diethyl ether/hexane, 1 : 9) to give (7a) as a colourless *oil* (5·20 g, 82%), b.p. 105°C/0·08 mmHg (Found: C, 83·0; H, 9·5. $C_{15}H_{20}O$ requires C, 83·3; H, 9·3%). ν_{max} (neat) 1683s cm^{-1} (C=O). ^{1}H n.m.r. δ 7·83, d, *J* 8·0 Hz, 1H, H 6′; 7·78, s, 1H, H 4′; 7·25, d, *J* 8·0 Hz, 1H, H 7′; 3·12, m, 2H, H 1′ and H 3′; 2·93, t, *J* 7·4 Hz, 2H, H 2; 2·50, dt, *J* 12·1, 7·0 Hz, 1H, H 2′$_a$; 1·78, sextet, *J* 7·4 Hz, 2H, H 3; 1·35, d, *J* 7·4 Hz, CH_3; 1·32, d, *J* 7·0 Hz, CH_3; 1·18, dt, *J* 12·1, 10·5 Hz, 1H, H 2′$_b$; 1·02, t, *J* 7·4 Hz, 3H, H 4. ^{13}C n.m.r. δ 200·9, C=O; 154·3, 149·2, 135·7, 3×Ar C_{quat}; 127·0, 122·8, 122·5, 3×Ar CH; 44·7, C 2′; 40·4, C 2; 38·0, 37·7, C 1′ and C 3′; 18·9, 18·7, 2×CH_3; 17·7, C 3; 13·6, C 4. Mass spectrum: *m/z* 216 (M^+, 11%), 188 (3), 173 (100), 145 (11), 91 (7).

*1-(*cis*-1′,3′-Dimethylindan-5′-yl)butan-1-ol (8a)*

The butanone (7a) (2·50 g, 11·56 mmol) was dissolved in methanol (25 ml) and the solution was cooled to −10°C. Sodium borohydride (0·66 g, 17·36 mmol) was added to the stirred solution in portions at a rate sufficient to maintain the reaction temperature between 0 and 2°C. Once the addition was complete, the mixture was stirred for 50 min as it warmed to room temperature. The reaction mixture was then poured onto water (40 ml) and the methanol was removed under reduced pressure. The aqueous residue was extracted with dichloromethane (3×30 ml), dried ($MgSO_4$) and the solvent removed to give the *title compound* (8a) as a colourless oil (2·47 g, 98%), b.p. 154°C/0·08 mmHg (Found: C, 82·2; H, 10·0. $C_{15}H_{22}O$ requires C, 82·5; H, 10·2%). ν_{max} (neat) 3385br cm^{-1} (OH). ^{1}H n.m.r. δ 7·15, m, 3H, ArH; 4·68, t, *J* 6·6 Hz, OCH; 3·08, m, 2H, H 1′ and H 3′; 2·50, dt, *J* 12·1, 7·0 Hz, 1H, H 2′$_a$; 1·95–1·20, m, 5H, H 2, H 3 and OH; 1·33, d, *J* 6·8 Hz, CH_3; 1·32, d, *J* 6·8 Hz, CH_3; 1·19, dt, *J* 12·1, 10·5 Hz, 1H, H 2′$_b$; 0·95, t, *J* 7·2 Hz, 3H, H 4. ^{13}C n.m.r. δ 149·0, (148·9), 148·0, 143·3, 3×Ar C_{quat}; 124·2, (123·9), 122·7, (122·6), 120·4, (120·3), 3×Ar CH; 74·6, (74·5), OCH; 44·9, C 2′; 41·0, C 2; 37·7, 37·5, C 1′ and C 3′; 18·98, 2×CH_3; 18·98, C 3; 13·6, C 4. Mass spectrum: *m/z* 218 (M^+, 3%), 203 (1), 176 (13), 175 (100), 145 (5), 105 (82), 91 (46).

cis-*5-(1′-Methoxymethyloxybutyl)-1,3-dimethylindan (9a)*

The methoxymethyl ether (9a) was prepared by the method of Stork and Takahashi.[23] To a stirred solution of the alcohol (8a) (1·0 g, 4·58 mmol) in dichloromethane (25 ml) at 0°C, methoxymethyl chloride (2·09 ml, 27·48 mmol) was added. Ethyldiisopropylamine (4·79 ml, 27·48 mmol) was added slowly to the solution. The reaction mixture was warmed to room temperature and it was stirred for a further 28 h until the reaction was complete. The reaction mixture was poured onto a mixture of ice and water (30 g) with stirring. The aqueous layer was separated and extracted with dichloromethane (3×15 ml). The organic layers were combined and washed with 10% hydrochloric acid solution (20 ml), saturated sodium hydrogen carbonate solution (2×20 ml) and saturated sodium chloride solution (20 ml). The organic layer was dried ($MgSO_4$) and the solvent was removed by distillation to give (9a) as a yellow *oil* (1·13 g, 94%), b.p. 80°C/0·8 mmHg (Found: C, 78·0; H, 9·7. $C_{17}H_{26}O_2$ requires C, 77·8; H, 10·0%). ν_{max} (neat) 1109 cm^{-1} (C–O). ^{1}H n.m.r. δ 7·11, s, 3×ArH; 4·53, m, OCH_2O and OCH; 3·39, (3·38), s, OCH_3; 3·06, m, 2H, H 1 and H 3; 2·48, dt, *J* 12·0, 7·0 Hz, 1H, H 2′$_a$; 1·85, m, 1H, H 2′$_a$; 1·69–1·25, br m, 3H, H 2′$_b$ and H 3′; 1·30, d, *J* 6·7 Hz, CH_3; 1·29, d, *J* 6·7 Hz, CH_3; 1·16, m, 1H, H 2$_b$; 0·93, t, *J* 7·3 Hz, 3H, H 4′. ^{13}C n.m.r. δ 148·8, 148·0, 140·4, 3×Ar C_{quat}; 125·1, 122·6, 121·4, (121·2), 3×Ar CH; 93·9, OCH_2O; 77·8, CHO; 55·3, OCH_3; 45·0, C 2; 40·2, C 2′; 37·7, 37·6, C 1 and C 3; 19·0, C 3′; 18·9, 2×CH_3; 13·6, C 4′. Mass spectrum: *m/z* 262 (M^+, 2%), 247 (1), 220 (15), 219 (70), 201 (10), 175 (21), 145 (27), 105 (52), 91 (100).

General Procedure used for Metalation Reactions with Butyllithium Reagents

An excess of the appropriate butyllithium was added under strictly anhydrous conditions to a stirred solution of the substrate in dry solvent under argon at 0°C. The reaction mixture was heated, usually to the boiling point of the solvent, and maintained at this temperature until a colour developed. The solution was then cooled, quenched with an electrophile, and stirred for a further 20 min. It was then diluted with diethyl ether and washed with water. After the aqueous washings were back-extracted with diethyl ether, the organic fractions were combined and dried ($MgSO_4$).

cis-*5,7-Dimethyl-3-propyl-3,5,6,7-tetrahydro-1*H*-indeno[5,6-c]furan-1-ol (10)*/cis-*6-(1′-Hydroxybutyl)-1,3-dimethylindan-5-carbaldehyde (11a)*

The general metalation procedure was followed for the lithiation of the alcohol (8a). The amounts of reagents and solvents used were as follows: alcohol (8a) (30 mg, 137 μmol) in dry, distilled heptane (2·5 ml) and 1·4 M t-butyllithium in pentane (880 μl, 1·23 mmol). The mixture was heated to reflux for 1 h. It was cooled and an excess of *N,N*-dimethylformamide (120 μl) was added. After workup, the residue was chromatographed (silica; ethyl acetate/light petroleum, 1 : 4) to afford an inseparable *mixture* of the title compounds (10) and (11a) as a colourless oil (29 mg, 85%), b.p. 79–80°C/0·8 mmHg (Found: C, 78·5; H, 8·8%; $M^{+\bullet}$, 246·1619. $C_{16}H_{22}O_2$ requires C, 78·0; H, 9·0%; $M^{+\bullet}$, 246·1620). ν_{max} (neat) 3380br cm^{-1} (OH). ^{1}H n.m.r. δ Minor component (11a): 10·09, s, CHO. Major component: 7·20, s, 1H, ArH; 6·97, s, 1H, ArH; 6·44, br s, (6·38, d, *J* 4·0 Hz), 1H, H 1; 5·38,

m, (5·12, m), 1H, H 3; 3·05, m, 2H, H 5 and H 7; 2·81, m, OH [exchangeable with D_2O]; 2·52, m, 1H, H 6_a; 1·8–1·2, br m, 5H, H 1′, H 2′ and H 6_b; 1·33, d, *J* 6·0 Hz, 2×CH_3; 0·99, t, *J* 6·0 Hz, (0·97, t, *J* 5·8 Hz), 3H, H 3′. ^{13}C n.m.r. *δ* 150·5, 149·05, (148·98), 141·23, (141·17), 137·72, 4×Ar C_{quat}; 117·11, (117·07), 115·43, (115·34), 2×Ar CH; 100·65, (100·56), OCHO; 82·96, (82·22), OCH; 45·35, (45·32), C 6; 37·69, 37·65, C 5 and C 7; 19·17, 19·11, 2×CH_3; 18·79, (18·58), C 1′; 18·44, (18·31), C 2′; 14·03, (13·99), C 3′. Mass spectrum: *m/z* 246 (M^+, 2%), 228 (35), 213 (70), 203 (100), 199 (91), 143 (27), 128 (32), 115 (30).

*1-(*cis*-5′-Bromo-1′,3′-dimethylindan-6′-yl)butan-1-ol (12a)*

The general lithiation procedure was followed. Reagents and solvents used were as follows: alcohol (8a) (1·0 g, 4·6 mmol) in heptane, 1·4 M t-butyllithium in pentane (50 mmol) and carbon tetrabromide (50 mmol) in heptane. The residue was chromatographed on silica (ethyl acetate/light petroleum, 1 : 9) to give recovered starting material (8a) (240 mg, 24%) and the *title compound* (12a) (1·02 g, 75%) as a colourless solid, m.p. 79–80°C (Found: C, 59·9; H, 7·3; Br, 26·8%; $M^{+\bullet}$, 296·0787. $C_{15}H_{21}BrO$ requires C, 60·6; H, 7·1; Br, 26·9%; $C_{15}H_{21}{}^{79}BrO$, $M^{+\bullet}$, 296·0776). ^{1}H n.m.r. *δ* 7·35, s, 1H, ArH; 7·30, (7·29), s, 1H, ArH; 5·10, m, 1H, OCH; 3·05, m, 2H, H 1′ and H 3′; 2·47, m, 1H, H $2'_a$; 1·89, m, 1H, OH; 1·71, m, 2H, H 2; 1·57–1·34, br m, 2H, H 3; 1·32, d, *J* 6·7 Hz, CH_3; 1·29, d, *J* 6·9 Hz, CH_3; 1·25, m, 1H, H $2'_b$; 0·98, m, 3H, H 4. ^{13}C n.m.r. *δ* 149·57, (149·46), 148·30, 141·42, (141·34), 3×Ar C_{quat}; 126·91, (126·88), 121·40, (121·35), 2×Ar CH; 119·69, (119·54), Ar CBr; 72·83, (72·64), OCH; 45·06, (44·97), C 2′; 39·92, (39·86), C 2; 37·79, (37·71), 37·69, C 1′ and C 3′; 19·11, CH_3; 19·07, (19·01), C 3; 18·97, CH_3; 13·88, C 4. Mass spectrum: *m/z* 298 (M^+, 5%), 296 (M^+, 5), 255 (91), 253 (100), 185 (25), 183 (26).

cis-*5-Bromo-6-(1′-methoxymethyloxybutyl)-1,3-dimethylindan (13a)*

The same method was used as that detailed above for preparing the methoxymethyl ether of (8a). The reagents and amounts used were as follows: indan (12a) (511 mg, 1·72 mmol), ethyldiisopropylamine (150 *μ*l, 850 *μ*mol) and methoxymethyl chloride (65 *μ*l, 850 *μ*mol). The reaction was complete after 26 h. The crude product was chromatographed (silica; ethyl acetate/light petroleum, 1 : 9) to give recovered starting material (12a) (40 mg, 8%) and (13a) as a colourless *oil* (532 mg, 91%), b.p. 70°C/1·3 mmHg (Found: $M^{+\bullet}$, 340·1037. $C_{17}H_{25}{}^{79}BrO_2$ requires $M^{+\bullet}$, 340·1038). ^{1}H n.m.r. *δ* 7·27, s, 1H, ArH; 7·25, s, 1H, ArH; 5·02, m, 1H, OCH; 4·55, d, *J* 6·5 Hz, (4·53, d, *J* 6·3 Hz), 4·52, d, *J* 6·6 Hz, (4·51, d, *J* 6·6 Hz), 2H, OCH_2O; 3·41, (3·40), s, OCH_3; 3·05, m, 2H, H 1 and H 3; 2·46, m, 1H, H 2_a; 1·72–1·21, m, 4H, H 2′ and H 3′; 1·28, d, *J* 7·0 Hz, 2×CH_3; 1·17, dt, *J* 12·1, 10·8 Hz, 1H, H 2_b; 0·97, m, 3H, H 4′. ^{13}C n.m.r. *δ* 149·51, 148·23, 139·35 (139·29), 3×Ar C_{quat}; 126·80, C 4; 121·85, C 7; 120·44, Ar CBr; 94·73, (94·59), OCH_2O; 76·63, (76·58), OCH; 55·72, OCH_3; 45·08, (44·99), C 2; 39·41, (39·28), C 2′; 37·78, 37·71, C 1 and C 3; 19·12, C 3′; 19·07, CH_3; 18·99, (18·94), CH_3; 13·79, C 4′. Mass spectrum: *m/z* 342 (M^+, 9%), 340 (M, 9), 299 (92), 297 (90), 269 (19), 267 (21), 253 (95), 251 (100), 239 (87), 237 (91).

cis-*6-(1′-Methoxymethyloxybutyl)-1,3-dimethylindan-5-carbaldehyde (14a)*

For the general procedure for the lithiation reaction see that used for the lithiation of the alcohol (8a). The amounts of reagents used were as follows: aryl bromide (13a) (532 mg, 1·56 mmol), 1·6 M butyllithium in hexane (1·95 ml, 3·12 mmol) and dimethylformamide (1·2 ml, 15·6 mmol). The crude product was chromatographed (silica; ethyl acetate/light petroleum, 1 : 9) to give the *title compound* (14a) as a colourless oil (367 mg, 81%), b.p. 62°C/1·0 mmHg (Found: $[M-1]^{+\bullet}$, 289·1804. $C_{18}H_{25}O_3$ requires *m/z*, 289·1804). ν_{max} (neat) 1700s (CHO), 1610m cm^{-1} (ArH). ^{1}H n.m.r. *δ* 10·33, (10·31), s, 1H, CHO; 7·64, s, 1H, H 4; 7·40, s, 1H, H 7; 5·44, m, 1H, OCH; 4·57, m, 2H, OCH_2O; 3·38, (3·37), s, OCH_3; 3·12, m, 2H, H 1 and H 3; 2·54, dt, *J* 12·1, 6·2 Hz, 1H, H 2_a; 1·94–1·16, m, 4H, H 2′ and H 3′; 1·36, (1·35), d, *J* 6·3 Hz, CH_3; 1·33, d, *J* 6·7 Hz, CH_3; 1·22, m, 1H, H 2_b; 0·95, t, *J* 7·2 Hz, 3H, H 4′. ^{13}C n.m.r. *δ* 192·37, (192·32), CHO; 155·27, 147·97, 144·42, 132·36, 4×Ar C_{quat}; 125·94, (125·81), 121·73, (121·63), 2×Ar CH; 94·85, (94·74), OCH_2O; 74·59, (74·33), OCH; 55·67, OCH_3; 44·82, (44·76), C 2; 41·09, (41·03), C 2′; 38·55, (38·46), 37·60, C 1 and C 3; 19·39, C 3′; 19·02, CH_3; 18·81, (18·78), CH_3; 13·79, C 4′. Mass spectrum: *m/z* 289 ($[M-1]^+$, 1%), 245 (100), 229 (29), 217 (15), 203 (70). Chemical-ionization mass spectrum: *m/z* 291 (MH^+, 11%), 289 (12), 259 (20), 245 (30), 229 (100).

Preparation of the Azidocinnamate (15a)

A mixture of the formylindan (14a) (350 mg, 1·21 mmol), freshly prepared ethyl azidoacetate[24] (2·50 g, 19·4 mmol) and dry, distilled ethanol (1·5 ml) was added dropwise to a stirred solution of sodium (345 mg, 15 mmol) and ethanol (20 ml) under argon at −15°C. The reaction mixture was kept between −15 and −10°C over 5·5 h and then was allowed to slowly warm to room temperature over 1 h. Water (20 ml) was added and the solution was extracted with dichloromethane (3×10 ml). The combined organic fraction was washed with a phosphate buffer solution (pH 6·8, 2×10 ml), dried ($MgSO_4$) and the solvent removed. The residue was chromatographed (silica; ethyl acetate/light petroleum, 1 : 9) to give (15a) as an unstable yellow oil (300 mg, 63%). ν_{max} (CH_2Cl_2) 2130s (N_3), 1715s cm^{-1} (C=O). ^{1}H n.m.r. *δ* 7·63, (7·62), s, 1H, H 4; 7·31, (7·30), s, 1H, H 7; 7·26, s, 1H, =CH; 4·85, m, 1H, OCH; 4·59, d, *J* 6·7 Hz and 4·54, d, *J* 6·6 Hz, (4·50, d, *J* 6·9 Hz), 2H, OCH_2O; 4·38, q, *J* 7·1 Hz, O**C**$\mathbf{H}_2$$CH_3$; 3·39, (3·38), s, OCH_3; 3·06, m, 2H, H 1 and H 3; 2·50, dt, *J* 11·9, 6·6 Hz, H 2_a; 1·84–1·13, m, 5H, H 2′, H 3′ and H 2_b; 1·40, t, *J* 7·1 Hz, 3H, $OCH_2C\mathbf{H}_3$; 1·37, d, *J* 6·8 Hz, (1·36, d, *J* 6·6 Hz), CH_3; 1·31, d, *J* 6·6 Hz, (1·30, d, *J* 6·8 Hz), CH_3; 0·95, t, *J* 6·9 Hz, (0·94, t, *J* 7·2 Hz), 3H, H 4′. ^{13}C n.m.r. *δ* 163·41, **C**O_2Et; 150·15, 147·28, 139·84, (139·80), 129·20, (129·14), 125·94, 5×C_{quat}; 123·82, (123·72), 123·66, (123·61), 120·85, 3×CH; 94·15, OCH_2O; 74·52, (74·49), OCH; 62·06, O**C**H_2CH_3; 55·50, OCH_3; 44·94, (44·90), C 2; 39·95, (39·89), C 2′; 38·16, (38·08), 37·74, C 1 and C 3; 19·19, C 3′; 19·07, CH_3; 18·97, CH_3; 14·05, OCH_2**C**H_3; 13·75, (13·64), C 4′. Mass spectrum: *m/z* 330 (1%), 288 (6), 270 (8), 245 (49).

Ethyl cis-*4-(1′-Methoxymethyloxybutyl)-6,8-dimethyl-1,6,7,8-tetrahydrocyclopent[g]indole-2-carboxylate (16a)*

A solution of the azidocinnamate (15a) (300 mg, 750 *μ*mol) in toluene (80 ml) was plunged into a preheated oil bath (140°C) and allowed to reflux for 45 min. The mixture was cooled and the toluene removed under reduced pressure. The residue was chromatographed (silica; ethyl acetate/light petroleum, 1 : 9) to yield as the major component the *title compound* (16a) as a yellow oil (228 mg, 81%), b.p. 82°C/1·8 mmHg (Found: $M^{+\bullet}$, 373·2253. $C_{22}H_{31}NO_4$ requires $M^{+\bullet}$, 373·2253). ν_{max} (neat) 3455m (N–H), 1700s cm^{-1} (C=O). ^{1}H n.m.r. *δ* 8·73, br s, 1H, NH; 7·41, (7·40), d, *J* 1·9 Hz, 1H, H 3; 6·97, s, 1H, H 5; 4·94, m, 1H, OCH; 4·56, m, 2H, OCH_2O; 4·41, q, *J* 7·2 Hz, 2H, O**C**$\mathbf{H}_2$$CH_3$; 3·45, m, 1H, H 6; 3·43, (3·41), s, OCH_3; 3·21, m, 1H, H 8; 2·64, m, 1H, H 7_a; 2·00, (1·80), m, 2H, H 2′; 1·51, (1·35), m, 2H, H 3′; 1·51, d, *J* 6·9 Hz, CH_3; 1·43, t, *J* 7·2 Hz, 3H, $OCH_2C\mathbf{H}_3$; 1·37, (1·36), d, *J* 6·9 Hz, CH_3; 1·35, m, 1H, H 7_b; 0·94, t, *J* 7·3 Hz, 3 H, H 4′. ^{13}C n.m.r. *δ* 162·1,

CO_2Et; 146·0, 134·7, (134·6), 134·1, 129·0, 126·4, 124·9, 6×Ar C_{quat}; 115·4, (115·1), C 5; 108·1, (108·0), C 3; 94·0, (93·9), OCH_2O; 77·1, C 1′; 60·8, O**C**H_2CH_3; 55·5, OCH_3; 44·1, C 7; 39·5, (39·4), C 2′; 39·0, C 8; 37·1, C 6; 20·8, CH_3; 20·6, CH_3; 19·6, C 3′; 14·3, OCH_2**C**H_3; 13·9, C 4′. Mass spectrum: *m/z* 373 (M^+, 11%), 330 (10), 312 (6), 284 (26), 270 (43), 258 (16), 240 (15), 228 (16), 224 (12), 212 (18), 86 (67), 84 (100).

The minor component was the isoquinoline (17a) which was isolated as a colourless *solid* (12 mg, 5%), m.p. 119·5–120°C (Found: $M^{+\bullet}$, 311·1886. $C_{20}H_{25}NO_2$ requires $M^{+\bullet}$, 311·1885). ^{1}H n.m.r. δ 8·39, s, 1H, H 4; 7·90, s, 1H, H 9; 7·67, s, 1H, H 5; 4·50, q, *J* 7·5 Hz, 2H, OC**H**$_2$CH$_3$; 3·41, m, 1H, H 6 or H 8; 3·36, t, *J* 7·7 Hz, 2H, H 1′; 3·24, m, 1H, H 6 or H 8; 2·60, dt, *J* 12·1, 7·2 Hz, 1H, H 7$_a$; 1·91, m, 2H, H 2′; 1·44, m, 9H, 3×CH$_3$; 1·32, m, 1H, H 7$_b$; 1·09, t, *J* 7·3 Hz, 3H, H 3′. ^{13}C n.m.r. δ 166·22, **C**O_2Et; 162·07, C 1; 152·64, 151·62, Ar C_{quat}; 139·90, C 3; 135·41, C 8a; 127·84, C 4a; 122·57, C 4; 121·61, C 5; 118·33, C 9; 61·34, O**C**H_2CH_3; 45·08, C 7; 38·10, C 6 or C 8; 37·83, C 8 or C 6; 37·71, C 1′; 23·12, C 2′; 18·64, CH_3; 18·46, CH_3; 14·30, CH_3; 14·26, CH_3. Mass spectrum: *m/z* 311 (M^+, 6%), 296 (7), 283 (100), 239 (11), 222 (19), 209 (69), 194 (30).

cis-*4-(1′-Methoxymethyloxybutyl)-6,8-dimethyl-1,6,7,8-tetrahydrocyclopent[g]indole-2-carboxylic Acid (18a)*

A stirred solution of the ester (16a) (12 mg, 32 μmol) in methanol (2·5 ml) with added sodium carbonate (20 mg) and water (1·5 ml) was heated to 50°C for 12 h. After the solution was cooled, the methanol was removed and the aqueous layer extracted with diethyl ether (3×3 ml). The aqueous layer was acidified with 4 M hydrochloric acid solution and extracted with diethyl ether (3×3 ml) and dichloromethane (3 ml). The combined organic extracts were dried ($MgSO_4$) and the solvent was evaporated to give the title compound (18a) as a colourless solid (12 mg). ^{1}H n.m.r. δ 8·87, s, 1H, NH; 8·61, br s, 1H, CO_2H (exchangeable with D_2O); 7·69, (7·68), d, *J* 1·8 Hz, 1H, H 3; 7·00, s, 1H, H 5; 4·97, m, 1H, OCH; 4·58, m, 2H, OCH_2O; 3·48, m, 1H, H 6; 3·43, (3·42), s, OCH_3; 3·22, m, 1H, H 8; 2·65, dt, *J* 6·9, 11·3 Hz, 1H, H 7$_a$; 2·02, m, 1H, H 2′$_a$; 1·82, m, 1H, H 2′$_b$; 1·5–1·25, m, 3H, H 3′ and H 7$_b$; 1·52, d, *J* 6·3 Hz, CH_3; 1·36, (1·35), d, *J* 6·4 Hz, CH_3; 0·94, t, *J* 7·0 Hz, 3H, H 4′. ^{13}C n.m.r. δ 166·15, CO_2H; 146·77, 135·06, (135·02), 134·95, 134·73, (134·70), 129·07, (129·02), 125·33, (125·09), 6×Ar C_{quat}; 115·55, (115·24), C 5; 110·34, (110·23), C 3; 93·93, OCH_2O; 77·07, OCH; 55·44, OCH_3; 44·00, C 7; 39·49, (39·38), C 2′; 39·09, (39·04), C 8; 37·04, C 6; 20·75, CH_3; 20·62, (20·55), CH_3; 19·50, C 3′; 13·83, C 4′. Mass spectrum: *m/z* 345 (M^+, 20%), 302 (23), 283 (25), 242 (100).

Decarboxylation of the Indole-2-carboxylic Acid (18a)

The indole-2-carboxylic acid (18a) (18 mg, 52 μmol), copper (6 mg, 94 μmol) and quinoline (4 ml) were stirred at 220–230°C for 1 h.[14] The mixture was cooled and poured onto an acid/ice slurry (4 ml hydrochloric acid and *c.* 10 g ice). It was stirred and extracted with dichloromethane (4×5 ml). The organic layer was washed with water (5 ml) and 5% sodium bicarbonate solution until the pH of the washings was 3–4. The aqueous layer was further extracted with diethyl ether (4×15 ml) and the organic fractions were combined, dried ($MgSO_4$) and the solvent was evaporated to give a red, viscous oil (17 mg). The oil was subjected to repeated flash chromatography under nitrogen (silica; ethyl acetate/light petroleum, 1:9 to 3:7) to yield (19a) as a pink *oil* (1·5 mg, 10%) (Found: $M^{+\bullet}$, 301·2042. $C_{19}H_{27}NO_2$ requires $M^{+\bullet}$, 301·2042). ^{1}H n.m.r. δ 8·11, s, 1H, NH; 7·16, m, 1H, H 2; 6·95, s, 1H, H 5; 6·69, m, 1H, H 3; 4·98, m, 1H, OCH; 4·60, d, *J* 6·7 Hz, (4·59, d, *J* 6·6 Hz), and 4·54, d, *J* 6·7 Hz, (4·53, d, *J* 6·6 Hz), 2H, OCH_2O; 3·46, m, 1H, H 6; 3·44, (3·43), s, OCH_3; 3·26, m, 1H, H 8; 2·61, dt, *J* 12·4, 7·5 Hz, 1H, H 7$_a$; 2·00, m, 1H, H 2′$_a$; 1·82, m, 1H, H 2′$_b$; 1·50–1·25, br m, 3H, H 3′ and H 7$_b$; 1·51, d, *J* 7·0 Hz, CH_3; 1·36, d, *J* 7·0 Hz, (1·35, d, *J* 6·8 Hz), CH_3; 0·94, t, *J* 7·4 Hz, 3H, H 4′. ^{13}C n.m.r. δ 142·62, 132·69, 132·48, 128·39, 125·13, 5×Ar C_{quat}; 122·90, 113·86, (113·57), 101·74, 3×Ar CH; 93·98, OCH_2O; 76·89, OCH; 55·43, OCH_3; 44·50, C 7; 39·26, C 2′; 38·70, C 8; 37·13, C 6; 20·84, CH_3; 20·55, CH_3; 19·56, C 3′; 13·87, C 4′. Mass spectrum: *m/z* 301 (M^+, 6%), 258 (9), 226 (8), 212 (8), 198 (100).

cis-*4-(1′-Methoxymethyloxybutyl)-6,8-dimethyl-1,6,7,8-tetrahydrocyclopent[g]indole-2-methanol (20a)*

To a solution of the ethyl indole-2-carboxylate (16a) (11 mg, 29 μmol) in toluene (2 ml) at −74°C under argon was added 1·5 M diisobutylaluminium hydride in toluene (22 μl, 32 μmol). The mixture was warmed to −41°C. After being stirred for 1 h at this temperature the reaction mixture was quenched with saturated ammonium chloride solution. The mixture was warmed to room temperature and extracted with diethyl ether (3×2 ml). The organic layer was washed with water (2 ml), dried ($MgSO_4$) and the solvent evaporated to yield a yellow oil (9 mg) that was identified as mainly starting material by ^{1}H n.m.r. spectroscopy. Trace amounts of another compound were present. The oil was then taken up in toluene (2 ml) and 1·5 M diisobutylaluminium hydride in toluene (48 μl, 72 μmol) was added dropwise. The reaction mixture was stirred at room temperature and monitored by t.l.c. The reaction was complete after 75 min. It was then cooled (ice bath) and saturated ammonium chloride solution (1 ml) was added. It was extracted with diethyl ether (3×3 ml) and the organic layer was washed with water (3 ml), dried ($MgSO_4$) and the solvent evaporated. The material was chromatographed (silica; ethyl acetate/light petroleum, 1:9) to yield the *title compound* (20a) as a yellow oil (7 mg, 88%) (Found: $M^{+\bullet}$, 331·2146. $C_{20}H_{29}NO_3$ requires $M^{+\bullet}$, 331·2147). ν_{max} (neat) 3460m (NH), 3500–3200br cm^{-1} (OH). ^{1}H n.m.r. δ 8·41, br s, 1H, NH; 6·91, s, 1H, H 5; 6·56, br s, 1H, H 3; 4·92, m, 1H, OCH; 4·81, s, 2H, C**H**$_2$–OH; 4·57, d, *J* 6·5 Hz, (4·56, d, *J* 6·6 Hz), and 4·52, d, *J* 6·7 Hz, (4·50, d, *J* 6·7 Hz), 2H, OCH_2O; 3·42, (3·41), s, OCH_3; 3·42, m, 1H, H 6; 3·19, m, 1H, H 8; 2·60, dt, *J* 12·3, 7·5 Hz, 1H, H 7$_a$; 2·01, m, 1H, H 2′$_a$; 1·82, m, 1H, H 2′$_b$; 1·5–1·25, br m, 4H, H 3′, H 7$_b$ and OH; 1·50, d, *J* 6·8 Hz, CH_3; 1·35, (1·34), d, *J* 6·9 Hz, CH_3; 0·93, t, *J* 7·4 Hz, (0·88, t, *J* 7·5 Hz), 3H, H 4′. ^{13}C n.m.r. δ 142·89, 136·45, 133·37, 132·30, 128·45, 125·45, 6×Ar C_{quat}; 114·09, (113·79), 99·95, (99·86), 2×Ar CH; 93·87, OCH_2O; 77·14, OCH; 58·73, CH_2OH; 55·40, OCH_3; 44·44, C 7; 39·17, C 2′; 38·71, C 8; 37·09, C 6; 20·90, (20·81), CH_3; 20·55, (20·48), CH_3; 19·57, C 3′; 13·87, C 4′. Mass spectrum: *m/z* 331 (M^+, 68%), 270 (36), 256 (57), 228 (100), 226 (100), 198 (74).

cis-*4-(1′-Methoxymethyloxybutyl)-6,8-dimethyl-1,6,7,8-tetrahydrocyclopent[g]indole-2-carbaldehyde (21a)*

Manganese dioxide (0·25 g, 2·63 mmol) was added to a stirred solution of the indole-2-methanol (20a) (109 mg, 329 μmol) and dichloromethane (50 ml) and the mixture heated to reflux temperature. After 30 min, another portion of manganese dioxide (0·25 g, 2·63 mmol) was added. After 6 h, the reaction mixture was filtered through a pad of Celite and the Celite was washed with hot toluene (250 ml). The toluene was removed and the residue was chromatographed (Florisil; dichloromethane) to yield (21a) as a yellow *solid* (71 mg, 65%) (Found: $M^{+\bullet}$, 329·1990. $C_{20}H_{27}NO_3$ requires $M^{+\bullet}$, 329·1991). ν_{max} (neat) 1660s cm^{-1} (C=O). ^{1}H n.m.r. δ 9·80, s, 1H, CHO; 8·82, br s, 1H, NH; 7·49, (7·48), d, *J* 1·9 Hz, 1H, H 3; 6·98, s, 1H, H 5; 4·92, m, 1H, OCH; 4·57, 4·56, m, 2H, OCH_2O; 3·44, m, 1H, H 6; 3·42, (3·40),

s, OCH_3; 3·21, m, 1H, H 8; 2·65, dt, *J* 12·5, 7·7 Hz, 1H, H 7_a; 2·02, m, 1H, H $2'_a$; 1·80, m, 1H, H $2'_b$; 1·50–1·20, br m, 3H, H 3′ and H 7_b; 1·50, d, *J* 6·9 Hz, CH_3; 1·36, d, *J* 6·9 Hz, (1·35, d, *J* 6·8 Hz), CH_3; 0·95, t, *J* 7·2 Hz, 3H, H 4′. ^{13}C n.m.r. *δ* 181·70, CHO; 148·30, 135·74, (135·62), 135·44, 135·26, 129·41, 124·93, 6×Ar C_{quat}; 116·00, (115·70), 114·99, (114·89), 2×Ar CH; 93·97, OCH_2O; 77·56, OCH; 55·51, OCH_3; 43·93, C 7; 39·50, (39·40), C 2′; 39·17, C 8; 37·01, C 6; 20·68, CH_3; 20·53, (20·48), CH_3; 19·52, C 3′; 13·85, C 4′. Mass spectrum: *m/z* 329 (M^+, 12%), 286 (10), 276 (19), 244 (22), 226 (34), 201 (30), 184 (89), 130 (100).

cis-*4-(1′-Methoxymethyloxybutyl)-6,8-dimethyl-1,6,7,8-tetrahydrocyclopent[g]indole (19a)*

A mixture of bis(triphenylphosphine)(carbonyl)rhodium(I) chloride (27 mg, 40 μmol) and mesitylene (40 ml) was heated to 85°C under oxygen-free conditions. This temperature was maintained until the rhodium complex had dissolved (20 min). A mixture of 1,3-bis(diphenylphosphino)propane (33 mg, 80 μmol) and mesitylene (5 ml), also under oxygen-free conditions, was added to the above rhodium solution. The mixture was stirred at 85°C for a further 20 min. A solution of oxygen-free indole-2-carbaldehyde (21a) (66 mg, 200 μmol) and mesitylene (2 ml) was added to the rhodium complex solution and it was immediately plunged into a Woods metal bath at 200°C. The bath temperature was maintained between 180 and 200°C. After 30 min t.l.c. (silica; ethyl acetate/light petroleum, 1 : 4) showed that the starting material had been consumed. The reaction mixture was cooled (ice bath) and the mesitylene was removed by distillation under reduced pressure. The residue was dissolved in dichloromethane (2 ml) and chromatographed (Florisil; dichloromethane, and then silica; ethyl acetate/light petroleum, 1 : 4) to yield the title compound (19a) as a yellow oil (39 mg, 65%). Its spectroscopic data were identical to those of the compound obtained by decarboxylation of the indole-2-carboxylic acid (18a). Attempted concomitant deprotection and dehydration of (19a) with *p*-toluenesulfonic acid in benzene according to the method of Natsume *et al.*[9,10] gave an intractable product.

N-*Acetylation of (19a)*

To a cooled suspension of potassium hydride (12 mg, 299 μmol) in dry tetrahydrofuran (1 ml) was added the indole (19a) (18 mg, 60 μmol) in tetrahydrofuran (1 ml) and the mixture heated to reflux temperature for 15 min. After the solution was cooled, acetic anhydride (24 mg, 238 μmol) was added and the reaction mixture stirred for a further 1 h. Water (1 ml) was then added and the solution extracted with dichloromethane (3×3 ml). The combined organic fractions were washed with saturated sodium chloride (3 ml) and dried ($MgSO_4$). The solvent was removed and the residue chromatographed (silica; ethyl acetate/light petroleum, 1 : 9) to give (22a) as a yellow *oil* (12 mg, 60%) (Found: $M^{+\bullet}$, 343·2146. $C_{21}H_{29}NO_3$ requires $M^{+\bullet}$, 343·2147). ν_{max} (neat) 1720s cm^{-1} (C=O). ^{1}H n.m.r. *δ* 7·35, (7·34), d, *J* 3·9 Hz, 1H, H 2; 7·10, s, 1H, H 5; 6·85, (6·84), d, *J* 3·9 Hz, 1H, H 3; 4·93, m, 1H, OCH; 4·52, m, 2H, OCH_2O; 4·20, (3·95), m, 1H, H 6; 3·41, s, OCH_3; 3·30, m, 1H, H 8; 2·70, m, 1H, H 7_a; 2·65, s, $COCH_3$; 2·00, m, 1H, H $2'_a$; 1·78, m, 1H, H $2'_b$; 1·6–1·3, br m, 3H, H 3′ and H 7_b; 1·35, (1·33), d, *J* 6·7 Hz, CH_3; 1·10, (1·08), d, *J* 6·8 Hz, CH_3; 0·94, t, *J* 7·1 Hz, 3H, H 4′. ^{13}C n.m.r. *δ* 167·5, NCO; 146·78, (146·28), 134·95, (134·57), 132·56, 128·53, 4×Ar C_{quat}; 125·15, 118·16, (117·83), 2×Ar CH; 110·73, Ar C_{quat}; 107·98, Ar CH; 93·9, OCH_2O; 76·06, OCH; 55·4, OCH_3; 42·76, (42·71), C 7; 39·53, (39·35), C 2′; 38·89, 37·21, C 8 and C 6; 24·52, (24·00), 23·17, (22·09), 21·36, (20·30), 3×CH_3; 19·32, C 3′; 13·81, C 4′. Mass spectrum: *m/z* 343 (M^+, 45%), 300 (25), 282 (19), 258 (40), 240 (64), 266 (57), 198 (100).

cis-*1-Acetyl-4-(1′-hydroxybutyl)-6,8-dimethyl-1,6,7,8-tetrahydrocyclopent[g]indole (23a)*

To a stirred solution of acetamide (22a) (8 mg, 23 μmol) in dry dichloromethane (1 ml), under argon at −78°C, was added an aliquot (200 μl) of a solution of dimethylboron bromide and dichloromethane (43 mg/ml). The solution turned green. After the solution was stirred for 15 min, triethylamine (30 μl) was added and then water (100 μl) was added dropwise. The reaction mixture was slowly warmed to room temperature and extracted with dichloromethane (3×3 ml). The combined organic fractions were washed with water (1 ml), saturated sodium chloride solution (1 ml) and dried ($MgSO_4$). The solvent was evaporated to give a colourless solid (15 mg). It was chromatographed (silica; ethyl acetate/light petroleum, 1 : 9) under nitrogen to give (23a) as a colourless solid (4·5 mg, 65%). ^{1}H n.m.r. *δ* 7·42, (7·41), d, *J* 2·1 Hz, 1H, H 5; 7·04, (7·03), d, *J* 3·7 Hz, 1H, H 2; 6·89, (6·88), d, *J* 3·7 Hz, 1H, H 3; 4·98, (4·93), m, 1H, OCH; 4·28, (4·18), m, 1H, H 6; 3·38, m, 1H, H 8; 2·63, m, 1H, H 7_a; 2·61, (2·58), s, $COCH_3$; 2·03, m, 1H, H $2'_a$; 1·82, m, 1H, H $2'_b$; 1·5–1·3, br m, 4H, H 3′, H 7_b and OH; 1·23, d, *J* 7·2 Hz, CH_3; 1·21, d, *J* 7·2 Hz, CH_3; 0·89, *J* 7·0 Hz, 3H, H 4′. Mass spectrum: *m/z* 299 (M^+, 4%), 281 (87), 266 (51), 239 (51), 224 (100).

Attempted elimination of water from (23a) by using *p*-toluenesulfonic acid in benzene failed to give any identifiable products.

3-Methylindan-1-one

A solution of crotonic acid (17·28 g, 201 mmol) in dry benzene (50 ml) was added over 20 min to a stirred suspension of aluminium trichloride (46·1 g, 345 mmol) in dry benzene (70 ml) that was cooled in an ice bath. The mixture was then heated to reflux for 17 h. The condensed solvent was passed through activated molecular sieves (4 Å) before being returned to the reaction flask. The mixture was poured onto ice (300 g) and stirred. It was extracted with dichloromethane (3×150 ml). The combined organic fractions were washed with water (200 ml), dried ($MgSO_4$) and the solvent was removed. The concentrate was distilled (100–105°C/0·8 mmHg) to give 3-methylindan-1-one as a colourless oil (22·7 g, 77%). ν_{max} (neat) 1710s cm^{-1} (C=O). ^{1}H n.m.r. *δ* 7·73, d, *J* 7·6 Hz, 1H, ArH; 7·61, t, *J* 7·6 Hz, 1H, ArH; 7·51, d, *J* 7·6 Hz, 1H, ArH; 7·39, t, *J* 7·6 Hz, 1H, ArH; 3·44, m, 1H, H 3; 2·93, dd, *J* 19·0, 7·4 Hz, 1H, H 2_a; 2·29, dd, *J* 19·0, 3·3 Hz, 1H, H 2_b; 1·42, d, *J* 7·1 Hz, CH_3. ^{13}C n.m.r. *δ* 206·6, C=O; 160·1, 136·4, 2×Ar C_{quat}; 134·8, 127·4, 125·3, 123·3, 4×Ar CH; 45·0, C 2; 32·4, C 3; 20·9, CH_3. Mass spectrum: *m/z* 146 (M^+, 65%), 131 (100), 117 (29), 103 (46), 91 (12), 77 (32).

cis-*1,3-Dimethylindan-1-ol (24)*

Iodomethane (17·31 ml, 278 mmol) in dry diethyl ether (30 ml) was added dropwise to a stirred suspension of magnesium turnings (3·38 g, 139 mmol) in dry diethyl ether (100 ml) under argon at a rate sufficient to maintain gentle reflux. After the addition was complete, the mixture was heated to reflux for a further 1 h. It was cooled and the solution was transferred to another flask, also under argon. A solution of 3-methylindan-1-one (10·16 g, 69·5 mmol) in dry diethyl ether (40 ml) was added dropwise to the stirred solution of Grignard reagent. The mixture was heated to reflux for 18 h. The reaction mixture was cooled and slowly poured onto a mixture of iced water (300 g) and hydrochloric acid (5 ml). The mixture was stirred vigorously and the aqueous layer was extracted with diethyl ether (6×100 ml). The organic fraction was washed with water (3×100 ml), saturated ammonium chloride solution (50 ml) and water (3×50 ml). The organic fraction was dried ($MgSO_4$), the solvent was removed and the residue was distilled to give the title compound (24) as a yellow oil (9·98 g, 89%). The spectroscopic data corresponded to those previously obtained for

cis-1,3-dimethylindan-1-ol prepared from the radical cyclization of 2-(2-bromophenyl)pent-4-en-2-ol.[3]

X-Ray Structure Determination of (24)[3]

A colourless block-shaped crystal of $C_{11}H_{14}O$, M_r 162·23, having dimensions of 0·23 by 0·21 by 0·13 mm was mounted on a quartz fibre. All measurements were made on a Rigaku AFC6R diffractometer with graphite monochromatized Cu Kα radiation and a 12 kW rotating anode generator. A liquid-nitrogen-refrigeration fixed tube low-temperature system was used to cool the crystal to avoid sublimation. Data were collected at a temperature of -73 ± 1°C. Cell constants and an orientation matrix for data collection, obtained from a least-squares refinement by using the setting angles of 25 carefully centred reflections in the range $97{\cdot}79 < 2\theta < 109{\cdot}12°$, corresponded to a primitive triclinic cell, space group $P\bar{1}$ (No. 2), with dimensions *a* 11·674(2), *b* 12·726(2), *c* 14·272(4) Å, α 86·67(2), β 66·37(1), γ 83·04(1)°, *V* 1928·2(6) Å^3, *Z* 8, D_{calc} 1·12 g cm^{-3}, μ 5·4 cm^{-1}, *F*(000) 704.

The structure was solved by direct methods (SHELXS86)[25] and expanded by using Fourier techniques (DIRDIF92).[26] Non-hydrogen atoms were refined with anisotropic displacement factors. The coordinates of the alcohol hydrogen atoms were refined, while the remaining hydrogen atoms were held fixed at geometrically determined positions. Least squares refinement was performed by using the minimizing function $\Sigma\, w(|F_o| - |F_c|)^2$, where $w = [\sigma^2(F_o) + 0{\cdot}000006F_o{}^2]^{-1}$. Maximum and minimum peaks on the final difference Fourier map corresponded to 0·89 and $-0{\cdot}34$ e/Å^3. Neutral atom scattering factors were taken from Cromer and Waber.[27] All calculations were carried out with the teXsan Crystal Structure Analysis Package (Molecular Structure Corporation).

The final *R* factor was 0·067 (R_w 0·064) for 4384 reflections with $I > 3\sigma(I)$. The crystallographic asymmetric unit consists of four chemically equivalent molecules of $C_{11}H_{14}O$, with very similar conformations, arranged in a hydrogen-bonded tetramer with an approximate $\bar{4}$ axis parallel to $\mathbf{a}-2\mathbf{c}$. A *C*-centred pseudo monoclinic cell can be found that has this direction as the unique *b*-axis. We have chosen the transformation: $\mathbf{a}' = \mathbf{a}$, $\mathbf{b}' = \mathbf{a}-2\mathbf{c}$, $\mathbf{c}' = -\mathbf{a}+\mathbf{b}$ (a' 11·674, b' 26·152, c' 16·194 Å, α' 90·79, β' 128·73, γ 89·49°, *Z* 16), making $\mathbf{a}'^* = \mathbf{a}^*+\mathbf{b}^*+\mathbf{c}^*/2$, $\mathbf{b}'^* = \mathbf{c}^*/2$, $\mathbf{c}'^* = \mathbf{b}^*$, and $h' = h$, $k' = h-2l$, $l' = -h+k$, $x' = x+y+z/2$, $y' = -z/2$, $z' = y$.

The centre of mass of the tetramer is at approximately $x, y, z = 1/2, 3/8, 1/4$ and this corresponds to $x', y', z' = 1, -1/8, 3/8$. Consequently, in the *C*-centred cell, there is an apparent local symmetry operation $2-x', y', 3/4-z'$ ($1{\cdot}25-x-z, 0{\cdot}75-y, z$ for our reference cell) as well as the true symmetry operations $x', y', z'; -x', -y', -z; 1/2+x', 1/2+y', z'; 1/2-x', 1/2-y', -z'$.

Closure under multiplication produces space group $C2/c$ for a unit cell $\mathbf{a}'$, $\mathbf{b}'$, $\mathbf{c}'/2$ and may be thought of as the true structure plus a pseudo-translation of $\mathbf{c}'/2$. A glide plane cannot be a symmetry element of the true structure as using the operator twice produces a $\mathbf{c}'/2$ translation which is not allowed. α' and γ' are significantly different from 90° and the structure is definitely triclinic, though half the reflection data have approximate monoclinic diffraction symmetry. The data were separated according to whether l' is even or odd, and merged assuming monoclinic diffraction symmetry. R_{merge} on *F* for l' even data was 36% while $R_{merge}(F)$ for l' odd was 53%. This shows the partial diffraction enhancement of the l' even data, but also shows that the local twofold rotation does not hold all that well. The structure can be described as an occupancy and displacive modulation of a 1 : 1 disordered $C2/c$ parent structure for a cell $\mathbf{a}'$, $\mathbf{b}'$, $\mathbf{c}'/2$ with associated monoclinic diffraction symmetry, viz. $l(h', k', l') = I(-h', k', -l')$ if l' is even but $I(h', k', l') = 0$ if l' is odd. Ordering, to select between sites $\mathbf{c}/2$ apart, creates extra reflections that do not have monoclinic diffraction symmetry, and displacive modulation lowers the symmetry of the parent structure as the local twofold axis need no longer hold exactly, nor need it be exactly located or oriented. The fit of the extra (l' odd) reflections confirms that the ordering is appropriate and unconstrained refinement behaves well. The partial diffraction enhancement may be reexpressed in terms of the primitive triclinic cell as $I(h,k,l) \approx I(-h,-k,l-h)$ if $h-k$ is even with the pseudo *c*-glide absences associated with a $C2/c$ parent symmetry corresponding to reflections $I(h,k,l)$, $h = 2l, h-k = 4n+2$. These reflections are systematically weak but are clearly observed.

Full details, including tables of atomic coordinates for hydrogen and non-hydrogen atoms, are in an Accessory Publication (available until 31 December 2003 from the Australian Journal of Chemistry, P.O. Box 1139, Collingwood, Vic. 3066).

Preparation of Raney Nickel Reagent

Raney nickel was prepared by a modification of the method of Pavlic and Adkins.[28] To a stirred solution of sodium hydroxide (32 g) and water (125 ml) at 50°C was added portions of nickel aluminium alloy (25 g, over *c.* 1 h) so as to maintain the temperature at 50±4°C. After the addition was complete, this temperature range was maintained for 1 h. The mixture was cooled, and washed with degassed water thoroughly until the pH of the washings ranged between 7·5 and 8·5. The Raney nickel suspension was washed with dried, distilled absolute ethanol (3×100 ml) and stored under ethanol.

Hydrogenolysis of cis*-1,3-Dimethylindan-1-ol (24)*

To a solution of *cis*-1,3-dimethylindan-1-ol (24) (2·50 g, 15 mmol) in distilled, degassed ethanol (100 ml) was added a suspension of freshly prepared Raney nickel (*c.* 25 g) and the reaction mixture heated to reflux. After 2 h, the spent Raney nickel was collected on a Celite pad. The solvent was removed by distillation to give a clear oil (2·04 g), identified as *trans*-1,3-dimethylindan (6b) by comparison of its ^{1}H n.m.r. spectrum with literature data.[29]

*1-(*trans*-1′,3′-Dimethylindan-5′-yl)butan-1-one (7b)*

The procedure followed that used for the synthesis of the *cis*-isomer (7a). The reagents and amounts used were as follows: *trans*-1,3-dimethylindan (6b) (10·3 g, 70 mmol), butyryl chloride (11 ml, 106 mmol) and aluminium trichloride (14·09 g, 106 mmol). The resulting oil was chromatographed on silica (ethyl acetate/light petroleum, 1 : 9) to give the *title compound* (7b) as a colourless oil (10·6 g, 70%) (Found: $M^{+\bullet}$, 216·1514. $C_{15}H_{20}O$ requires $M^{+\bullet}$, 216·1514). ^{1}H n.m.r. δ 7·82, d, *J* 8·0 Hz, 1H, H 6′; 7·78, s, 1H, H 4′; 7·24, d, *J* 8·0 Hz, 1H H 7′; 3·31, m, 2H, H 1′ and H 3′; 2·95, (2·94), t, *J* 7·3 Hz, 2H, H 2; 1·94, t, *J* 6·8 Hz, 2H, H 2′; 1·76, sextet, *J* 7·3 Hz, 2H, H 3; 1·27, d, *J* 6·9 Hz, CH_3; 1·25, d, *J* 6·9 Hz, CH_3; 1·01, t, *J* 7·4 Hz, 3H, H 4. ^{13}C n.m.r. δ 200·33, C=O; 153·90, 148·80, 135·84, 3×Ar C_{quat}; 126·88, 123·24, 122·99, 3×Ar CH; 42·76, C 2′; 40·48, C 2; 37·61, 37·28, C 1′ and C 3′; 20·41, 20·34, 2×CH_3; 17·86, C 3′; 13·88, C 4′. Mass spectrum: *m/z* 216 (M^+, 30%), 201 (3), 188 (7), 173 (100), 145 (14).

*1-(*trans*-1′,3′-Dimethylindan-5′-yl)butan-1-ol (8b)*

This was prepared according to the method used for the synthesis of the *cis*-isomer (8a). The reagents and amounts used were as follows: butyroylindan (7b) (10·6 g, 49 mmol) and sodium borohydride (2·78 g, 74 mmol). Compound (8b) was isolated as a colourless *oil* (10·13 g, 95%), b.p. 130°C/0·02 mmHg (Found: $M^{+\bullet}$, 218·1670. $C_{15}H_{22}O$ requires $M^{+\bullet}$, 218·1671). ^{1}H n.m.r. δ 7·16, d, *J* 6·2 Hz, 2H, H 6′ and H 7′; 7·15, s, 1H, H 4′; 4·66, m, 1H, OCH; 3·26, m, 2H, H 1′ and H 3′; 1·91, t, *J* 6·7 Hz, 2H, H 2′; 1·77, m, 2H, H 2_a and OH; 1·69, m, 1H, H 2_b; 1·50–1·30, m, 2H, H 3; 1·25, (1·24), d, *J* 7·0 Hz, CH_3; 1·23, d, *J* 7·0 Hz, CH_3; 0·94, t, *J* 7·3 Hz, 3H, H 4. ^{13}C n.m.r. δ 148·57, 147·7, 143·18, 3×Ar C_{quat}; 124·09, 123·16, 120·80,

(120·75), 3×Ar CH; 74·55, OCH; 43·02, C 2′; 41·16, (41·11), C 2; 37·43, 37·22, C 1′ and C 3′; 20·45, 2×CH_3; 19·11, C 3; 13·88, C 4. Mass spectrum: *m/z* 218 (M^+, 20%), 175 (100), 145 (11), 131 (16), 105 (54).

*1-(*trans*-5′-Bromo-1′,3′-dimethylindan-6′-yl)butan-1-ol (12b)*

This was prepared according to the procedure used for the *cis*-isomer (12a). The reagents and amounts used were as follows: hydroxybutylindan (8b) (2·0 g, 9·2 mmol), 1·7 M t-butyllithium in pentane (27 ml, 46 mmol) and carbon tetrabromide (14·5 g, 44 mmol). The product was chromatographed on silica (ethyl acetate/light petroleum, 1 : 9) to give recovered starting material (8b) (0·74 g, 37%) and (12b) as a yellow *oil* (1·44 g, 52%) (Found: $M^{+\bullet}$, 296·0776. $C_{15}H_{21}{}^{79}BrO$ requires $M^{+\bullet}$, 296·0776). ^{1}H n.m.r. δ 7·36, s, 1H, ArH; 7·30, s, 1H, ArH; 5·08, m, 1H, OCH; 3·24, m, 2H, H 1′ and H 3′; 1·91, t, *J* 6·8 Hz, 2H, H 2′; 1·80–1·30, br m, 5H, H 2, H 3 and OH; 1·24, (1·23), d, *J* 7·4 Hz, CH_3; 1·21, d, *J* 7·2 Hz, CH_3; 0·96, t, *J* 7·3 Hz, 3H, H 4. ^{13}C n.m.r. δ 149·51, (149·28), 148·26, (148·19), 141·456, (141·41), 3×Ar C_{quat}; 127·34, 121·92, 2×Ar CH; 119·63, Ar CBr; 72·62, (72·58), OCH; 42·99, C 2′; 39·90, (39·85), C 2; 37·75, (37·65), 37·25, (37·13), C 1′ and C 3′; 20·31, (20·22), CH_3; 20·18, CH_3; 19·08, C 3; 13·82, C 4. Mass spectrum: *m/z* 298 (M^+, 14%), 296 (M^+, 16), 255 (97), 253 (100), 185 (28), 183 (27).

trans-*5-Bromo-6-(1′-methoxymethyloxybutyl)-1,3-dimethylindan (13b)*

To a stirred solution of indanol (12b) (0·80 g, 2·7 mmol) and dichloromethane (75 ml) at 0°C were added 4-dimethylaminopyridine (33 mg, 0·3 mmol), ethyldiisopropylamine (2·4 ml, 13·5 mmol) and methoxymethyl chloride (1 ml, 13·5 mmol). The reaction mixture was warmed to room temperature and stirred for 17 h. The usual workup and purification procedure (as for the corresponding *cis*-compound (13a)) gave (13b) as a yellow *oil* (0·88 g, 95%) (Found: $M^{+\bullet}$, 340·1037. $C_{17}H_{25}{}^{79}BrO_2$ requires $M^{+\bullet}$, 340·1038). ^{1}H n.m.r. δ 7·29, s, 1H, ArH; 7·26, (7·25), s, 1H, ArH; 5·03, m, 1H, OCH; 4·53, m, 2H, OCH_2O; 3·41, (3·39), s, OCH_3; 3·23, m, 2H, H 1 and H 3; 1·90, t, *J* 6·8 Hz, 2H, H 2; 1·75–1·20, br m, 4H, H 2′ and H 3′; 1·23, (1·21), d, *J* 7·0 Hz, CH_3; 1·20, (1·19), d, *J* 7·0 Hz, CH_3; 0·96, t, *J* 7·4 Hz, 3H, H 4′. ^{13}C n.m.r. δ 148·18, 139·51, 2×Ar C_{quat}; 127·36, C 4; 122·46, (122·37), C 7; 120·45, Ar CBr; 111·33, C_{quat}; 94·76, OCH_2O; 76·09, OCH; 55·72, OCH_3; 42·98, (42·90), C 2; 39·36, (39·26), C 2′; 37·70, (37·65), 37·24, (37·21), C 1 and C 3; 20·32, CH_3; 20·27, (20·26), CH_3; 19·06, C 3′; 13·79, C 4′. Mass spectrum: *m/z* 342 (M^+, 11%), 340 (M^+, 12), 299 (99), 297 (100), 269 (20), 267 (22), 253 (89), 251 (84), 239 (73), 237 (75).

trans-*6-(1′-Methoxymethyloxybutyl)-1,3-dimethylindan-5-carbaldehyde (14b)*

To a stirred solution of the aryl bromide (13b) (0·60 g, 1·8 mmol) and heptane (50 ml) under argon at −78°C was added 1·6 M butyllithium in hexane (2·2 ml, 3·5 mmol) dropwise. It was stirred for a further 10 min while slowly warming to 0°C. The reaction mixture turned dark yellow and a precipitate formed. The mixture was stirred for a further 15 min and then cooled to −78°C. Dimethylformamide (2 ml) was added dropwise and the reaction mixture slowly warmed to room temperature. The same workup and purification procedures were employed as those used for the corresponding *cis*-compound (14a), to provide the *title compound* (14b) as a colourless oil (0·33 g, 65%) (Found: $[M-1]^{+\bullet}$, 289·1804. $C_{18}H_{25}O_3$ requires *m/z*, 289·1804). ν_{max} (neat) 1695s (CHO), 1610m cm^{-1} (Ar–H). ^{1}H n.m.r. δ 10·30, s, 1H, CHO; 7·65, s, 1H, H 4; 7·41, s, 1H, H 7; 5·44, m, 1H, OCH; 4·58, d, *J* 6·7 Hz, and 4·53, d, *J* 6·6 Hz, 2H, OCH_2O; 3·38, (3·36), s, OCH_3; 3·30, m, 2H, H 1 and H 3; 1·95, t, *J* 6·8 Hz, 2H, H 2; 1·80–1·20, br m, 4H, H 2′ and H 3′; 1·27, d, *J* 6·6 Hz, (1·26, d, *J* 6·4 Hz), CH_3; 1·25, d, *J* 7·0 Hz, CH_3; 0·95, t, *J* 7·3 Hz, 3H, H 4′. ^{13}C n.m.r. δ 192·23, (192·20), CHO; 155·07, 147·66, 144·43, 132·33, 4×Ar C_{quat}; 126·66, (126·63), 122·16, 2×Ar CH; 94·71, (94·56), OCH_2O; 74·43, (74·14), OCH; 55·48, OCH_3; 42·56, C 2; 40·88, C 2′; 37·86, (37·78), 36·91, C 1 and C 3; 20·14, CH_3; 19·95, (19·91), CH_3; 19·25, C 3′; 13·67, C 4′. Mass spectrum: *m/z* 289 ($[M-1]^+$, 5%), 259 (7), 245 (100), 229 (34), 217 (25), 203 (58), 201 (56), 199 (57). Chemical ionization mass spectrum: *m/z* 291 (MH^+, 9%), 259 (27), 245 (57), 229 (100).

Ethyl trans-*4-(1′-Methoxymethyloxybutyl)-6,8-dimethyl-1,6,7,8-tetrahydrocyclopent[g]indole-2-carboxylate (16b) via the Azidocinnamate (15b)*

The azidocinnamate (15b) was prepared according to the method used for the corresponding *cis*-azidocinnamate (15a). The reagents and amounts used were as follows: dimethylindancarbaldehyde (14b) (215 mg, 740 μmol), ethyl azidoacetate (1·75 g, 13·6 mmol) and sodium (218 mg, 9·5 mmol) in ethanol (10 ml). After the usual workup and purification procedures, (15b) was obtained as an unstable yellow oil (160 mg, 54%). ν_{max} (neat) 2110s (N_3), 1715s cm^{-1} (C=O). ^{1}H n.m.r. δ 7·67, (7·66), s, 1H, H 4; 7·28, m, 2H; 4·83, m, 1H, OCH; 4·58, m, and 4·54, m, 2H, OCH_2O; 4·38, q, *J* 7·1 Hz, 2H, 2H, OC**H**$_2$$CH_3$; 3·41, (3·38), s, OCH_3; 3·27, m, 2H, H 1 and H 3; 1·92, t, *J* 6·8 Hz, 2H, H 2; 1·80–1·20, br m, 4H, H 2′ and H 3′; 1·40, t, *J* 7·1 Hz, 3H, OCH_2C**H**$_3$; 1·27, d, *J* 6·8 Hz, CH_3; 1·23, d, *J* 6·2 Hz, (1·19, d, *J* 6·6 Hz), CH_3; 0·94, t, *J* 7·2 Hz, (0·92, t, *J* 7·3 Hz), 3H, H 4′. ^{13}C n.m.r. δ 163·37, **C**O_2Et; 150·00, (149·97), 147·23, (147·19), 139·98, 129·26, 125·79, 5×C_{quat}; 124·46, 123·56, 121·61, 3×CH; 94·20, (94·15), OCH_2O; 74·81, (74·26), OCH; 62·00, O**C**H_2CH_3; 55·48, OCH_3; 42·83, C 2; 39·89, C 2′; 37·51, 37·30, (37·28), C 1 and C 3; 20·41, (20·37), CH_3; 20·17, (20·12), CH_3; 19·17, (19·10), C3′; 14·03, OCH_2**C**H_3; 13·70, C 4′.

A solution of the azidocinnamate (15b) (42 mg, 105 μmol) in toluene (20 ml) was plunged into a reaction bath maintained at 135°C and heated for 2 h. The mixture was cooled and the toluene removed by distillation. The residue was chromatographed (silica; ethyl acetate/light petroleum, 1 : 9) to yield the *title compound* (16b) as a yellow oil (31 mg, 79%) (Found: $M^{+\bullet}$, 373·2253. $C_{22}H_{31}NO_4$ requires $M^{+\bullet}$, 373·2253). ν_{max} (neat) 3455m (NH), 1700s cm^{-1} (C=O). ^{1}H n.m.r. δ 8·73, br s, 1H, NH; 7·42, (7·41), d, *J* 1·8 Hz, 1H, H 3; 6·97, s, 1H, H 5; 4·93, m, 1H, OCH; 4·56, m, 2H, OCH_2O; 4·40, q, *J* 7·1 Hz, 2H, OC**H**$_2$$CH_3$; 3·53, m, 1H, H 6; 3·43, (3·42), s, OCH_3; 3·41, m, 1H, H 8; 2·06, 3H, H 7 and H 2′$_a$; 1·80, m, 1H, H 2′$_b$; 1·6–1·3, br m, 2H, H 3′; 1·43, t, *J* 7·1 Hz, 3H, OCH_2C**H**$_3$; 1·33, d, *J* 7·1 Hz, (1·30, d, *J* 7·0 Hz), CH_3; 1·29, d, *J* 6·9 Hz, CH_3; 0·95, t, *J* 7·3 Hz, 3H, H 4′. ^{13}C n.m.r. δ 162·18, **C**O_2Et; 145·44, 134·75, (134·67), 133·84, 129·45, 126·51, 124·70, 6×Ar C_{quat}; 115·36, (115·21), 108·26, (108·23), 2×Ar CH; 93·93, OCH_2O; 77·07, (77·01), OCH; 60·85, O**C**H_2CH_3; 55·46, OCH_3; 43·35, C 7; 39·41, (39·36), C 2′; 37·93, (37·88), 35·91, C 6 and C 8; 20·30, CH_3; 19·71, (19·67), CH_3; 19·56, C 3′; 14·34, OCH_2**C**H_3; 13·85, C 4′. Mass spectrum: *m/z* 373 (M^+, 40%), 330 (49), 312 (27), 284 (61), 270 (100), 240 (24), 224 (17), 212 (22).

trans-*4-(1′-Methoxymethyloxybutyl)-6,8-dimethyl-1,6,7,8-tetrahydrocyclopent[g]indole-2-methanol (20b)*

This was synthesized according to the procedure used to prepare the isomeric *cis*-compound (20a). The reagents and amounts used were as follows: the ethyl indole-2-carboxylate (16b) (160 mg, 428 μmol) and 1·5 M diisobutylaluminium hydride in toluene (860 μl, 1·29 mmol). The usual workup and

purification steps were employed to yield the *title compound* (20b) as a yellow oil (73 mg, 51%) (Found: $M^{+\bullet}$, 331·2146. $C_{20}H_{29}NO_3$ requires $M^{+\bullet}$, 331·2147). ^{1}H n.m.r. δ 8·42, br s, 1H, NH; 6·91, s, 1H, H 5; 6·56, s, 1H, H 3; 4·94, m, 1H, OCH; 4·81, s, 2H, C**H**$_2$OH; 4·58, d, *J* 6·8 Hz, (4·57, d, *J* 6·6 Hz), and 4·52, d, *J* 6·7 Hz, (4·50, d, *J* 6·7 Hz), 2H, OCH_2O; 3·50, m, 1H, H 6; 3·42, (3·41), s, OCH_3; 3·23, m, 1H, H 8; 2·02, m, 3H, H 2′$_a$ and H 7; 1·83, m, 1H, H 2′$_b$; 1·60–1·20, br m, 3H, H 3′ and OH; 1·31, (1·29), d, *J* 7·0 Hz, CH_3; 1·25, d, *J* 7·1 Hz, (1·24, d, *J* 7·0 Hz), CH_3; 0·94, t, *J* 7·3 Hz, 3H, H 4′. ^{13}C n.m.r. δ 142·30, 136·56, 133·05, 132·34, 128·88, 125·09, 6×Ar C_{quat}; 114·09, (113·98), 100·02, 2×Ar CH; 93·86, OCH_2O; 77·12, OCH; 58·69, CH_2OH; 55·41, OCH_3; 43·61, C 7; 39·18, C 2′; 37·71, (37·33), C 8; 35·95, C 6; 20·68, (20·62), CH_3; 20·60, (20·40), CH_3; 19·59, C 3′; 13·91, (13·90), C 4′. Mass spectrum: *m/z* 331 (M^+, 67%), 288 (13), 271 (49), 270 (43), 256 (87), 228 (100), 226 (92), 198 (64).

trans-*4-(1′-Methoxymethyloxybutyl)-6,8-dimethyl-1,6,7,8-tetrahydrocyclopent[g]indole-2-carbaldehyde (21b)*

This was synthesized according to the procedure used to prepare the corresponding *cis*-compound (21a). The reagents and amounts used were as follows: the indole-2-methanol (20b) (123 mg, 371 μmol) and manganese dioxide (0·60 g, 6·2 mmol). The usual workup and chromatographic procedures were employed to give (21b) as a yellow *oil* (79 mg, 65%) (Found: $M^{+\bullet}$, 329·1990. $C_{20}H_{27}NO_3$ requires $M^{+\bullet}$, 329·1991). ν_{max} (neat) 1600s cm^{-1} (C=O). ^{1}H n.m.r. δ 9·80, s, 1H, CHO; 8·90, (8·87), br s, 1H, NH; 7·49, d, *J* 2·1 Hz, 1H, H 3; 6·98, s, 1H, H 5; 4·92, m, 1H, OCH; 4·54, m, 2H, OCH_2O; 3·46, m, 1H, H 6; 3·42, (3·41), s, OCH_3; 3·25, m, 1H, H 8; 2·00, m, 3H, H 7 and H 2′$_a$; 1·80, m, 1H, H 2′$_b$; 1·60–1·20, br m, 2H, H 3′; 1·32, d, *J* 7·3 Hz, CH_3; 1·28, d, *J* 7·0 Hz, CH_3; 0·95, t, *J* 7·3 Hz, 3H, H 4′. ^{13}C n.m.r. δ 181·64, CHO; 147·69, 135·69, 135·30, 129·78, 124·63, 5×Ar C_{quat}; 115·78, 115·03, 2×Ar CH; 110·73, C_{quat}; 93·94, OCH_2O; 77·04, OCH; 55·42, OCH_3; 43·21, C 7; 39·34, C 2′; 38·06, C 8; 35·83, C 6; 20·13, CH_3; 19·51, CH_3, 19·43, C 3′; 13·77, C 4′. Mass spectrum: *m/z* 329 (M^+, 55%), 286 (33), 268 (26), 258 (40), 240 (35), 226 (100), 198 (62).

trans-*4-(1′-Methoxymethyloxybutyl)-6,8-dimethyl-1,6,7,8-tetrahydrocyclopent[g]indole (19b)*

This was prepared according to the procedure used for the synthesis of the corresponding *cis*-compound (19a). The reagents and amounts used were as follows: the indole-2-carbaldehyde (21b) (60 mg, 182 μmol), bis(triphenylphosphine)(carbonyl) rhodium(I) chloride (25 mg, 36 μmol) and 1,3-bis(diphenylphosphino)propane (30 mg, 72 μmol). The usual workup and purification procedures were followed to yield the *title compound* (19b) as a yellow oil (35 mg, 64%) (Found: $M^{+\bullet}$, 301·2042. $C_{19}H_{27}NO_2$ requires $M^{+\bullet}$, 301·2042). ^{1}H n.m.r. δ 8·08, br s, 1H, NH; 7·17, d, *J* 5·4 Hz, 1H, H 2; 6·95, s, 1H, H 5; 6·71, d, *J* 5·4 Hz, (6·70, d, *J* 5·4 Hz), 1H, H 3; 4·98, m, 1H, OCH; 4·61, d, *J* 6·7 Hz, (4·60, d, *J* 6·7 Hz), and 4·57, d, *J* 6·6 Hz, (4·55, d, *J* 6·7 Hz), 2H, OCH_2O; 3·56, m, 1H, H 6; 3·44, (3·43), s, OCH_3; 3·40, m, 1H, H 8; 2·00, m, 3H, H 7 and H 2′$_a$; 1·85, m, 1H, H 2′$_b$; 1·60–1·30, br m, 2H, H 3′; 1·33, d, *J* 7·0 Hz, CH_3; 1·30, d, *J* 6·8 Hz, (1·29, d, *J* 6·8 Hz), CH_3; 0·95, t, *J* 7·3 Hz, 3H, H 4′. ^{13}C n.m.r. δ 142·11, 132·64, 132·40, 128·78, 124·97, 5×Ar C_{quat}; 122·95, 113·95, (113·81), 101·89, 3×Ar CH; 94·02, OCH_2O; 77·11, OCH; 55·45, OCH_3; 43·51, C 7; 39·28, C 2′; 37·76, C 8; 36·00, C 6; 20·67, CH_3; 19·84, CH_3; 19·60, C 3′; 13·90, C 4′. Mass spectrum: *m/z* 301 (M^+, 49%), 258 (53), 240 (27), 226 (35), 212 (27), 198 (100).

(±)-*Iso*-trans-*trikentrin B (5)*

To a well stirred solution of the methoxymethyl ether (19b) (7 mg, 23 μmol) and dry dichloromethane (2 ml), under argon at −78°C, was added an aliquot (105 μl) of a solution of dimethylboron bromide and dichloromethane (80 mg/ml). The reaction mixture darkened. After the mixture was stirred for 4 min, triethylamine (100 μl) was added and the reaction mixture turned orange. It was stirred for 5 min and water (1 ml) was added. The mixture was warmed to room temperature and extracted with dichloromethane (3×3 ml). The combined organic fractions were washed with water (1 ml), saturated sodium chloride solution (1 ml) and dried ($MgSO_4$). The solvent was evaporated to give an oil. Repeated flash chromatography under nitrogen (silica; ethyl acetate/light petroleum, 1 : 9) of the residue gave as the major fraction a yellow oil, identified as (±)-iso-*trans*-trikentrin B (5)[1,5] (5 mg, 63%) (Found: $M^{+\bullet}$, 239·1673. Calc. for $C_{17}H_{21}N$: $M^{+\bullet}$, 239·1674). ν_{max} (CH_2Cl_2) 3475s cm^{-1} (NH). ^{1}H n.m.r. δ 8·04, br s, 1H, NH; 7·19, dd, *J* 2·7, 3·0 Hz, 1H, H 2; 7·09, s, 1H, H 5; 6·80, d, *J* 15·7 Hz, 1H, H 1′; 6·75, dd, *J* 2·3, 3·0 Hz, 1H, H 3; 6·41, dt, *J* 15·8, 6·6 Hz, 1H, H 2′; 3·51, m, 1H, H 6; 3·44, m, 1H, H 8; 2·32, m, 2H, H 3′; 2·00, m, 2H, H 7; 1·33, d, *J* 7·0 Hz, CH_3; 1·31, d, *J* 7·2 Hz, CH_3; 1·15, t, *J* 7·5 Hz, 3H, H 4′. ^{13}C n.m.r. δ 142·46, Ar C_{quat}; 132·35, CH; 128·99, 128·38, 2×Ar C_{quat}; 127·22, CH; 125·12, Ar C_{quat}; 123·17, 112·31, 2×CH; 110·73, Ar C_{quat}; 101·61, CH; 43·59, C 7; 37·68, C 8; 35·93, C 6; 26·40, C 3′; 20·68, CH_3; 19·82, CH_3; 13·88, C 4′. Mass spectrum: *m/z* 239 (M^+, 89%), 224 (100), 198 (19), 182 (23), 154 (9).

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