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Structure–function relationship of Yuehchukene II. The effect of C-6 indole rotation on anti-implantation activity

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Summary — In a first attempts to define the structural requirements for the expression of anti-implantation activity in Yuehchukene (YCK), it was found that the relative position or planarity of the aromatic centres may be crucial. New synthetic routes leading to analogues with modification of C-7 substituents were established. Results indicated that a bulky group at C-7 that served to restrict the rotation of the C-6 indole was indispensable. Further steric hindrance by 2'-methyl would increase potency in all weak analogues. It was concluded that YCK required an optimal conformation that was defined by a narrowly-fixed angle between the planes of the C-6 indole and the tetracyclic unit.

Yuehchukene (YCK) / analog syntheses / anti-implantation activity / steric requirement

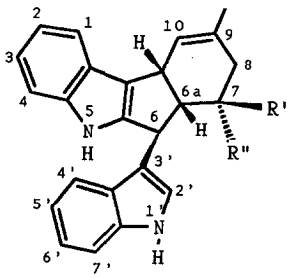
Introduction

(±) Yuehchukene (YCK) is a bis-indole alkaloid with potent anti-implantation activity in rats. As this animal model is sensitive to estrogen, one important reservation in developing YCK as a novel type anti-fertility agent for human use resides in its estrogenicity. While it could be reasonably assumed that YCK became estrogenic only after hydroxylation of its aromatic centres through hepatic transformation, previous attempts in defining the structure–function relationship of YCK (see paper I of this series) [1] revealed that the 2,5'-dihydroxy analogues were actually inactive. These results left the question of what was the structural basis for the expression of estrogenicity in YCK, assuming for simplicity of argument, that YCK blocked implantation in rats by virtue of its estrogenic activity. As YCK has no oxygen function, insight into this structural requirement may possibly lead to the discovery of new mechanisms in estrogenic action, particularly regarding receptor binding.

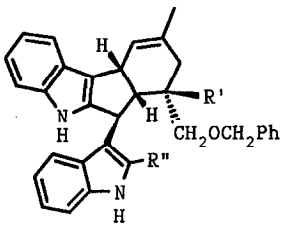
In our previous study (paper I of this series) [1] it was also observed that substitution on the indole nitrogen would abolish activity. There could be 2 explanations. Firstly, a bulky N-substitution would restrict the degree of rotation of the C-6 indole and push it out of a favourable conformation optimal for activity. Secondly, the lone pair of electrons on the nitrogen atom must be freely accessible in order to be active. The present paper addresses the first hypothesis by examining the relationship between the C-6 indole rotation and the potent of anti-implantation. As regards the second hypothesis, serious efforts are underway to replace both the indole moieties with benzofuran. The combination of these results would eventually shed light on the action mechanism, whether estrogenic or not, of YCK as an anti-implantation agent.

Chemistry

Our laboratory provided the first synthesis of YCK [2] by acid dimerization of the 3-dehydroprenylindole (**11**). We have also synthesized a few YCK analogues by the same strategy [1] by employing substituted 3-dehydroprenylindole. However, this dimerization strategy cannot provide YCK analogues with functionalized substituents at C-7 necessary for the present study. We therefore developed a more general synthetic approach which would provide access to YCK analogues with possible variation of substituent both at C-7 and C-6. The key synthetic intermediate for



	R'	R"
1	Me	Me
2	H	H
3	H	CH_2OCH_2Ph
4	Me	CH_2OCH_2Ph



	R'	R"
5	H	Me
6	Me	Me
7	H	Ph

this approach was based on the tetracyclic ketoester (**12**) which we have successfully synthesized [3]. In this paper we report the transformation of **12** into the YCK analogues **3**, **4**, **5**, **6**, **7** and **8**.

Analogues **9** and **10** were synthesized *via* the tetracyclic ketone **13** which was prepared by another entirely different route [4].

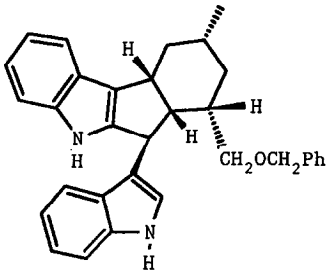
Synthesis of analogues 3, 5 and 7

Conversion of **12** into YCK analogues **3**, **5** and **7** was achieved *via* the diol **14** (scheme 1), adopting a procedure we had developed in the synthesis of 7,7-bisnor-YCK (**2**) [5]. Treatment of **12** with lithium aluminium hydride stereoselectively afforded the 6α-hydroxy derivative (**14**). Treatment of the diol (**14**) with benzyl bromide in the presence of tetrabutylammonium hydrogen sulphate, a phase transfer catalyst, selectively benzylated only the primary alcohol giving rise to **15** in quantitative yield. Benzoylation of the 6α-hydroxy group in **15** to yield **16** was achieved with benzoyl chloride-triethylamine in the presence of stoichiometric amount of 4-(dimethylamino)-pyridine (DMAP) [6] an active esterification catalyst. Bimolecular nucleophilic displacement of the 6α-benzoate with the indol-3-yl moiety was accomplished by treating **16** with the indolyl Grignard reagent to give **17**. Finally, detosylation of **17** with sodium amalgam in methanol in the presence of disodium hydrogen phosphate buffer [7] afforded analogue **3**.

Treatment of the benzoate (**16**) with 2-methylindol-3-yl Grignard or the alcohol (**15**) with 2-phenylindole in BF_3 etherate yielded **18** or **19** which upon detosylation gave analogues **5** or **7** respectively.

Synthesis of analogues 4 and 6

The ketoester (**12**) was first treated with sodium borohydride at –10°C whereby lactone **20** was isolated



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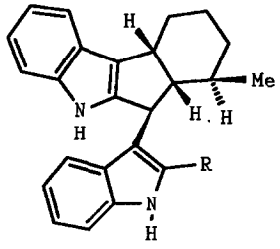
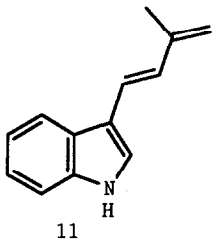


9 R = Me

10 R = H



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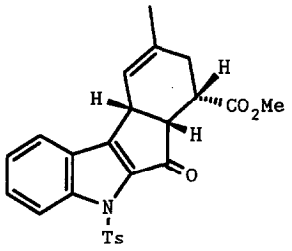
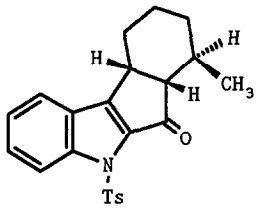


12 Ts = p-toluenesulphonyl



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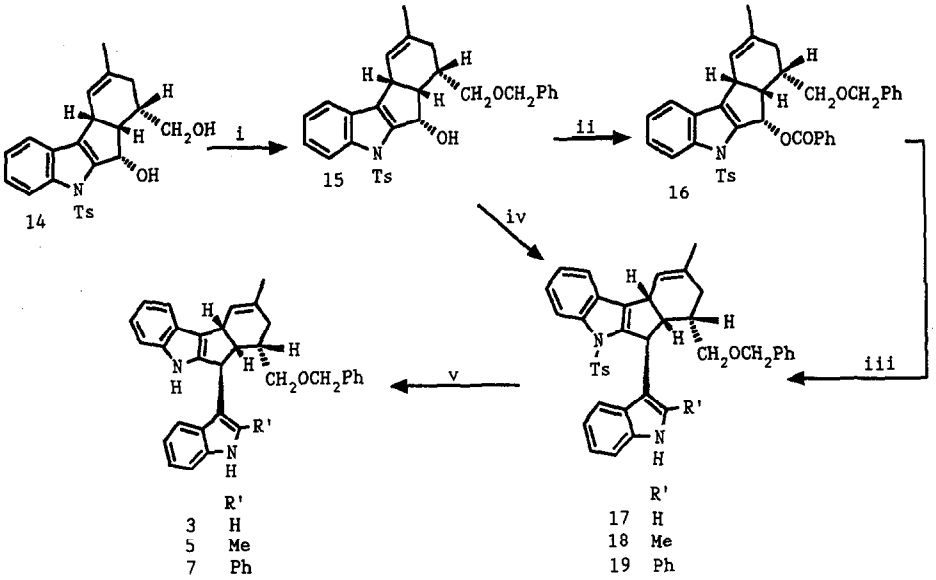
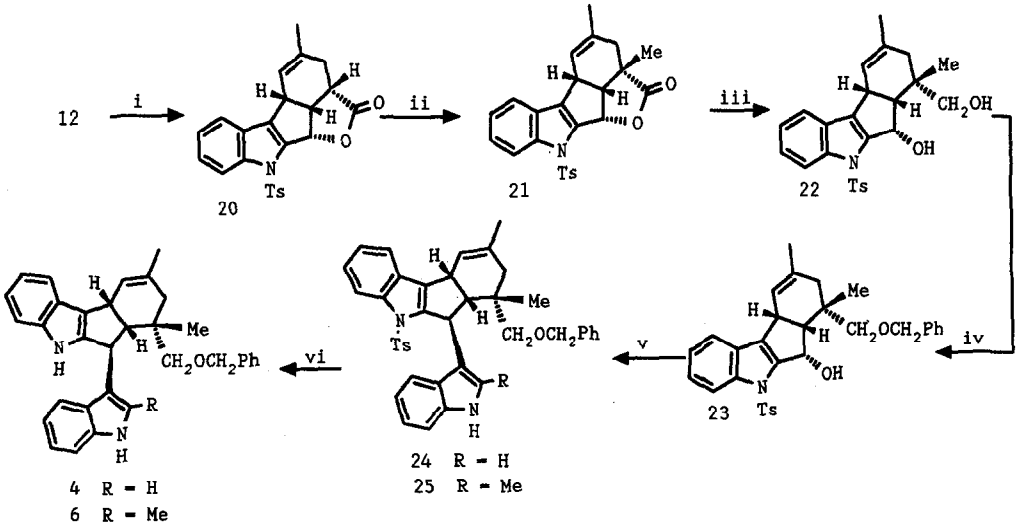
(scheme 2). Methylation of **20** in the presence of lithium diisopropylamide and methiodide at –90°C resulted in the formation of 7-methyl derivative **21**. Lithium aluminium hydride reduction of **21** gave the diol **22** which was converted to 7-benzyloxymethyl derivative **23**. Introduction of an indole moiety at C-6 was achieved by treating **23** with indole or 2-methylindole in the presence of BF_3 etherate whereby **24** and **25** were obtained respectively. Final detosylation afforded analogues **4** and **6**.

Synthesis of analogue 8

Conversion of **12** into **8** was achieved *via* the diol (**27**) which was obtained by first saturation of the C-9, C-10 double bond in **12** by catalytic hydrogenation to **26**, followed by lithium aluminium hydride reduction (scheme 3). The diol (**27**) thus obtained was transformed into the analogue **8** by a reaction sequence similar to the synthesis of **3** from the diol (**15**).



Scheme 1. Reagents: i, nBu$_4$NHSO$_4$, NaOH, C$_6$H$_6$, PhCH$_2$Br; ii, Et$_3$N, DMAP, CHCl$_3$, PhCOCl; iii, (16 → 17) indolyl-MgBr, C$_6$H$_6$; (16 → 18) 2-methylindolyl-MgBr, C$_6$H$_6$; iv, BF$_3$, Et$_2$O. Et$_3$N, 2-phenylindole; v, Na-Hg, Na$_2$HPO$_4$, MeOH.



Scheme 2. Reagents: i, NaBH$_4$, MeOH; ii, LiN(iPr)$_2$, CH$_3$I, THF; iii, LiAlH$_4$, THF; iv, nBu$_4$NHSO$_4$, NaOH, PhCH$_2$Br, C$_6$H$_6$; v, (23 → 24) BF$_3$·Et$_2$O, THF, indole; (23 → 25) BF$_3$·Et$_2$O, THF, 2-methylindole; vi, Na-Hg, Na$_2$HPO$_4$, MeOH.

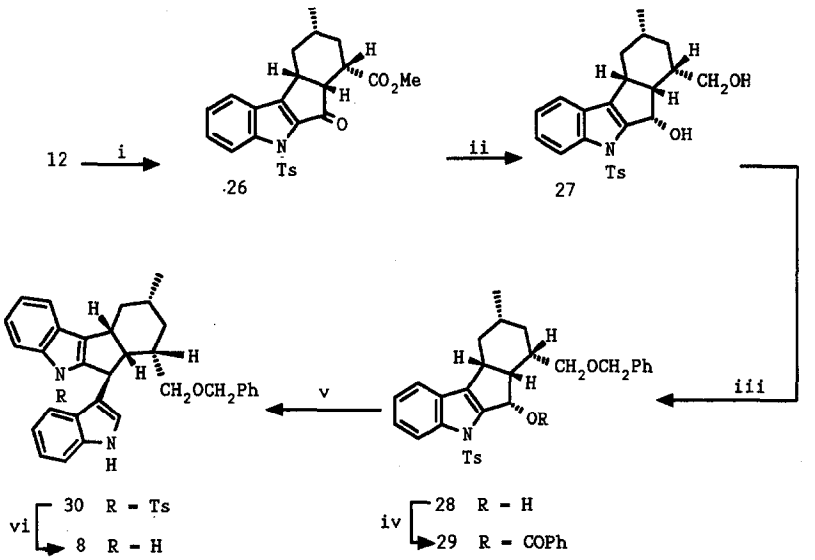
Bioassay

Details of the methods for treatment of animals in anti-implantation and formulation of test samples have been previously reported (see paper I of this series) [1].

Structure–function relationship

Group I: modification at C-7

YCK (**1**) was 100% active at 1.25 mg/kg, but deletion of the 7,7-di-methyl group in bis-nor-YCK (**2**) rendered the analogue totally inactive up to a dose level of 40 mg/kg. This dose was so heavy that the rats began to suffer from toxic effects and one rat died in this group. The replacement of the gem-methyl group by a bulky benzyloxymethyl group as in 7-nor-7α-BM-YCK (**3**) was able to restore the activity such that **3** was active at 10 mg/kg, although not 100%; the re-introduction of a methyl group as in 7β-Me-7α-BM-YCK (**4**) further enhanced the activity to reach 100% at the same dose level (10 mg/kg).



Scheme 3. Reagents: i, PtO_2/C, H_2, THF; ii, $LiAlH_4$, THF; iii, nBu$_4$NHSO$_4$, NaOH, $PhCH_2Br$, C_6H_6; iv, DMAP, Et_3N, PhCOCl, CH_3Cl; v, C_6H_6, indolyl-MgBr; vi, Na-Hg, Na_2HPO_4, MeOH.

Group II: modification at C-7 and C-2'

Inasmuch as compound (**3**) was active but not at 100%, the introduction of a methyl group at C-2' as in 2'-Me-7-nor-7α-BM-YCK (**5**) made it 100% active at the same dose level (10 mg/kg). While this enhancement could be effected with the re-introduction of a methyl group at C-7 as in **4**, the additional substitution of 2'-methyl as in 2',7β-DiMe-7α-BM-YCK (**6**) could greatly increase the potency of this analogue by reaching 100% activity at 3 mg/kg. On the contrary, the introduction of a phenyl group at C-2' as in 2'-Ph-7-nor-7α-BM-YCK (**7**) completely abolished activity when compared with the introduction of a small alkyl group at the same position in **5** and tested at the same dose level (10 mg/kg).

Group III: modification at C-7 and saturation of C-9, C-10 double bond

It has been previously reported that (see paper I of this series), 9,10-dihydro-YCK, which was obtained by hydrogenation of the parent compound, was equipotent with YCK in all aspects (anti-implantation and estrogenic activity). By the same token, 7-nor-7α-BM-YCK (**3**) was hydrogenated to yield 9,10-dihydro-7-nor-7α-BM-YCK (**8**) which was more or less equipotent compared with its parent compound (**3**) tested at the same dose level. While the reduction in potency was not due to hydrogenation, the concurrent deletion of 7α- and 9-methyl as in 7α,9-bisnor-9,10-dihydro-YCK (**10**) raised the minimal effective dose to 10 mg/kg. This substantial reduction in potency could be partly restored by the introduction of 2'-methyl group as in 2'-Me-7α,9-bisnor-9,10-dihydro-YCK (**9**). With this compound (**9**), the 100% active dose could be lowered to 6 mg/kg.

Discussion

When highly pure YCK was consistently obtained and stored in a stable form (lyophilised from aqueous suspension), it was tested routinely at 1.25 mg/kg with 100% anti-implantation activity in rats. This dose level was now considered the minimal effective dose. Analogues reported in this paper were not always as pure as YCK, which stood at 95% or above. But then if the minimal effective dose was raised by several-fold or more, a lesser degree of purity became indifferential.

From our previous study based on 10 analogues obtained by substitution of the parent compound, it became obvious that 3 structural features were essential to the expression of biological activity. 1) Hydroxylation of the aromatic centres at C-2 and C-5' abolished activity. 2) It is indispensable that both nitrogen atoms be unsubstituted. 3) The relative position or planarity of the aromatic centres was crucial to the full expression of biological activity.

In order to address the last point, analogues with variation of substituents at C-7 were synthesized. They were designed to restrict the degree of rotation of the free indole moiety so as to examine its

Table I. Anti-implantation activity of C-7 and C-2' YCK analogues Vehicle controls in all experiments were pregnant, *ie* all rat groups were 100% fertile. Anti-implantation activity is positive (+ve), negative (–ve), or equivocal (±ve).

Compound	*Dose (mg/kg, PD_{1-4})*	*No preg No tested*	*Remarks*
YCK (**1**)	1.25	0/5	+ve
Group I: modification at C-7			
7,7-Bisnor-YCK (**2**)	25.6	5/5	–ve
	40.0	4/5	–ve
7α-BM-7-Nor-YCK (**3**)	2.5	5/5	–ve
	10.0	2/5	+ve
7α-BM-7β-Me-YCK (**4**)	10.0	0/5	+ve
Group II: modification at C-7 and C-2'			
2'-Me-7-Nor-7α-BM-YCK (**5**)	10.0	0/5	+ve
2',7β-DiMe-7α-BM-YCK (**6**)	1.5	5/5	–ve
	3.0	0/5	+ve
2'-Ph-7-Nor-7α-BM-YCK (**7**)	5.0	5/5	–ve
	10.0	5/5	–ve
Group III: modification at C-7 and saturation of $\Delta^{9,10}$			
9,10-DiH-7-Nor-7α-BM-YCK (**8**)	10.0	3/5	±ve
2'-Me-7α,9-Bisnor-9,10-DiH-YCK (**9**)	6.0	0/5	+ve
7α,9-Bisnor-9,10-DiH-YCK (**10**)	3.6	2/5	+ve
	10.0	0/5	+ve

consequence on potency. The results reported here seem to bear out the rationale of this approach. Indeed, the deletion of 7,7-dimethyl group (**2**) totally abolished the activity which was not observed until the free indole ring was rotating within the steric constraints imposed by a 7α-benzyloxymethyl group (**3**). Rotation of the free indole moiety hinged at C-6 round the tetracyclic unit plane was further restricted by the introduction of 7β-methyl group. This additional steric hindrance favoured a corresponding increase in potency. Hence, results from Group I analogues led to the unequivocal conclusion that a restricted rotation plane of the free indole moiety would increase the probability of YCK falling into an optimal conformation required for receptor binding prior to the expression of biological activity. The increased potency in compounds **5**, **6**, and **9** clearly indicated that where the potency of an analogue was weakened by removing substituents at C-7, steric hindrance afforded by 2'-methyl substitution could partly restore the biological activity. This was true with 3 different degrees of substitution at C-7 as evidenced in compounds **3**, **4** and **10**. The importance of 2'-substitution as a differential factor in structure–function relationship was corroborated with the introduction of a phenyl group at C-2' (**7**) which rendered the weakened analogue still less active. Here either the bulky size of a phenyl group, or the aromaticity of the phenyl ring or both elements could prevent the appearance of an optimal conformation as reasoned above. The neutral effect of saturating the C-9, C-10 double bond by hydrogenation had been dealt with and the further deletion of the 9-methyl group did not seem to affect the expression of biological activity (compare **9** with **4** at the same dose level), possibly because it was away from the rotation plane of the free indole moiety. But here again, the introduction of a 2'-methyl group could substantially increase the potency, strongly suggesting the existence of an optimal conformation. Thus the synthesis of an analogue with more restricted rotation of the indole at C-6 may yield a more potent analogue with minimal change in structure of the parent coumpound.

Experimental protocols

Mps were measured on a Reichert–Kofler hot-stage apparatus and are uncorrected. IR spectra were recorded on a Perkin–Elmer 577G spectrophotometer or a Nicolet 20SXC FT-IR spectrometers and calibrated with polystyrene. NMR spectra

were recorded on a JEOL FX-90Q spectrometer, a JEOL GSX-270 spectrometer or a Varian XL-400 spectrometer in deuteriochloroform unless otherwise stated with tetramethylsilane as internal standard. Mass spectra were recorded on a Hitachi RMS-4 and VG 70-70F high resolution mass spectrometers. Flash chromatography used Kieselgel 60 (Merck) as the stationary phase [8]. Analytical HPLC was performed on a Beckmann Model 331 HPLC System with UV–vis detector. Light petroleum refers to 40–60°C fraction which was redistilled before use. All reactions requiring anhydrous conditions used dry solvents and were conducted in apparatus oven-dried at 120°C and under a dry nitrogen static atmosphere. New compounds whose elemental compositions were established through accurate mass determination were shown to be homogeneous by spectroscopic and chromatographic methods. Analyses indicated by the symbols of the elements were within ± 0.4% of the theoretical values. All compounds described were racemic.

*6α-Hydroxy-7α-hydroxymethyl-9-methyl-5-tosyl-5,6β,6aβ,7β,8,10aβ-hexahydroindeno[2,1-b]indole (**14**)*

To lithium aluminium hydride (70.8 mg) in anhydrous THF (2 ml) at 0°C was added the ketoester **12** (0.2 g, 0.45 mmol) in anhydrous THF (7 ml). The mixture was stirred at room temperature for 2 h. Usual work-up and chromatography of the residue on silica gel eluted with ether–light petroleum (1:1) yielded **14** (164 mg, 86%) as white solids, mp 103–105°C; Anal $C_{24}H_{25}NO_4S$ (C, H, N); ν_{max} (Nujol) 3400, 1370, 1180, 755, and 680 cm^{-1}; δ_H (90 MHz) 1.63 (3H, br s, 9-Me), 1.79–2.60 (3H, m, 8-H_2 and 7-H), 2.20 (3H, s, ArMe), 3.04 (1H, m, 6a-H), 3.32 (2H, br s, exchangeable with D_2O, 2 x OH), 3.56 (1H, m, 10a-H), 4.01 (2H, br d, *J* 4.4 Hz, 7-CH_2), 5.58 (1H, br s, 10-H), 5.61 (1H, d, *J* 6.1 Hz, 6-H), 7.06–7.55 and 7.78–8.02 (8H, m, ArH); δ_c (22.5 MHz) 21.34 (ArMe), 23.88 (9-Me), 31.09 (C-8), 38.24, 38.56 (C-7, C-10a), 46.91 (C-6a), 65.38 (7-CH_2), 71.93 (C-6) 114.46 (C-4), 119.88 (C-1), 120.58 (C-10), 123.40 (C-2), 124.59 (C-3), 125.84 (C-10b), 126.81 (2 x C-2'), 129.74 (2 x C-3'), 131.25 (C-10c), 133.75 (C-9), 135.32 (C-11), 139.81 (C-5a), 142.52 (C-4a), and 144.80 (C-4'); *m/z* 423 (*M*+, 16%), 405 (*M*–H_2O, 91), 374 (36), 250 (64), 232 (43), 220 (100), 218 (55), 204 (55), and 158 (66).

*7α-Benzyloxymethyl-6α-hydroxy-9-methyl-5-tosyl-5,6β-6aβ,7β,8,10aβ-hexahydroindeno[2,1-b]indole (**15**)*

A mixture of **14** (0.2 g, 0.47 mmol) and tetrabutylammonium hydrogen sulphate (0.16 g, 0.47 mmol) in benzene (4.7 ml), and NaOH (50% w/w, 0.47 ml) at 0°C was vigorously stirred at rt for 10 min. The resulting greenish brown solution was cooled to 0°C and benzyl bromide (0.11 ml, 0.94 mmol) was added. The whole was then stirred at room temperature for 0.5 h, poured into water, and extracted with ether. Usual work-up and flash chromatography of the residue on silica gel eluted with ether-light petroleum (1:5) afforded **15** (0.243 g, 99%) as a white powder, mp 145–147°C; Anal $C_{31}H_{31}NO_4S$ (C, H, N); λ_{max} (EtOH) 215 (log ε 4.40), and 258 nm (4.09); ν_{max} (Nujol) 3550, 3450, 3040, 1600, 1370, 1235, 1180, 1100, 995, 750, 710, and 670 cm^{-1}; δ_H (90 MHz) 1.65 (3H, s, 9-Me), 1.88–2.48 (3H, m, 8-H_2 and 7-H), 2.33 (3-H, s, ArMe), 2.77 (1H, d, $J_{6,OH}$ 4.8 Hz, exchangeable with D_2O, OH), 3.06 (1H, m, 6a-H), 3.68 (1H, m, 10a-H), 3.81–3.88 (2H, m, 11-H_2), 4.66 (2H, s, 12-H_2), 5.51 (1H, dd, $J_{6,OH}$ 4.8 Hz and $J_{6,6a}$ 6.2 Hz, collapses to d, *J* 6.1 Hz upon deuteriation, 6-H), 7.15–7.56 and 7.80–8.02 (13H, m, ArH); δ_c (22.5 MHz), 21.45 (ArMe), 23.94 (9-Me), 31.64 (C-8), 36.60 (C-10a), 38.35 ((C-7), 46.59 (C-6a), 71.94 (C-6), 73.19, 73.40 (C-11, C-12), 114.52 (C-4), 119.89 (C-1), 120.91 (C-10), 123.52 (C-2), 124.54 (C-3), 125.90 (C-10b), 126.98 (2 x C-2'), 127.69 (C-4"), 127.79 (2 x C-2"), 128.44 (3 x C-3"), 129.75 (2 x C-3'), 131.05 (C-10c), 133.59 (C-9), 135.60 (C-1'), 138.47 (C-5a), 139.82 (C-1"), 143.01 (C-4a), and 144.70 (C-4'); *m/z* 513 (*M*+, 4%), 495 (*M*–H_2O, 4), 405 (*M*–$PhCH_2OH$, 7), 374 (14), 231 (25), 220 (25), 218 (32), 204 (22), 90 (32), and 91 (100).

*6α-Benzoyloxy-7α-benzyloxymethyl-9-methyl-5-tosyl-5,6β,6aβ,7β,8,10aβ-hexahydroindeno[2,1-b]indole (**16**)*

To a solution of **15** (0.25 g, 0.49 mmol) in anhydrous $CHCl_3$ (2.13 ml) was added 4-dimethylaminopyridine (DMAP) (0.18 g, 1.47 mmol), triethylamine (0.14 ml, 0.98 ml), and benzoyl chloride (0.11 ml, 0.98 mmol). After refluxing for 1 h, dichloromethane was added. The organic layer was washed with aqueous copper sulphate, water and brine, dried, and evaporated to dryness. Flash chromatography of the residue on silica gel eluted with ether–light petroleum (1:4) afforded the benzoate **16** as white solid (275 mg, 91%), mp 181–183.5°C; λ_{max} (EtOH) 220 (log ε 4.14), and 264 nm (4.00); ν_{max} (Nujol) 3060, 1710, 1610, 1375, 1270, 1125, 1180, 710, and 670 cm^{-1}; δ_H (400 MHz) 1.65 (3H, s, 9-Me), 1.81 [1H, t (dd), *J* 14.63 Hz, 8-H], 1.92 (1H, dd, $J_{7,8}$ 5.60 Hz and $J_{8,8}$ 17.4 Hz, 8-H), 2.21 (3H, s, ArMe), 2.51 (1H, m, 7-H), 3.34 [1H, q (ddd), $J_{6,6a}$, $J_{6a,7}$, $J_{6a,10a}$ 5.71 Hz, 6a-H], 3.55 (1H, dd, $J_{7,11}$ 6.81 Hz and $J_{11,11}$ 9.19 Hz, 11-H), 3.69 [1H, t (dd), $J_{7,11}$ and $J_{11,11}$ 8.94 Hz, 11-H], 3.71 (1H, br s, 10-a-H), 4.55 and 4.71 (2H, ABq, *J* 11.59 Hz, 12-H_2), 5.71 (1H, br s, 10-H), 6.95 (2H, d, *J* 8.03 Hz, ArH), 7.09 (1H, d, $J_{6,6a}$ 5.99 Hz, 6-H), 7.25–7.42 and 7.52–7.60 (11H, m, ArH), 7.64 (2H, d, *J* 10.4 Hz, ArH), 7.90 (2H, d, *J* 8.59 Hz, ArH), and 8.06 (1H, d, *J* 8.11 Hz, ArH).

*7α-Benzyloxymethyl-6β-indol-3'-yl-9-methyl-5-tosyl-5,6α,-6aβ,7β,8,10aβ-hexahydroindeno[2,1-b]indole (**17**)*

To a suspension of magnesium turnings (30 mg, 1.2 mmol) in anhydrous ether (1.5 ml) was added bromoethane (0.093 ml, 1.2 mmol). When the reaction has ceased, indole (133 mg, 1.1 mmol) in anhydrous benzene (7 ml) was added. After replacing the ether solvent with benzene, this freshly prepared indolylmagnesium bromide was added to **16** (637 mg, 1 mmol) in benzene (6 ml) and the mixture was refluxed for 0.5 h. The mixture was then treated with aqueous ammonium chloride, extracted with ether, washed successively with water and brine, dried, and evaporated to dryness. Flash chromatography of the residue on silica gel eluted with ether–light petroleum (7:13) yielded **17** (604 mg, 96%) as pale yellow solids, mp 88–90°C; Anal $C_{39}H_{36}N_2O_3S$ (C, H, N); λ_{max} (EtOH) 217 (log ε 4.75), and 265 nm (4.25); ν_{max} (Nujol) 3400, 3030, 1600, 1375, 1120, 780, and 710 cm^{-1}; δ_H (400 MHz, C_6D_6) 1.576 (3H, S, 9-Me), 1.680 (3H, s, ArMe), 1.960 (1H, dd, $J_{7,8}$ 2.38 Hz and $J_{8,8}$ 16.26 Hz, 8-H), 2.123 (1H, dd, $J_{7,8}$ 9.02 Hz and $J_{8,8}$ 16.57 Hz, 8-H), 2.472 (1H, m, 7-H), 3.26 (1H, dd, *J* 6.98 Hz and 14.12 Hz, 11-H), 3.336 (1H, dd, *J* 8.86 Hz and 17.10 Hz, 11-H), 3.638 [1H, q (ddd), *J* 5.5 Hz, 6a-H], 3.900 (1H, br m, 10a-H), 3.928 (2H, s, 12-H_2), 5.091 (1H, dd, *J* 1.81 Hz and 4.96 Hz, 6-H), 5.783 (1H, br s, 10-H), 6.216 (2H, d, *J* 8.33 Hz, ArH), 6.520 (2H, br s, NH and 2'-H), 7.202–6.805 (11H, m, ArH), 7.477 and 8.407 (2H, m, ArH); δ_c (22.5 MHz), 21.24 (ArMe), 23.94 (9-Me), 29.90 (C-8), 37.98, 38.52, 39.00 (C-6, C-7, C-10a), 51.68 (C-6a), 72.59, 72.75 (C-11, C-12), 111.22 (C-7'), 114.74 (C-4), 117.83 (C-3'), 119.13, 119.95 (C-4', C-5', C-1), 121.35, 122.27, 123.03, 123.52 (C-2, C-10, C-2', C-6'), 125.57 (C-3 and C-3'a), 126.01 (C-11b), 126.55 (2 x C-2"), 127.25 (C-4'"), 127.58 (2 x C-2'"), 128.12 (2 x C-3'"), 128.77 (2 x C-3"), 129.20 (C-10c), 133.32 (C-9), 135.87 (C-1"), 136.35 (C-7'a), 138.30 (C-5a); 140.69 (C-1'"), 143.40 (C-4a), and 143.99 (C-4"); *m/z* 612 (*M*+, 4%), 458 (22), 457 (*M*–$C_7H_7SO_2$, 58), 404 (25), 335 (25), 130 (28), 117 (26), and 91 (100).

7α-Benzyloxymethyl-6β-indol-3'-yl-9-methyl-5,6α,6aβ,7β,8,10aβ-hexahydroindeno[2,1-b]indole, 7-Nor-7α-BM-YCK (3)
A mixture of **17** (90 mg, 0.15 mmol) in anhydrous ether (1.5 ml) and methanol (3 ml), disodium hydrogen phosphate (1.22 g), and sodium amalgam (5%; 1.22 g) was stirred at room temperature for approx 1 h. Work-up and flash chromatography on silica gel eluted with ether–light petroleum (7:20) gave 7-nor-7α-BM-YCK (**3**) (Found: M^+, 458.2359. $C_{32}H_{30}N_2O$ requires M, 458.2358) (62 mg, 90%) as white solids (from ether), mp 213–215°C (dec); λ_{max} (EtOH) 224 (log ε 4.76), and 281 nm (4.13); λ_{max} (Nujol) 3420, 3380, 1110, and 740 cm^{-1}; δ_H [270 MHz, $(CD_3)_2CO$], 1.653 (3H, br s, 9-Me), 2.168 (2H, m, 8-H_2), 2.404 (1H, m, 7-H), 3.371 (2H, m, 11-H_2), 3.779–3.854 (2H, m, 6a-H and 12-H), 3.931–3.973 (2H, m, 10a-H and 12-H), 4.960 (1H, d, $J_{6,6a}$ 8.4 Hz, 6-H), 5.679 (1H, br s, 10-H), 6.858–7.534 (14H, m ArH), 9.562 (1H, br s, 5-NH), and 10.080 (1H, br s, 1'-NH); δ_c [22.5 MHz, $(CD_3)_2CO$] 24.02 (9-Me), 30.11 (C-8), 36.47 (C-6), 39.06 (C-7), 40.63 (C-10a), 52.68 (C-6a), 73.12 (C-12), 74.15 (C-11), 112.29, 112.56 (C-4, C-7'), 117.59 (C-3'), 118.74, 119.37, 119.59, 120.06, 120.67, 121.99 (C-1, C-2, C-3, C-4', C-5', C-6'), 120.09 (C-10b), 123.97 (C-2'), 125.20 (C-3'a), 125.71 (C-10), 127.78 (C-4"), 128.42 (2 x C-2"), 128.72 (2 x C-3"), 131.38 (C-10c), 137.85, 138.00 (C-4a, C-7'a), 139.65 (C-5a), 141.74 (C-1"), and 146.72 (C-9); *m/z* 458 (M^+, 100%), 367 (M–C_7H_7, 55), 337 (M–367–H_2O, 20), 335 (21), 220 (24), 162 (63), 130 (32), and 91 (38).

7α-Benzyloxymethyl-9-methyl-6β-(2'-methylindol-3'-yl)-5-tosyl-5,6α,6aβ,7β,8,10aβ-hexahydroindeno[2,1-b]indole (18)
Applying a procedure similar to the preparation of **17**, reaction of **16** (241 mg) with 2-methylindolylmagnesium bromide gave **18** (194 mg, 79%) as pale yellow solid, mp 113–114°C; Anal $C_{40}H_{38}N_2O_3S$ (C, H, N); ν_{max} (Nujol) 3380, 3020, 1370, 1175, 745, and 680 cm^{-1}; δ_H (90 MHz, C_6D_6) 1.55 (3H, s, 9-Me), 1.71 (3H, s, 2'-Me), 2.09 (2H, m, 8-H_2), 2.32 (3H, s, ArMe), 2.32 (1H, m, 7-H), 3.26 (2H, m, 11-H_2), 3.96 (4H, s and m, 10a-H, 6a-H, 12-H_2), 4.91 (1H, m, 6-H), 5.71 (1H, br s, 10-H), 6.19 (2H, 1/2ABq, *J* 8.1 Hz, ArH), 6.48–7.52 (14H, m, ArH), and 8.34 (1H, m, ArH); δ_c (22.5 MHz, C_6D_6) 12.38 (2'-Me), 21.05 (ArMe), 24.03 (9-Me), 30.47 (C-8), 38.38, 38.57, 39.33 (C-6, C-7, C-10a), 50.82 (C-6a), 73.03, 73.24 (C-11, C-12), 110.51 (C-7'), 112.95 (C-7'), 115.39 (C-4), 119.26, 119.37, 120.35 (C-1, C-4', C-5'), 123.19, 123.49, 123.92 (C-2, C-10, C-6'), 125.63 (C-3), 126.49 (C-10b), 126.93 (2 x C-2"), 127.33 (C-4'"), 127.77 (2 x C-2'"), 128.31 (2 x C-3'"), 128.93 (2 x C-3" and C-3'a), 129.75 (C-10c), 131.72 (C-2'), 133.40 (C-9), 135.84 (C-1"), 136.90 (C-7'a), 139.31 (C-5a), 141.61 (C-1'"), 142.99 (C-4a), and 144.51 (C-4"); *m/z* 626 (M^+, 17%), 505 (M–$PhCH_2OCH_2$, 11), 471 (M–$C_7H_7SO_2$, 38), 374 (38), 349 (31), 234 (21), 232 (21), 220 (39), 146 (20), 144 (58), 131 (35), 130 (56), and 91 (100).

7α-Benzyloxymethyl-9-methyl-6β-(2'methylindol-3'-yl)-5,6α,6aβ,7β,8,10aβ-hexahydroindeno[2,1-b]indole, 2'-Me-7-nor-7α-BM-YCK (5)
Applying the same procedure as in the preparation of **3**, detosylation of **18** (194 mg) yielded 2'-Me-7-nor-7α-BM-YCK (**5**) (120 mg, 80%) as white needles (from dichloromethane–ether), mp 226–227.5°C (Found: M+, 472.2519. $C_{33}H_{32}N_2O$ requires M, 472.2513); λ_{max} (EtOH) 226 (log ε 4.79), and 280 nm (4.21); ν_{max} (Nujol) 3400, 3380, 3040, 1615, 1100, and 740 cm^{-1}; δ_H (90 MHz), 1.68 (3H, br s, 9-Me), 2.08 (2H, br d, *J* 7.9 Hz, 8-H_2), 2.22 (3H, s, 2'-Me), 2.44 (1H, m, 7-H), 3.21 (2H, double ABq, $J_{7,11}$ 7.6 Hz and $J_{11,11}$ 8.3 Hz, 11-H_2), 3.82 (2H, s, 12-H_2), 3.96 (2H, m, 10a-H and 6a-H), 4.57 (1H, d, $J_{6,6a}$ 8.8 Hz, 6-H), 5.66 (1H, br s, 10-H), 6.77–7.27 and 7.46–7.62 (15H, m, ArH); δ_c (22.5 MHz), 12.27 (2'-Me), 23.81 (9-Me), 30.58 (C-8), 34.75 (C-6), 38.03 (C-7), 40.09 (C-10a), 51.41 (C-6a), 72.81, 73.51 (C-11, C-12), 110.30 (C-7'), 111.73 (C-4), 112.14 (C-3'), 118.34, 119.15, 119.59, 119.67 (C-1, C-2, C-4', C-5'), 120.62, 121.67 (C-3, C-6'), 121.62 (C-10b), 124.60 (C-10), 127.28 (C-4" and C-3'a), 127.66 (2 x C-2"), 128.15 (2 x C-3"), 131.10, 131.29 (C-4a, C-10c, C-2'), 135.65 (C-7'a), 138.06 (C-5a), 140.47 (C-1"), and 144.91 (C-9); *m/z* 472 (M^+, 100%), 381 (M–$C_6H_5CH_2$, 24), 351 (M–$PhCH_2OCH_2$, 42), 341 (M–2-methylindole, 20), 220 (100), 144 (54), and 91 (31).

7α-Benzyloxymethyl-9-methyl-6β-(2'-phenylindol-3'-yl)-5-tosyl-5,6α,6aβ,7β,8,10aβ-hexahydroindeno[2,1-b]indole (19)
Applying a procedure similar to the preparation of **24**, condensation of **15** (200 mg) with 2-phenylindole afforded **19** (235 mg, 88%) as white fine needles (from dichloromethane–light petroleum), mp 161–163°C; Anal $C_{45}H_{40}N_2O_3S$ (C, H, N); λ_{max} (EtOH) 213 (log ε 4.90), 260sb (4.44), 298 (4.42), and 306 nm (4.42); ν_{max} (Nujol) 3250, 1600, 1280, 1030, and 720 cm^{-1}; δ_H (90 MHz) 1.59 (3H, br s, 9-Me), 1.81 (1H, m, 8-H), 2.07 (4H, s + m, 8-H, ArMe), 2.73 [11H, t (dd), $J_{7,11}$ 8.3 Hz and $J_{11,11}$ 8.8 Hz, 11-H], 2.99 (1H, dd, $J_{7,11}$ 5.5 Hz and $J_{11,11}$ 9.0 Hz, 11-H), 3.57 (1H, m, 6a-H), 3.86 (2H, s, 12-H_2), 3.98 (1H, m, 10a-H), 5.18 (1H, d, *J* 5.0 Hz, 6-H), 5.59 (1H, br s, 10-H), 6.44–7.59 and 7.96–8.17 (23H, m, ArH); δ_c (22.5 MHz) 21.29 (ArMe), 23.84 (9-Me), 30.26 (C-8), 38.06, 38.38, 39.00 (C-6, C-7, C-10a), 52.28 (C-6a), 72.70, 73.19 (C-11, C-12), 110.70 (C-7'), 114.28 (C-3'), 114.85 (C-4), 119.02, 119.51, 120.61 (C-1, C-4', C-5'), 121.48, 122.24, 122.97 (C-2, C-10, C-6'), 123.62 (C-3), 125.55 (2 x C-2+), 125.71 (C-10b), 127.17 (C-4'"), 127.33 (2 x C-2"), 127.88 (C-4+), 128.09 (2 x C-2" and C-10c), 128.44 (2 x C-3'"), 128.61 (2 x C-3"), 129.20 (2 x C-3+), 129.93 (C-3'a), 133.43 (C-9), 133.70, 134.08 (C-2', C-1+), 135.62, 136.06 (C-7'a, C-1"), 138.60 (C-5a), 140.82 (C-1'"), 143.29 (C-4a), and 143.72 (C-4"); *m/z* 688 (M^+, 8%), 567 (M–$PhCH_2OCH_2$, 6), 533 (M–$C_7H_7SO_2$, 31), 411 (22), 374 (21), 218 (24), 206 (39), 204 (26), 193 (21), and 91 (100).

7α-Benzyloxymethyl-9-methyl-6β-(2'-phenylindol-3'-yl)-5,6α,6aβ,7β,8,10aβ-hexahydroindeno[2,1-b]indole, 2'-Ph-7-nor-7α-BM-YCK (7)
Following a procedure similar to the preparation of **3**, detosylation of **19** (214 mg) with sodium amalgam gave 2'-Ph-7-nor-7α-BM-YCK (**7**) (Found: M^+, 534.2675. $C_{38}H_{34}N_2O$ requires M, 534.2671) (160 mg, 97%) as white solids (from dichloromethane–ether), mp 231–233°C (dec); λ_{max} (EtOH) 205sh (log ε 4.74), 226 (4.78), and 298 nm (4.33); ν_{max} (Nujol) 3360, 1600, 1330, 1125, 790, and 740 cm^{-1}; δ_H (90 MHz), 1.56 (3H, br s, 9-Me), 1.74 (2H, m, 8-H_2), 2.25 (1H, m, 7-H), 2.96 (2H, br d, *J* 7.2 Hz, 11-H_2), 3.67 (1H, m, 6a-H), 3.81 (2H, s, 12-H_2), 3.95 (1H, m, 10a-H), 4.87 (1H, dd, *J* 3.4 Hz and $J_{6,6a}$ 6.9 Hz, 6-H), 5.62 (1H, br s, 10-H), 6.67–7.64 (18H, m, ArH), 7.64 (1H, br s, NH), and 8.03 (1H, br s, NH); δ_c [22.5 MHz, $(CD_3)_2CO$] 23.89 (9-Me), 30.63 (C-8), 36.16 (C-6), 39.09 (C-7), 40.77 (C-10a), 51.41 (C-6a), 73.30, 74.22 (C-11, C-12), 112.08, 112.57 (C-4, C-7'), 113.47 (C-3'), 118.75, 119.70 (C-1, C-4', C-5), 120.75, 121.02, 122.38 (C-2, C-3, C-6'), 121.62 (C-10b), 125.38 (C-3'a), 125.68 (C-10), 127.71 (C-4"), 128.28 (2 x C-2'"), 128.66 (2 x C-2" and C-4"), 128.96 (C-10c), 129.64 (2 x C-3"), 129.88 (2 x C-3'"), 131.32, 134.51 (C-2', C-1'"), 136.71 (C-7'a), 137.90 (C-4a), 139.71 (C-5a), 141.91 (C-1"), and 146.46 (C-9); *m/z* 534 (M^+, 10%), 443 (M–$PhCH_2$, 19), 413 (M–$PhCH_2OCH_2$, 24), 220 (84), 206 (73), and 91 (47).

*9-Methyl-5-tosyl-5,6β,6aβ,7β,8,10aβ-hexahydroindeno[2,1-b]-indole-7α,6α-carbolactone (**20**)*
A mixture of **12** (500 mg, 1.11 mmol) in THF (11 ml) and methanol (11 ml) and sodium borohydride (126 mg, 3.33 mmol) was stirred at –10°C for 15 min, followed at room temperature for 2 h. Usual work up and flash chromatography of the crude product on silica gel eluted with ether–light petroleum (3:2) yielded **20** (292 mg, 63%), mp 213–215°C (dec.); Anal $C_{24}H_{21}NO_4S$ (C, H, N); λ_{max} (EtOH) 217 (log ε 4.15), and 259 nm (3.84); ν_{max} (Nujol) 3040, 1770, 1600, 1375, 1180, 980, 740, and 660 cm^{-1}; δ_H (90 MHz) 1.72 (3H, s, 9-Me), 2.32 (3H, s, ArMe), 2.45 (2H, m, 8-H_2), 3.18 (1H, m, 7-H), 3.78–4.03 (2H, m, 6a-H and 10a-H), 5.67 (1H, br s, 10-H), 6.11 (1H, d $J_{6,6a}$ 6.1 Hz, 6-H), 7.21–7.57 (5H, m, ArH), and 7.93–8.07 (3H, m, ArH); δ_c (22.5 MHz) 21.59 (ArMe), 24.16 (9-Me), 27.57 (C-8), 35.35 (C-10a), 38.17 (C-7), 44.56 (C-6a), 78.55 (C-6), 114.63 (C-4), 120.18 (C-1), 121.94 (C-10), 123.52 (C-2), 124.68 (C-10b), 125.60 (C-3), 127.71 (2 x C-2'), 129.91 (2 x C-3'), 133.21 (C-9), 133.32 (C-10c), 135.05 (C-1'), 135.60 (C-5a), 140.12 (C-4a), 145.16 (C-4'), and 177.69 (CO, ketone); *m/z* 419 (*M*+, 86%), 299 (24), 221 (100), 204 (90), and 91 (79).

*7β,9-Dimethyl-5-tosyl-5,6β,6aβ,7β,8,10aβ-hexahydroindeno-[2,1-b]indole-7α,6α-carbolactone (**21**)*
To a solution of freshly distilled diisopropylamine (0.1 ml, 0.72 mmol) in anhydrous THF (0.4 ml) at –10°C was added *n*-butyllithium (1.5 M in hexane, 0.48 ml, 0.72 mmol). The resulting mixture was stirred at less than 0°C for 15 min. To this freshly prepared lithium diisopropylamine (LDA) at –90°C was added dropwise the lactone (**20**) (200 mg, 0.48 mmol) in anhydrous THF (0.8 ml). After stirring at –78°C for 10 min, methyl iodide (0.12 ml, 1.92 mmol) was added. The resulting mixture was warmed to room temperature in 2 h, poured into aqueous ammonium chloride, and extracted with ether. Flash chromatography of the residue on silica gel eluted with ether–light petroleum (7:3) afforded **21** (175 mg, 84%) as white crystals (from dichloromethane–ether), mp 215–216°C; λ_{max} (EtOH) 215 (log ε 4.38), 260 (4.03), and 293 nm (3.51); ν_{max} (Nujol) 3030, 1760, 1600, 1385, 1180, 1020, and 710 cm^{-1}; δ_H (90 MHz) 1.47 (3H, s, 7-Me), 1.69 (3H, br s, 9-Me), 2.31 (3H, s, ArMe), 2.10 and 2.48 (2H, ABq, *J* 16.2 Hz, 8-H_2), 3.47 (1H, dd, $J_{6,6a}$ 6.4 Hz and $J_{6a,10a}$ 8.8 Hz, 6a-H), 3.75 (1H, br m, 10a-H), 5.62 (1H, br s, 10-H), 6.12 (1H, d, $J_{6,6a}$ 6.4 Hz, 6-H), 7.13–7.56 and 7.93–8.05 (8H, m, ArH); δ_c (22.5 MHz), 21.51 (ArMe), 23.84 (9-Me), 25.92 (7-Me), 36.27 (C-8), 43.72 (C-7), 53.17 (C-6a), 36.57 (C-10a), 72.28 (C-6), 114.74 (C-4), 120.16 (C-1), 122.05 (C-10), 123.54 (C-2), 124.84 (C-10b), 125.57 (C-3), 127.69 (2 x C-2'), 129.86 (2 x C-3'), 133.24 (C-10c), 134.08 (C-9), 135.35 (C-1'), 138.58 (C-5a), 140.34 (C-4a), 145.10 (C-4'), and 180.04 (CO); *m/z* 433 (*M*+, 53%), 389 (*M*–CO_2, 14), 299 (20), 234 (*M*–CO_2–$C_7H_7SO_2$, 82), 218 (69), 204 (53), and 91 (100).

*6α-Hydroxy-7α-hydroxymethyl-7β,9-dimethyl-5-tosyl-5,6β,6aβ,7β,8,10aβ-hexahydroindeno[2,1-b]indole (**22**)*
Following the procedure same as in the preparation of **14**, reduction of **21** (155.6 mg, 0.36 mmol) with lithium aluminium hydride yielded **22** (71 mg, 45%) as white solids, mp 180–182.5°C; λ_{max} (EtOH) 220 (log ε 4.75), 259 (4.34), and 298 nm (3.82), ν_{max} (Nujol) 3250, 1600, 1390, 1255, 1200, 790, and 710 cm^{-1}; δ_H (90 MHz) 1.09 (3H, s, 7-Me), 1.57 (1H, br d, *J* 15.3 Hz, 8-H), 1.65 (3H, br s, 9-Me), 2.31 (3H, s, ArMe), 2.58 (1H, m, 8-H), 2.69 (1H, m, 6a-H), 2.80 (2H, v br, exchangeable with D_2O, OH), 3.61 (H, m, 10a-H), 3.83 (2H, ABq, *J* 10.7 Hz, 7-CH_2), 5.54 (1H, d, *J* 6.1 Hz, 6-H), 5.58 (1H, br s, 10-H), 7.12–7.58 and 7.77–8.08 (8H, m, ArH); δ_c (22.5 MHz) 21.51 (ArMe), 24.08 (9-Me), 25.81 (7-Me), 37.00 (C-10a), 37.19 (C-8), 37.95 (C-7), 52.82 (C-6a), 70.97 (C-11), 71.83 (C-6), 114.68 (C-4), 119.75, 119.94 (C-1, C-10), 123.52 (C-2), 124.76 (C-3), 125.98 (C-10b), 126.98 (2 x C-2'), 129.91 (2 x C-3'), 130.88 (C-10c), 132.45 (C-9), 135.89 (C-1'), 140.07 (C-5a), 142.75 (C-4a), and 144.89 (C-4'); *m/z* 437 (*M*+, 65), 419 (*M*–H_2O, 17), 388 (*M*–H_2O–CH_2OH, 39), and 91 (100).

*7α-Benzyloxymethyl-6α-hydroxy-7β,9-dimethyl-5-tosyl-5,6β,6aβ,7,8,10aβ-hexahydroindeno[2,1-b]indole (**23**)*
Following the same procedure as in the preparation of **15**, benzylation of **22** (0.2 g, 0.46 mmol) with benzyl bromide gave **23** (210.9 mg, 87%) as a white solid, mp 168–170°C (from $CDCl_3$); Anal $C_{32}H_{33}NO_4S$ (C, H, N); λ_{max} (EtOH) 215 (log ε 4.50), and 260 nm (4.20); ν_{max} (Nujol) 3400, 3040, 3020, 1600, 1390, 1260, 1210, 1200, 1125, 1025, 790, 750, and 710 cm^{-1}; δ_H (90 MHz), 1.12 (3H, s, 7-Me), 2.21 (1H, br m, 8-H), 2.21 (3H, br s, 9-Me), 2.50 (1H, br m, 8-H), 2.62 (1H, br d, $J_{6,6a}$ 5.5 Hz, 6a-H), 2.96 (1H, d, $J_{6,OH}$ 5.0 Hz, exchangeable with D_2O, OH), 3.58 (1H, m, 10a-H), 3.54 and 3.79 (2H, ABq, *J* 8.8 Hz, 11-H_2), 4.64 (2H, s, 12-H_2), 5.48 (1H, dd, $J_{6,OH}$ 5.0 Hz, $J_{6,6a}$ 5.5 Hz, collapses to a d, *J* 5.5 Hz upon deuteriation, 6-H), 5.55 (1H, br s, 10-H), 7.02–7.51 and 7.79–8.03 (13H, m, ArH); δ_c (22.5 MHz) 21.34 (ArMe), 24.03 (9-Me), 26.11 (7-Me), 36.59 (C-10a), 37.14 (C-8), 37.81 (C-7), 52.66 (C-6a), 71.67 (C-12), 73.73 (C-6), 78.44 (C-11), 114.58 (C-4), 119.75, 119.91 (C-1, C-10), 123.30 (C-2), 124.44 (C-3), 126.06 (C-10b), 127.04 (2 x C-2'), 127.61 (C-4"), 127.77 (2 x C-2"), 128.44 (2 x C-3"), 129.96 (2 x C-3'), 130.53 (C-10c), 131.99 (C-9), 135.92 (C-1'), 138.58 (C-5a), 139.93 (C-1"), 143.29 (C-4a), and 144.56 (C-4').

*7α-Benzyloxymethyl-6β-indol-3'-yl-7β,9-dimethyl-5-tosyl-5,6α,6aβ,7,8,10aβ-hexahydroindeno[2,1-b]indole (**24**)*
To the alcohol **23** (192 mg, 0.365 mmol) and indole (53 mg, 0.438 mmol) in anhydrous THF (8 ml) was added freshly distilled BF_3·Et_2O (0.058 ml, 0.468 mmol). The resulting mixture was stirred at room temperature for 4 h, poured into aqueous $NaHCO_3$, and extracted with ether. Usual work-up and flash chromatography of the residue on silica gel eluted with ether–light petroleum (2:3) gave **24** (172 mg, 75%) as white solid, mp 104–105°C; λ_{max} (EtOH) 219 (log ε 4.75) and 266 nm (4.23); ν_{max} (Nujol) 3380, 3020, 1600, 1375, 1180, 790, and 770 cm^{-1}; δ_H (90 MHz) 1.23 (3H, s, 7-Me), 1.65 (3H, br s, 9-Me), 1.71 (1H, m, 8-H), 2.11 (3H, s, ArMe), 2.23 (1H, m, 8-H), 2.04 [1H, t (dd), $J_{6a,6}$ 3.6 Hz and $J_{6a,10a}$ 3.6 Hz, 6a-H], 3.08 and 3.27 (2H, ABq, *J* 8.8 Hz, 11-H_2), 4.00 (1H, br, 10a-H), 4.03 (2H, s, 12-H_2), 4.13 (1H, br d, $J_{6,6a}$ 3.5 Hz, 6-H), 5.73 (1H, br s, 10-H), 6.60–6.69 and 6.79–7.35 (16H, m, ArH), 7.56 (1H, dd, *J* 3.5 Hz and 6.0 Hz, ArH), 7.79 (1H, br s, NH), and 8.03 (1H, dd, *J* 3.5 Hz and 6.4 Hz, ArH); δ_c (22.5 MHz) 21.26 (ArMe), 23.97, 24.16 (7-Me, 9-Me), 37.49 (C-7), 37.79 (C-8), 37.79, 39.25 (C-6, C-10a), 59.67 (C-6a), 72.94 (C-12), 75.60 (C-11), 111.06 (C-7'), 114.82 (C-4), 118.50 (C-3'), 119.24, 119.43, 119.56 (C-1, C-4', C-5'), 120.70, 121.56, 122.68, 123.08 (C-2, C-10, C-2', C-6'), 123.52 (C-3), 126.06 (2 x C-2'), 126.06, 126.66 (C-3', C-10b), 127.06 (C-4'), 127.25 (2 x C-2'"), 128.07 (2 x C-3'"), 128.26 (C-10c), 128.85 (2 x C-3"), 132.10 (C-9), 136.30, 136.52 (C-7'a, C-1"), 139.04 (C-5a), 140.80 (C-1'"), 143.53 (C-4a), and 144.21 (C-4"); *m/z* 626 (*M*+, 2.9%), 471 (*M*–C_7H_7SO, 34), 249 (*M*–155–$PhCH_2OCH_2$, 30), 130 (28), 105 (25), and 91 (86).

*7α-Benzyloxymethyl-6β-indol-3'-yl-7β,9-dimethyl-5,6α,6aβ,7,8,10aβ-hexahydroindeno[2,1-b]indole, 7α-BM,7β-Me-YCK (**4**)*

Following the procedure same as in the preparation of **3**, detosylation of **24** (160.5 mg) with sodium amalgam afforded the YCK analogue **4** (103 mg, 85%) as white solid (Found: M^+, 472.2502. $C_{33}H_{32}N_2O$ requires M, 472.2515), mp 103–104°C; λ_{max} (EtOH) 222 (log ε 4.49), 280 (3.85), and 290sh nm (3.80); ν_{max} (Nujol) 3370, 3030, 1325, 1275, 1150, and 785 cm^{-1}; δ_H (90 MHz, C_6D_6) 1.35 (3H, s, 7-Me), 1.63 (3H, br s, 9-Me), 1.70 and 2.26 (2H, ABq, *J* 17.7 Hz, 8-H_2), 3.10 (2H, s, 12-H_2), 3.42 [1H, t (dd), $J_{6,6a}$ 8.0 Hz and $J_{6a,10a}$ 8.0 Hz, 6a-H], 3.56 and 3.72 (2H, ABq, *J* 12.0 Hz, 11-H_2), 4.01 (1H, m, 10a-H), 4.51 (1H, d, $J_{6,6a}$ 8.3 Hz, 6-H), 5.80 (1H, br s, 10-H), 6.46 and 6.68–7.30 (14H, m, ArH), 7.45 and 7.69 (2H, m, ArH); δ_c (22.5 MHz, C_6D_6) 24.08, 24.16 (7-Me, 9-Me), 37.05 (C-7), 38.11 (C-8), 37.05, 38.25 (C-6, C-10a), 58.72 (C-6a), 72.43 (C-12), 78.39 (C-11), 111.46 (C-7'), 112.08 (C-4), 117.88 (C-3'), 118.69, 119.34, 119.94 (C-1, C-2, C-4', C-5'), 120.29 (C-10b), 120.83, 122.29, 122.38 (C-10, C-2', C-6'), 124.33 (C-3), 124.84 (C-3'a), 127.17 (C-4"), 127.31 (2 x C-2"), 127.66 (C-10c), 128.26 (2 x C-3"), 128.80 (C-7'a), 136.54 (C-4a), 139.58 (C-5a), 140.74 (C-1"), and 145.56 (C-9); *m/z* 472 (M^+, 35%), 317 (27), 267 (35), 217 (32), 212 (41), 182 (2), 162 (100), 151 (34), 132 (32), 113 (71), and 91 (20).

*7α-Benzyloxymethyl-7β,9-dimethyl-6β-dimethyl-6β-(2'-methylindol-3'-yl)-5-tosyl-5,6α,7,8,10aβ-hexahydroindeno[2,1-b]indole (**25**)*

Adopting a procedure same as in the preparation of **24**, condensation of **23** (192 mg, 0.365 mmol) with 2-methylindole gave **25** (201 mg, 87%), as pale yellow solids, mp 105–107°C; λ_{max} (EtOH) 220 (log ε 4.57), and 265 nm (4.08); ν_{max} (Nujol) 3370, 3020, 1615, 1380, 1150, 850, and 720 cm^{-1}; δ_H (90 MHz) 1.15 (3H, s, 7-Mc), 1.66 (3H, s, 9-Mc), 1.89 (1H, br m, 8-H), 2.04 (3H, s, ArMe), 2.14 (br m, 8-H), 2.38 (3H, s, 2'-Me), 3.27 (1H, m, 6a-H), 3.18 (2H, ABq, *J* 8.8 Hz, 11-H_2), 4.01 (1H, m, 10a-H), 4.12 (2H, ABq, 12-H_2), 4.73 (1H, d, $J_{6,6a}$ 5.5 Hz, 6-H), 5.68 (1H, br s, 10-H), 6.43–6.65 and 6.76–7.35 (15H, m, ArH), 7.59 and 7.99 (2H, m, ArH), and 7.65 (1H, br s, NH); δ_c (22.5 MHz), 12.35 (2'-Me), 21.18 (ArMe), 23.67 and 24.00 (7-Me, 9-Me), 36.97 (C-7), 37.62 (C-8), 37.62, 38.68 (C-6, C-10a), 57.15 (C-6a), 72.89 (C-12), 76.66 (C-11), 110.13 (C-7'), 112.60 (C-3'), 114.63 (C-4), 118.72, 119.02, 120.02 (C-1, C-4', C-5'), 121.38, 122.97, 123.35 (C-2, C-10, C-6'), 125.00 (C-3), 125.79 (C-10b), 127.09 (2 x C-2" and C-4'"), 127.47 (C-3'a), 127.98 (2 x C-2'"), 128.07 (C-10c and 2 x C-3'"), 128.61 (2 x C-3"), 131.37 (C-9 and C-2'), 135.30, 135.73 (C-7'a, C-1"), 138.82 (C-5a), 140.77 (C-1'"), 143.10 (C-4a), and 143.88 (C-4"); *m/z* 640 (M^+, 12%), 519 (M–$PhCH_2OCH_2$, 16), 485 (M–$C_7H_7SO_2$, 20), 234 (23), 144 (30), 130 (30), and 981 (100).

*7α-Benzyloxymethyl-7β,9-dimethyl-6β-(2'-methylindol-3'-yl)-5,6α,6aβ,7,8,10aβ-hexahydroindeno[2,1-b]indole, 2',7β-DiMe-7α-BM-YCK (**6**)*

By the same procedure as in the preparation of **3**, detosylation of **25** (200 mg) with sodium amalgam afforded the YCK analogue **6** (Found: M^+, 486.2657. $C_{34}H_{34}N_2O$ requires *M*, 486.2671) (124 mg, 82%) as white solids, mp 127–128°C; λ_{max} (EtOH) 226 (log ε 4.81), 280 (4.19), and 290 nm (4.15); ν_{max} (Nujol) 3360, 3040, 1610, 1225, 1110, 785, and 740 cm^{-1}; δ_H (90 MHz, C_6D_6) 1.34 (3H, s, 7-Me), 1.63 (3H, br s, 9-Me), 1.76 (3H, s, 2'-Me), 2.00 (2H, ABq, *J* 23.6 Hz, 8-H_2), 3.09 (2H, s, 12-H_2), 3.54 (1H, m, 6a-H), 3.57 (2H, ABq, *J* 11.8 Hz, 11-H_2), 4.01 (1H, br m, 10a-H), 4.46 (1H, d, *J* 9.0 Hz, 6-H), 5.77 (1H, br s, 10-H), 6.34 (1H, br s, NH), 6.44 (1H, br s, NH), 6.86–7.25 (11H, m, ArH), 7.37 and 7.71 (2H, m, ArH); δ_c (22.5 MHz) 12.05 (2'-Me), 23.94, 24.13 (7-Me, 9-Me), 36.46, 38.17 (C-6, C-10a), 37.14 (C-7), 38.03 (C-8), 57.18 (C-6a), 72.38 (C-12), 78.42 (C-11), 110.51 (C-7'), 112.00 (C-4), 112.30 (C-3'), 118.64, 118.96, 119.80 (C-1, C-4', C-5'), 119.91 (C-10b), 120.46, 120.70, 121.21 (C-2, C-10, C-6'), 124.46 (C-3), 124.92 (C-3'a), 127.31 (C-10c and C-4"), 128.01 (2 x C-3"), 128.63 (C7'a), 131.26 (C-2'), 135.51 (C-4a), 139.60 (C-5a), 140.66 (C-1"), 144.94 (C-9), and 128.17 (2 x C-2"); *m/z* 486 (M^+, 100%), 395 (M–C_7H_7, 32), 365 (M–$PhCH_2OCH_2$, 83), 234 (86), 144 (57), and 91 (52).

*7α-Methoxycarbonyl-9α-methyl-6-oxo-5-tosyl-5,6,6aβ-7β,8,9β-10aβ-octahydroindeno[2,1-b]indole (**26**)*

A mixture of the ketoester (**12**) (0.2 g, 0.45 mmol) and Adam's catalyst in THF (3 ml) was hydrogenated at 40 psi for 2 h. The mixture was filtered and after removal of solvent, the filtrate gave a white powder. Chromatography of the crude product on silica gel eluted with ether–light petroleum (1:1) afforded **26** (202 mg, 99%) as white crystals (from ether–dichloromethane), mp 154–155°C; Anal $C_{25}H_{25}NO_5S$ (C, H, N); λ_{max} (EtOH) 224 (log ε 4.26), 242 (4.14), and 290 nm (4.31); ν_{max} (Nujol) 3040, 1740, 1710, 1600, 1370, 1090, and 670 cm^{-1}; δ_H (270 MHz) 0.496 [1H, dt (ddd), $J_{9,10}$ 11.96 Hz, $J_{10,10a}$ 11.96 Hz and $J_{10,10}$ 13.19 Hz, axial 10-H], 0.855 (3H, d, *J* 6.35 Hz, 9-Me), 1.068 [1H, dt (ddd), $J_{8,9}$ 11.96 Hz, $J_{7,8}$ 11.96 Hz and $J_{8,8}$ 12.2 Hz, 8-H], 1.559 (1H, br m, 9-H), 1.992 (1H, br d, $J_{8,8}$ 13.67 Hz, 8-H), 2.272 (1H, br d, $J_{10,10}$ 13.35 Hz, 10-H), 2.356 (3H, s, ArMe), 2.742 (1H, ddd, $J_{7,eq\text{-}8}$ 3.9 Hz, $J_{6a,7}$ 6.35 Hz and $J_{7,8}$ 12.70 Hz, 7-H), 3.487 [1H, dt (ddd), $J_{6a,10a}$ 5.86 Hz, $J_{10a,10}$ 5.86 Hz and $J_{10a,10}$ 11.23 Hz, 10a-H], 3.745 [1H, t (dd), $J_{6a,10a}$ 5.98 Hz and $J_{6a,7}$ 5.98 Hz, 6a-H], 3.825 (3H, s, OMe), 7.242 (2H, 1/2ABq, 2 x 3'-H), 7.325 (1H, t, *J* 7.2 Hz, 2-H), 7.515 (1H, t, *J* 7.94 Hz, 3-H), 7.613 (1H, d, *J* 7.61 Hz, 1-H), 7.989 (2H, 1/2ABq, *J* 8.3 Hz, 2 x 2'-H), and 8.256 (1H, d, *J* 8.79 Hz, 4-H); δ_c (22.5 MHz) 21.53 (ArMe), 21.97 (9-Me), 30.15 (C-9), 32.69 (C-8), 34.13 (C10a), 41.31 (C-10), 41.58 (C-7), 51.76 (OMe), 53.82 (C-6a), 115.58 (C-4), 121.51 (C-1), 124.00 (C-2), 124.25 (C-10b), 127.36 (2 x C-2'), 128.96 (C-3), 129.83 (2 x C-3'), 135.54 (C-10c and C-1'), 142.58 (C-5a), 145.16 (C-4'), 155.96 (C-4a), 173.73 (7-CO, ester), and 188.85 (C-10, ketone;); δ_c (67.6 MHz) 21.64 (ArMe), 21.99 (9-Me), 30.27 (C-9), 32.67 (C-8), 34.20 (C-10a), 41.41 (C-10), 41.62 (C-7), 51.92 (OMe), 53.80 (C-6a), 115.64 (C-4), 121.41 (C-1), 123.92 (C-2), 124.21 (C-10b), 127.47 (2 x C-2'), 128.96 (C-3), 129.88 (2 x C-3'), 135.49, 135.53 (C-10c, C-1'), 142.52 (C-5a), 145.14 (C-4'), 155.69 (C-4a), 173.85 (7-CO, ester), and 188.83 (C-6), ketone); *m/z* 451 (M^+, 23%, 268 (33), 236 (M–$C_7H_7SO_2$–CH_3OH–CO, 79), 208 (59), 167 (33), 116 (25), and 91 (100).

*6α-Hydroxy-7α-hydroxymethyl-9α-methyl-5-tosyl-5,6β,6aβ,7β,8,9β,10,10aβ-octahydroindeno[2,1-b]indole (**27**)*

Following a procedure similar to the preparation of **14**, lithium aluminium hydride reduction of **26** (200 mg) afforded the diol **27** (68 mg, 36%) as white solids (67.5 mg, 36%), mp 101–102°C; λ_{max} (EtOH) 222 (log ε 4.33), and 254 nm (4.03); ν_{max} (Nujol) 3380, 3030, 1600, 1370, 1180, 740, and 680 cm^{-1}; δ_H [270 MHz, $(CD_3)_2CO$–D_2O] 0.921 (3H, d, $J_{9,Me}$ 6.34 Hz, 9-Me), 1.625–0.965 (4H, m, 8-H_2, equatorial 10-H, and 9-H), 2.182 (2H, m, 7-H, and axial 10-H), 2.313 (3H, s, ArMe), 2.789 (1H, q (ddd), $J_{6a,6}$ 5.86 Hz, $J_{6a,7}$ 5.86 Hz, and $J_{6a,10a}$ 5.86 Hz, 6a-H], 3.000 [1H, dt (ddd), $J_{6a,10a}$ 6.35 Hz, $J_{10a,eq\text{-}10}$ 6.35 Hz and $J_{10a,ax\text{-}10}$ 12.69 Hz, 10a-H], 3.950 (1H, dd, $J_{7,11}$ 5.37 Hz and $J_{11,11}$ 10.50 Hz), 4.049 (1H, dd, $J_{7,11}$ 6.35 Hz and $J_{11,11}$ 10.50 Hz, 11-H), 5.717 (1H, d, $J_{6,6a}$ 5.86 Hz, 6-H), 7.179–7.320 (4H, m, 2-H, 3-H, and 2 x 3'-H), 7.510 (1H, d, *J* 7.81 Hz, 1-H), 7.956–8.016 (3H, m, 2 x 2'-H and 4-H); δ_c

[22.5 MHz, $(CD_3)_2CO$] 21.37 (ArMe), 22.94 (9-Me), 33.13 (C-9), 36.35 (C-8), 39.09 (C-10a), 41.79 (C-10), 42.39 (C-7), 50.49 (C-6a), 65.77 (C-11), 72.32 (C-6), 115.28 (C-4), 120.78 (C-1), 124.11 (C-2), 124.92 (C-32), 128.07 (2 x C-2'), 130.53 (2 x C-3'), 127.23 (C-10b), 135.08 (C-10c), 136.38 (C-1'), 140.31 (C-5a), 145.27 (C-4a), and 145.83 (C-4'); *m/z* 425 (M^+, 38%), 407 (M–H_2O, 53), 270 (M–$C_7H_7SO_2$, 49), 252 (M–H_2O–$C_7H_7SO_2$, 42), 222 (43), 180 (42), 168 (33), 167 (37), 130 (62), and 91 (100).

7α-Benzyloxymethyl-6α-hydroxy-9α-methyl-5-tosyl-5,6β,6aβ,7β,8,9β,10,10aβ-octahydroindeno[2,1-b]indole (28)
Adopting a procedure similar to the preparation of **15**, the diol (**27**) (370 mg) yielded **28** (409 mg, 90%) as white crystals (from ether–dichloromethane), mp 159.5–160°C; Anal $C_{31}H_{33}NO_4S$ (C, H, N); λ_{max} (EtOH) 216 (log ε 4.26), and 257 nm (397); ν_{max} (Nujol) 3500, 3080, 1600, 1380, 1190, 1060, 780, and 710 cm^{-1}; δ_H (90 MHz) 0.93 (3H, d, *J* 5.5 Hz, 9-Me), 1.11–1.56 (4H, m, 8-H_2, 9-H, and equatorial 10-H), 2.07–2.24 (2H, m, 7-H, and axial 10-H), 2.32 (3H, s, ArMe), 2.76 (1H, m, 6a-H), 2.98 (1H, m, 10a-H), 3.36 (1H, d, *J* 2.9 Hz, exchangeable with D_2O, OH), 3.85 (2H, m, 11-H_2), 4.64 (2H, s, 12-H_2), 5.47 (1H, dd, $J_{6\text{-OH}}$ 2.9 Hz and $J_{6,6a}$ 5.3 Hz, collapses to d, *J* 5.5 Hz upon deuteriation, 6-H), 7.12–7.48 and 7.83–8.01 (13H, m, ArH); δ_c (22.5 MHz) 21.45 (ArMe), 22.37 (9-Me), 32.34 (C-9), 35.70 (C-8), 38.41 (C-10a), 39.49 (C-7), 41.01 (C-10), 49.08 (C-6a), 71.73 (C-6), 73.57, 73.73 (C-11, C-12), 114.41 (C-4), 119.83 (C-1), 123.14 (C-2), 124.17 (C-3), 126.17 (C-10b), 127.04 (2 x C-2'), 127.14 (C-4"), 128.01 (2 x C-2"), 128.50 (2 x C-3"), 129.64 (2 x C-3'), 133.97 (C-11c), 135.65 (C-1'), 138.14 (C-5a), 139.44 (C-1"), 143.61 (C-4a), and 144.53 (C-4'); *m/z* 515 (M^+, 56%), 406 (M–H_2O–C_7H_7, 49), 268 (15), and 91 (100).

6α-Benzoyloxy-7α-benzyloxymethyl-9α-methyl-5-tosyl-5,6β,6aβ,7β,8,9β,10,10aβ-octahydroindeno[2,1-b]indole (29)
Following a procedure similar to the preparation of **16**, benzoylation of **28** (215 mg) gave **29** (215 mg 83%) as colourless prisms (from ether–dichloromethane), mp 158–159°C; λ_{max} (EtOH) 220 (log ε 4.25), and 257 nm (3.91); ν_{max} (Nujol) 3060, 3030, 1710, 1660, 1280, 1150, and 710 cm^{-1}; δ_H (90 MHz) 0.92 (3H, d, *J* 6.1 Hz, 9-Me), 1.01–1.65 (4H, m, 8-H_2, 9-H, and equatorial 10-H), 2.19 (3H, s, ArMe), 2.28 (2H, m, 7-H, and axial 10-H), 2.35–3.09 (2H, m, 10a-H and 6a-H), 3.52 (1H, ABdd, *J* 9.0 Hz, 11-H), 3.61 (1H, ABdd, *J* 9.2 Hz, 11-H), 4.52 and 4.76 (2H, ABq, *J* 11.6 Hz, 12-H_2), 6.91–7.64 (4H, ABq, *J* 7.9 Hz, 2 x 2'-H and 2 x 3'-H), 7.10 (1H, d, *J* 4.8 Hz, 6-H), 7.22–7.69 and 7.90–8.13 (14H, m, ArH), δ_c (22.5 MHz) 21.40 (ArMe), 22.54 (9-Me), 31.80 (C-9), 34.83 (C-8), 38.08 (C-10a), 39.17 (C-10), 41.17 (C-7), 48.11 (C-6a), 72.43 (C-6), 73.03, 73.30 (C-11, C-12), 114.96 (C-4), 119.99 (C-1), 123.41 (C-2), 125.03 (C-3), 125.57 (C-10b), 126.49 (2 x C-2'), 127.42 (2 x C-2'"), 127.90 (2 x C-3"), 128.28 (2 x C-3'" and C-4'"), 129.64 (2 x C-2"), 129.85 (2 x C-3'), 130.50 (C-1"), 132.78 (C-4"), 135.70 (C-1'), 137.49 (C-10c), 138.85 (C-5a), 139.82 (C-1'"), 140.25 (C-4a), 144.48 (C-4'), and 164.96 (CO); *m/z* 619 (M^+, 0.31%), 377 (23), 376 (89), 222 (30), 220 (21), 122 (96), 105 (68), and 91 (100).

7α-Benzyloxymethyl-6β-indol-3'-yl-9α-methyl-5-tosyl-5,6α,6aβ,7β,8,9β,10,10aβ-octahydroindeno[2,1-b]indole (30)
Following a procedure similar to the preparation of **17**, reaction of **29** (356 mg) with indolylmagnesium bromide afforded **30** (186 mg, 53%) as white powder, mp 129–130°C; ν_{max} (Nujol) 3400, 3040, 1590, 1240, 1180, 1090, and 675 cm^{-1}; δ_H (90 MHz, C_6D_6) 0.57 (1H, m, axial 8-H), 0.81 (3H, d, *J* 6.1 Hz, 9-Me), 0.94 (1H, m, axial 10-H), 1.10 (1H, m, equatorial 8-H), 1.30 (1H, m, 9-H), 1.75 (3H, s, ArMe), 1.90 (2H, m, 7-H and equatorial 10-H), 3.08 (3H, m, 10a-H and 11-H_2), 3.57 (1H, m, 6a-H), 3.86 (2H, ABq, *J* 12.0 Hz, 12-H_2), 4.89 (1H, d, *J* 8.8 Hz, 6-H), 6.29 (2H, 1/2ABq, *J* 8.3 Hz, ArH), 6.68 (1H, d, *J* 2.2 Hz, 2'-H), 6.74–7.50 (14H, m, ArH), and 8.412 (1H, m, ArH); δ_c (22.5 MHz, C_6D_6) 21.05 (ArMe), 22.64 (9-Me), 30.77 (C-9), 34.62 (C-8), 38.22, 38.68 (C-6, C-10a), 41.01 (C-7 and C-10), 53.63 (C-6a), 72.78, 74.14 (C-11, C-12), 111.46 (C-7'), 115.66 (C-4), 117.77 (C-3'), 119.34, 119.61, 120.13, 121.27 (C-1, C-4', C-5', C-6'), 123.49, 123.89 (C-2, C-2'), 124.14 (C-3), 125.84 (2 x C-2"), 126.74 (C-3'a), 127.31 (C-10b and C-4'"), 127.77 (2 x C-2'"), 128.28 (2 x C-3'"), 128.99 (2 x C-3"), 132.37 (C-10a), 136.65 (C-1"), 136.90 (C-7'a), 139.33 (C-5a), 141.55 (C-1'"), 143.10 (C-4a), and 144.91 (C-4");; *m/z* 614 (M^+, 2%), 459 (M–$C_7H_7SO_2$, 21), 407 (22), 181 (100), 103 (21), and 91 (68).

7α-Benzyloxymethyl-6β-indol-3'-yl-9α-methyl-5,6α,6aβ,7β,8,-9β,10,10aβ-octahydroindeno[2,1-b]indole, 9,10-DiH-7-nor-7α-BM-YCK (8)
Following a same procedure same as in the preparation of **3**, detosylation of **30** (158 mg) afforded 9,10-DiH-7-nor-7α-BM-YCK **8** (95.9 mg, 81%) as a white amorphous solid, mp 225–226°C (dec) (Found: M^+, 460.2520. $C_{32}H_{32}N_2O$ requires M, 460.2513); λ_{max} (EtOH) 224 (log ε 4.56), and 282 nm (4.08); ν_{max} (Nujol) 3410, 3380, 1090, 750, and 740 cm^{-1}; δ_H [90 MHz, $CDCl_3$–$(CD_3)_2CO$] 0.73 (1H, m, axial 10-H), 0.93 (3H, d, *J* 6.1 Hz, 9-Me), 1.07 (1H, m, axial 8-H), 1.48 (1H, br m, 9-H), 1.80 (1H, br d, *J* 11.4 Hz, equatorial 8-H), 2.12 (2H, m, 7-H and equatorial 10-H), 3.16 (2H, br d, *J* 7.4 Hz, 11-H_2), 3.28–3.58 (2H, m, 6a-H and 10a-H), 3.82 (2H, s, 12-H_2), 4.55 (1H, d, $J_{6,6a}$ 10.0 Hz, 6-H), 7.05 (1H, d, *J* 2.4 Hz, 2'-H), 6.84–7.54 (13H, m, ArH), 7.99 (1H, br s, 5-H), and 8.77 (1H, br s, 1'-H); δ_c [22.5 MHz, $CDCl_3$–$(CD_3)_2CO$] 22.59 (9-Me), 31.15 (C-9), 34.97 (C-8), 35.40 (C-6), 39.36 (C-10a), 41.17 (C-7), 41.26 (C-10), 54.09 (C-6a), 72.62, 74.27 (C-11, C-12), 111.46, 111.76 (C-4, C-7'), 116.93 (C-3'), 118.53, 119.37, 119,51 (C-1, C-2, C-4', C-5'), 120.35, 121.92, 122.81 (C-3, C-2', C-6'), 123.65 (C-10b), 124.38 (C-3'a), 127.20 (C-4" and C-10c), 127.69 (2 x C-2"), 128.15 (2 x C-3"), 136.87 (C-7'a), 138.82 (C-5a), 140.25 (C-1"), and 145.43 (C-4a); *m/z* 460 (M^+, 100%), 369 (M–$PhCH_2$, 62), 283 (2), 269 (15), 257 (15), 130 (33), and 91 (23).

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