SYNTHETIC STUDIES ON INDOLE ALKALOIDS. IV.[1] STUDIES OF *N*-PHENYLSULFONYL-2-METHYLINDOLES ON INTRAMOLECULAR CYCLIZATIONS

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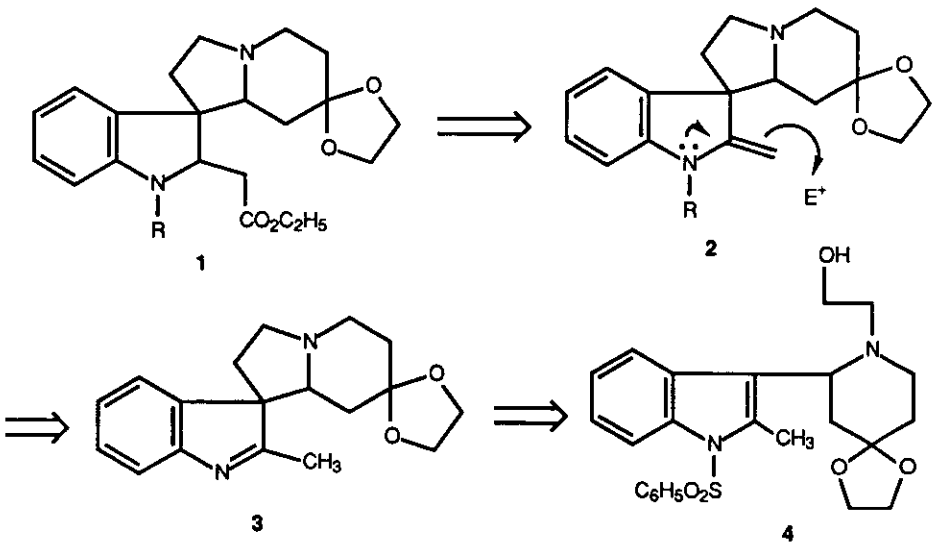
Abstract--The synthesis of 1-(2-hydroxyethyl)-2-[2-methyl-*N*-(phenylsulfonyl)-2-indolyl]-4-piperidone ethylene ketal (4) by two alternative ways and the study of its intramolecular cyclization using potassium *tert*-butoxide are reported.

Following our interest in the intramolecular cyclization of N_b-(hydroxyethyl)piperidyl-N_a-(phenylsulfonyl)indoles by the action of potassium *tert*-butoxide[2-6] we have proposed a related process using a starting piperidylindole which has a methyl group at the indole C-2 position. Thus, such intramolecular cyclization would lead to spiroindolenine (3) which by means of imine–enamine equilibrium and *via* acylation of **2** would provide spiroindoline (**1**). A similar spiroindoline with an acetate chain at the C-2 position of indoline ring has previously been reported by Wenkert *et al.*[7,8] as a potential synthetic intermediate to *Aspidosperma* and *Strychnos* alkaloids.

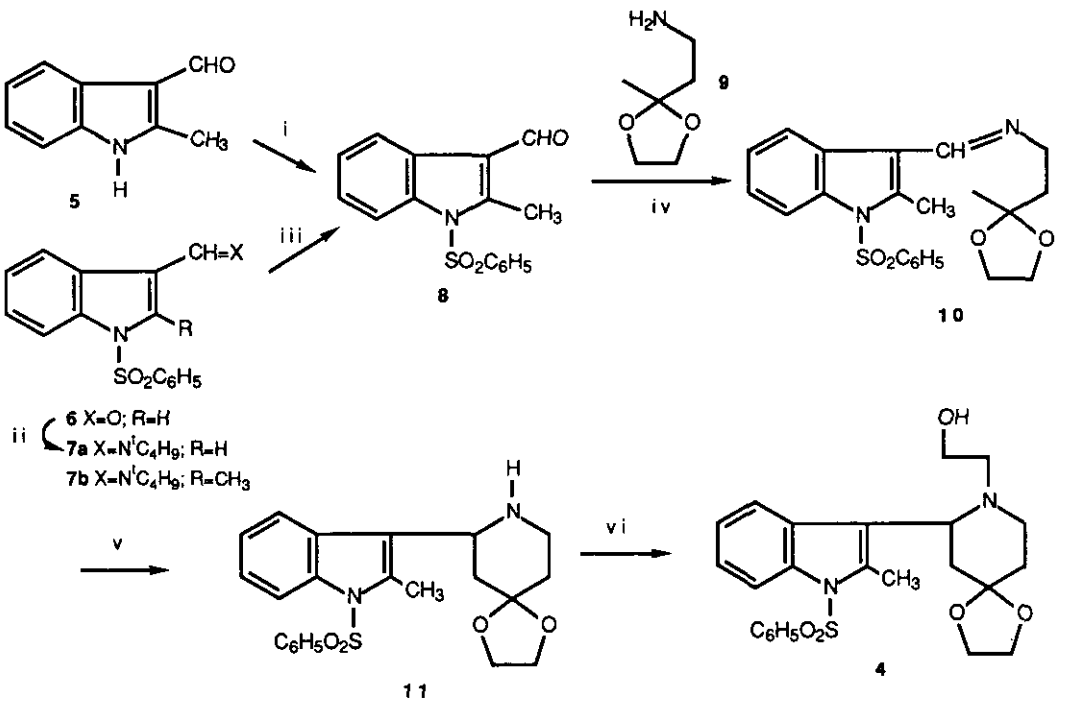


Scheme 1

Moreover, a similar acylation of a 2-methyl-3-spiroindolenine with trifluoroacetic anhydride *via* an enamine intermediate has also been reported.[9,10] More recently, *N*-(*p*-methoxyphenylsulfonyl)-2-methylindoles have been used by Magnus *et al.* [11,12] as intermediates of [ABCD] framework of *Aspidosperma* alkaloids *via* intramolecular cyclization of indole-2,3-quinodimethanes.

In the present paper we report the latest results obtained in the studies of the intramolecular cyclization of 1-(2-hydroxyethyl)-2-[2-methyl-1-(phenylsulfonyl)-3-indolyl]-4-piperidone ethylene ketal (**4**) by the action of potassium *tert*-butoxide.

The starting *N*-hydroxyethylpiperidine (**4**) was prepared by alkylation of piperidine (**11**) with 2-bromoethanol in the presence of anhydrous potassium carbonate. The secondary piperidine (**11**) was initially obtained by an intramolecular Mannich reaction of iminoketal (**10**) according to our general procedure for the synthesis of 2-



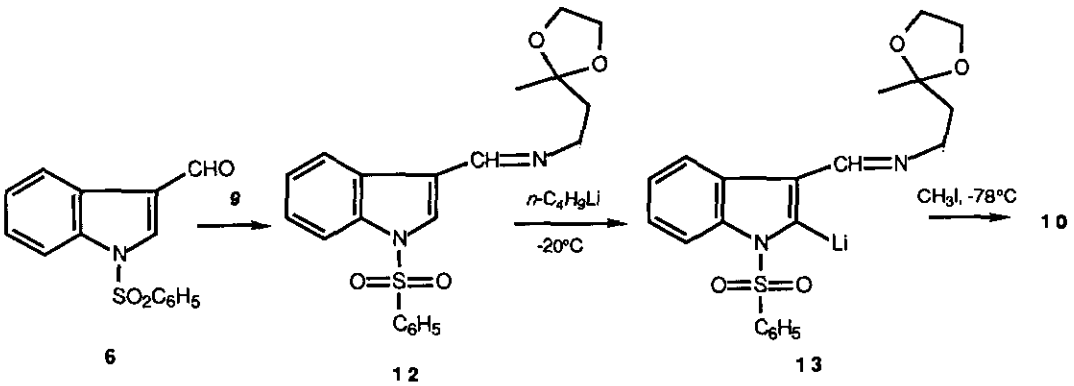
Reagents and Conditions: i) benzene, $C_4H_9N^+HSO_4^-$, 50% NaOH, $ClSO_2C_6H_5$, room temperature, 21 h. ii) *t*-$C_4H_9NH_2$, anhyd. Na_2SO_4, 4Å sieves, CH_2Cl_2, room temperature,1 h, and Δ ,18 h; or *t*-$C_4H_9NH_2$, dry benzene, room temperature, 1 h, Δ, 2 h, and Dean-Stark 16 h. iii) 1. *n*-C_4H_9Li, THF, -15°C, 30 min; CH_3I -78°C; 2. H_3O^+ or silica gel. iv) dry benzene, 30 min at 0°C, 6h Δ, 16 h Dean-Stark. v) *p*-TsOH, dry benzene, Δ, 1 h. vi) $BrCH_2CH_2OH$, K_2CO_3, C_2H_5OH, Δ, 15 h.

Scheme 2

aryl-4-piperidone ethylene ketals.[13-18] Thus, condensation between 2-methyl-1-phenylsulfonyl-3-indolylcarbaldehyde (**8**) and the primary amine (**9**), furnished the corresponding imine (**10**), which by acid cyclization was led to the expected piperidine (**11**) in 72% yield.

The indolylcarbaldehyde (**8**) was prepared by two alternative routes consisting of the protection of the indole nitrogen atom of commercially available aldehyde (**5**) with benzenesulfonyl chloride or of chemoselective lithiation of the indole C-2 position[11] of **7a**, obtained from 1-phenylsulfonyl-3-indolylcarbaldehyde (**6**)[19] and *tert*-butylamine, by the action of *n*-butyllithium at -78°C followed by methyl iodide alkylation.

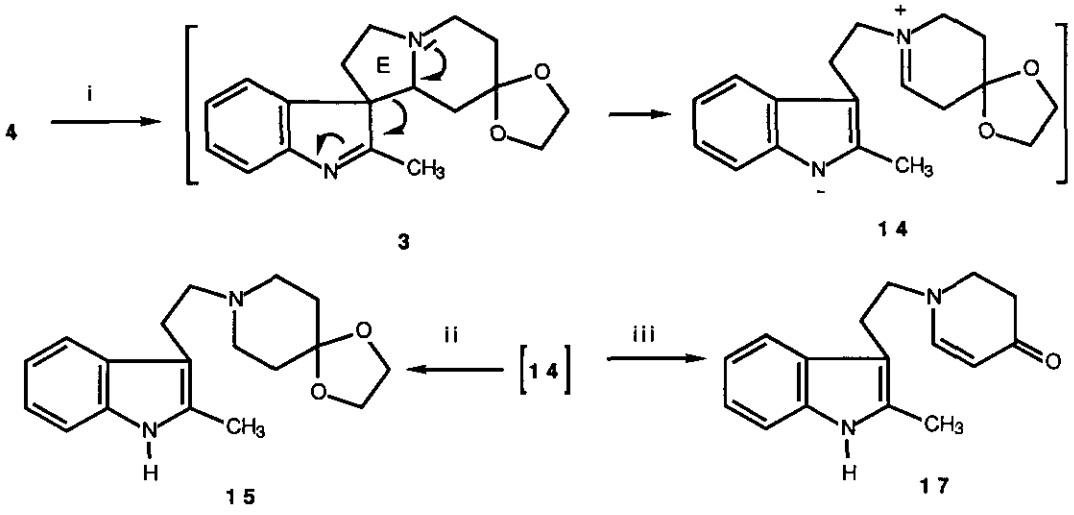
An alternative way to obtain imine (**10**) was developed as an extension of the method reported by Magnus *et al.*[11] Thus, alkylation of the indole 2-position has been carried out directly upon imine (**12**),[3] by lithiation with *n*-butyllithium followed by addition of methyl iodide upon intermediate (**13**).



Scheme 3

Hydroxyethylpiperidine (**4**) was submitted to potassium *tert*-butoxide treatment (2 eq., dry THF, 0°C, 3 h, argon atmosphere), leading to the indolenine intermediate (**3**) which was further reduced with $NaBH_4$. In this reaction only the *N*-indolylethylpiperidine (**15**) was isolated in 31 % yield, resulting from the reduction of tetrahydropyridinium salt (**14**) generated by ring opening of **3** such as shown in Scheme 4.

Alternatively, when spiroindolenine (**3**) obtained by the action of potassium *tert*-butoxide was treated *in situ* with a solution of 4*N* HCl in methanol, enaminone (**16**) was obtained in 23% yield. The same compound (**16**) was previously reported by Winterfeld[20] by reduction of 4-methoxy-1-(2-methyl-3-indolyl)ethylpyridinium bromide.

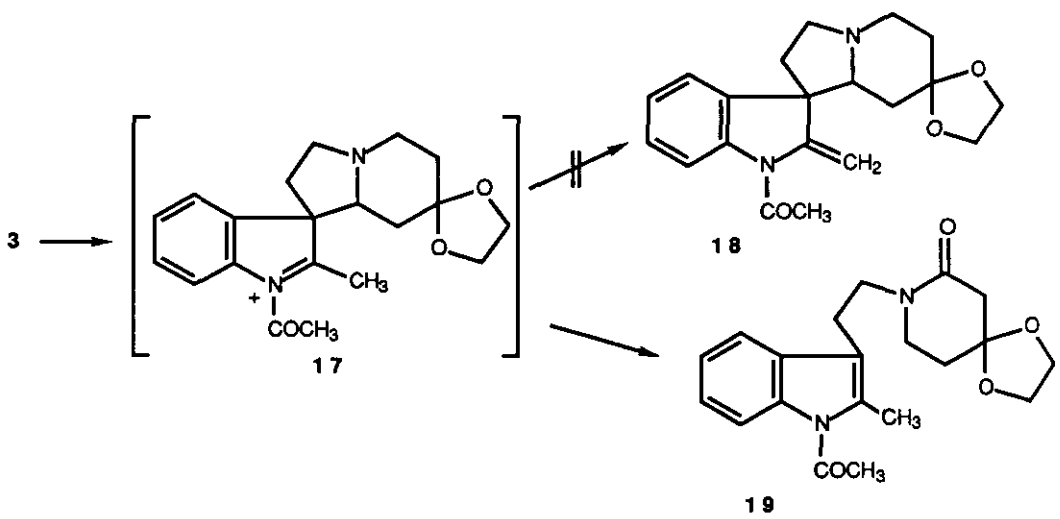


Reagents and Conditions: i) *t*-C_4H_9OK, THF, 0°C, 30 min. ii) $NaBH_4$, THF, Δ, 12 h. iii) 4*N* HCl, CH_3OH, Δ, 3 h.

Scheme 4

In order to avoid the competitive reaction of E ring opening an alternative process was assayed consisting of the acylation of spiroindolenine (**3**) to isolate the exocyclic enamide. Thus, by treatment of **3** with acetyl chloride in the presence of triethylamine, lactam (**19**) was obtained, compound (**18**) not being detected. Formation of **19** can be rationalized by considering an oxidation of the intermediate iminium salt as already observed in analogous cases.[21]

With this study we make clear that the preparation of spiroindoline (**1**) cannot be carried out from 2-methylspiroindolenine (**3**), since in this case the ring opening, promoted by the nitrogen (N_b) electron lone pair which leads to the iminium salt, is much quicker than the tautomeric imine–enamine equilibrium, even in the case in which the indolenine nitrogen atom is acylated.



Scheme 5

EXPERIMENTAL

General. Melting points were determined in a capillary tube on a Büchi apparatus and are uncorrected. ^{1}H- and ^{13}C-nmr spectra were recorded in $CDCl_3$ (unless otherwise indicated) on a Varian Gemini-200 spectrometer using TMS as an internal standard. Chemical shifts are reported in ppm downfield (δ) from TMS. Ir spectra were registered with a Perkin-Elmer 1430 spectrophotometer and only noteworthy absorptions (reciprocal centimeters) are listed. Mass spectra were determined on a Hewlett-Packard 5930A mass spectrometer. Tlc was carried out on SiO_2 (silica gel 60, Merck 0.0063-0.200 mm), and the spots were located with uv light or iodoplatinate reagent. Flash column chromatography was carried out on SiO_2 (silica gel 60, 0.040-0.063 mm, Macherey Nagel). Drying of organic extracts during workup of reaction mixtures was performed over anhydrous sodium sulfate. Microanalyses were performed on a Carlo-Erba 1106 analyzer by Departament de Química Orgànica Biològica, Barcelona.

2-Methyl-1-(phenylsulfonyl)-3-indolylcarbaldehyde (8). Method A. To a mixture of 2-methyl-3-indolylcarbaldehyde (5) (3 g, 18.86 mmol), benzene (180 ml), tetrabutylammonium bisulfate (226 mg, 0.66 mmol), and 50% aqueous NaOH (60 ml) was added benzenesulfonyl chloride (3.64 ml, 28.3 mmol). After being stirred at room temperature for 15 h, the organic layer was separated and washed with brine (3 x 30 ml), dried, and evaporated to give aldehyde(8)(3.8 g, 69%) as a solid after flash chromatography (Et_2O): mp 153-155 °C (Et_2O); ir (KBr) 1660 (CO); ^{1}H nmr 2.93 (s, 3H, CH_3), 7.00-8.40 (m, 9H, ArH), 10.27 (s, 1H, CHO); ^{13}C nmr 12.3 (CH_3), 113.9 (Ind.-C7), 121.3 (Ind.-C4), 125.1 (Ind.-C5), 125.6 (Ind.-C6), 126.1 (Ind.-C2), 126.4 (Ar-ortho), 126.5 (Ar-

meta), 129.3 (Ar-C3a), 129.4 (Ar-*para*), 129.7 (Ind.-C7a), 134.6 (Ar-*ipso*), 147.7 (Ind.-C3), 185.8 (CHO); ci ms (*m/z*, %) 317 (M^++18, 48), 272 (39), 194 (42), 177 (100), 123 (9). Anal. Calcd for $C_{16}H_{13}NO_5S$: C, 64.19; H, 4.38; N, 4.68. Found: C, 64.36; H, 4.42; N, 4.54.

Method B. To a THF solution (40 ml) of imine(**7a**) (395 mg, 1.16 mmol), prepared from aldehyde (**6**)(330 mg, 1.16 mmol) and excess of *t*-$C_4H_9NH_2$ in dry benzene was added *n*-C_4H_9Li (1.6 *M*, 0.87 ml, 1.39 mmol) at -15°C. After stirring for 1 h 15 min at -15°C, the mixture was cooled to -78°C and CH_3I (0.086 ml, 1.39 mmol) was added. After warming to room temperature the mixture was stirred for 5 h, then poured into water, and the product was extracted with ether. The combined extracts were dried and evaporated to give imine(**7b**)(225 mg, 55 %) as a white solid, mp 113-114°C (hexane-ether): ^{1}H nmr 1.29 (s, 9H, CH_3), 2.75 (s, 3H, Ind.-CH_3), 7.20-7.50 (m, 4H, Ind.-H), 7.80-8.00 (m, 2H, Ind.-H), 8.22 (m, 1H, Ind.-4H), 8.45 (m, 1H, Ind.-7H), 8.55 (s, 1H, =CH); ^{13}C-nmr 12.4 (Ind.-CH_3), 29.5 (CCH_3), 57.2 (CCH_3), 113.9 (In-C7), 122.2 (Ind.-C5), 124.2 (Ind.-C4), 124.8 (Ar-*ortho*), 129.4 (Ar-*meta*), 134.0 (Ar-*para*), 135.9 (Ind.-C7a), 138.8 (Ar-*ipso*), 148.9 (=CH). Anal. Calcd for $C_{20}H_{22}N_2O_2S$: C, 67.76; H, 6.27; N, 7.91; S, 9.04. Found: C, 67.95; H, 6.37; N, 8.07; S, 8.99. After aqueous acid hydrolysis (2*N* HCl, reflux, 2 h) aldehyde (**8**) was obtained quantitatively.

3,3-(Ethylenedioxy)-*N*-[[2-methyl-1-(phenylsulfonyl)-3-indolyl]methylene]butylamine (10).

Method A. A solution of aminoketal(**9**)(1.91 g, 14.59 mmol) and aldehyde(**8**)(4.8 g, 16.05 mmol) in dry benzene (100 ml) was stirred at 0°C for 30 min at room temperature for 1 h, and then under reflux for 4 h. After 16 h of additional refluxing with removal of water by a Dean-Stark trap, the solvent was evaporated to give an oily mixture of *E* and *Z* imines (**10**) (6.2 g, 98%) after flash chromatographic filtration (95:5, CH_2Cl_2-diethylamine), which was used without separation; ir (NaCl) 1630 (C=N), 1175, 1370; ^{1}H nmr 1.32 and 1.40* (Major isomer peak is indicated by an asterisk) (2 s, 3H each, CCH_3), 1.95 and 2.10* (2 t, *J*=7 Hz, 2H each, CH_2), 2.74 (s, 3H, Ind.-CH_3), 3.65 and 3.75* (2 t, *J*=7 Hz, 2H each, NCH_2), 3.95 (s, 4H , OCH_2), 7.00-8.20 (m, 9H, ArH), 8.50* and 8.95 (2 s, 1H each, =CH); ^{13}C nmr 12.1* and 15.8 (CH_3) , 23.9 and 24.0* (Ind.-CH_3), 36.4 and 40.2* (NCH_2CH_2), 47.2 and 57.7* (NCH_2), 64.3 and 64.4 (OCH_2), 109.2 and 109.8* (OCO), 112.7 and 113.8* (Ind.-C7), 121.9 (Ind.-C5), 124.1 (Ind.-C4), 126.3 (Ar-*ortho*), 126.7 (Ind.-C6), 129.3 (Ar-*meta*), 129.4 (Ind.-C3a), 133.9 (Ar-*para*), 136.3 (Ind.-C7a), 138.6* and 139.4 (Ar-*ipso*), 154.3 and 160.6 (C=N); ms (*m/z*, %) 412 (M^+, 1), 300 (15), 284 (100), 257 (8), 141 (43), 115 (14), 87 (21), 77 (55).

Method B. To a solution of imine(**12**)[3] (400 mg, 1.0 mmol) in THF (25 ml) was added *n*-C_4H_9Li (1.6 *M*, 0.76 ml, 1.2 mmol) at -15°C under argon atmosphere. After stirring for 1 h at -15°C the reaction mixture was cooled to

-78°C, and CH_3I (75 µl, 1.2 mmol) was added. After stirring overnight at room temperature the reaction mixture was poured upon water and extracted with ether. The organic layers were dried and evaporated to yield **10** (200 mg, 48%) as an oil after flash chromatography (95:5, CH_2Cl_2-CH_3OH).

2-[2-Methyl-1-(phenylsulfonyl)-3-indolyl]-4-piperidone Ethylene Ketal (11). A stirred solution of the iminoketal(**10**)(5.6 g, 13.62 mmol) and anhydrous *p*-TsOH (5.2 g, 27.36 mmol) in dry benzene (200 ml) was refluxed under N_2 for 1 h. The cooled mixture was poured on ice-water and basified with Na_2CO_3. The organic layer was separated and washed with saturated aqueous Na_2CO_3, dried, and evaporated to give piperidine(**11**) (4.02 g, 72%) as an oil after flash chromatography (95:5, CH_2Cl_2-CH_3OH); ir (KBr) 2600-3300 (NH), 1350, 1150; ^1H nmr 1.60-1.90 (m, 2H, 5-H), 2.13 (t, J=12 Hz, 1H, 3-Ha), 2.63 (s, 3H, Ind.-CH_3), 2.93 (td, J=12, 3.5 Hz, 1H, 6-Ha), 3.15 (br d, J=12 Hz, 1H, 6-He), 3.90-4.00 (br s, 4H, OCH_2), 4.13 (dd, J=12, 2.5 Hz, 1H, 2-Ha), 7.23 (br t, J=8 Hz, 1H, Ind.-5H), 7.25 (d, J=7 Hz, 2H, Ar-*ortho*), 7.41 (t, J=7 Hz, Ar-*meta*), 7.50 (br t, J=8 Hz, 1H, Ind.-6H), 7.74 (d, J=8 Hz, 1H, Ind.-4H), 7.90 (m, 1H, Ar-*para*), 8.19 (br d, J=8 hz, 1H, Ind.-7H); ^{13}C nmr 12.5 (CH_3), 35.1 (C-5), 40.7 (C-3), 44.2 (C-6), 51.9 (C-2), 64.0 and 64.2 (OCH_2), 107.7 (C-4), 114.4 (Ind.-C7), 120.6 (Ind.-C4), 122.8 (Ind.-C6), 123.1 (Ind.-C2), 123.9 (Ind.-C3), 124.3 (Ar-*ortho*), 126.3 (Ar-*meta*), 126.8 (Ind.-C3), 129.2 (Ar-*para*), 129.3 (Ind.-C7a), 133.7 (Ar-*ipso*); ci ms (*m/z*, %) 430 (M^++18, 50), 413 (M^++1), 73; 375 (36), 340 (38), 305 (42), 273 (91), 209 (67), 194 (79), 177 (100), 150 (44), 125 (71). The hydrochloride, as a crystalline solid, melted at 229-231 °C (acetone); ^1H nmr 1.82 (d, J=12 Hz, 1H, 5-He), 2.20 (m, 1H, 3-He), 2.77 (s, 3H, Ind.-CH_3), 3.94 (br s, 4H, OCH_2), 4.45 (t, J=12 Hz, 1H, 2-Ha), 7.00-8.15 (m, 9H, ArH); ^{13}C nmr 13.4 (CH_3), 31.1 (C-5), 37.5 (C-3), 42.7 (C-6), 51.3 (C-2), 64.5 and 64.6 (OCH_2), 105.1 (C-4), 114.2 (Ind.-C7), 121.0 (Ind.-C4), 123.7 (Ind.-C6), 124.6 (Ind.-C2), 126.4 (Ar-*ortho*), 129.5 (Ar-*meta*), 133.9 (Ar-*ipso*), 135.9 (Ind.-C7a), 137.9, 138.7. Anal. Calcd for $C_{22}H_{24}N_2O_4S.HCl$: C, 58.27; H, 5.67; N, 6.18. Found: C, 57.93; H, 5.65; N, 6.03.

***N*-(2-Hydroxyethyl)-2-[2-methyl-1-(phenylsulfonyl)-2-indolyl]-4-piperidone Ethylene Ketal (4).** 2-Bromoethanol (0.57 ml, 7.27 mmol) was added dropwise to a mixture of piperidine (**11**) (2 g, 4.85 mmol) and anhydrous K_2CO_3 (2 g, 14.5 mmol) in absolute ethanol (200 ml). The resulting mixture was refluxed under N_2 for 15 h. The ethanol was evaporated, and the residue was dissolved in CH_2Cl_2 and washed with brine (3x 30 ml). The dried organic phase was evaporated and purified by flash chromatography (95:5, CH_2Cl_2-CH_3OH) to give pure alcohol(**4**)(1.57 g, 71%) as an oil; ir (KBr) 3300-3500 (OH), 1370, 1170; ^1H nmr 1.82 (td, J=13 and 3 Hz, 1H, 3-Ha), 1.95 (br d, J=13 Hz, 1H, 3-He), 2.26 (td, J=13 and 3 Hz, 1H, 6-Ha), 2.58 (br s, 3H, Ind.-CH_3), 3.15 (br d, J=13 Hz,

1H, 6-He), 3.95 (m, 1H, 2-H), 3.98 (s, 4H, OCH_2), 7.00-7.50 (m, 7H, ArH), 7.69 (d, *J*=7 Hz, 1H, Ind.-4H), 8.22 (d, *J*=7 Hz, 1H, Ind.-7H); ^{13}C nmr 12.1 (CH_3), 34.6 (C-5), 40.2 (C-3), 49.0 (C-6), 54.4 (NCH_2), 58.0 (C-2), 58.4 (OCH_2), 64.0 and 64.1 (OCH_2), 106.7 (C-4), 114.8 (Ind.-C7), 120.9 (Ind.-C5), 123.4 (Ind.-C4), 124.2 (Ind.-C6), 126.1 (Ind.-C3a), 127.1 (Ar-*ortho*), 129.0 (Ar-*meta*), 129.2 (Ind.-C3), 133.6 (Ar-*para*), 133.7 (Ind.-C7a), 139.0 (Ar-*ipso*); ci ms (*m/z*, %) 457 (M^++1, 46), 349 (41), 301 (39), 232 (58), 194 (74), 127 (100), 163 (23), 123 (38). Anal. Calcd for $C_{24}H_{28}N_2O_5S$: C, 63.14; H, 6.18; N, 6.13. Found: C, 63.24; H, 6.07; N, 5.96.

***N*-[2-(2-Methyl-3-indolyl)ethyl]-4-piperidone Ethylene Ketal (15).** To a solution of piperidine(**4**)(350 mg, 0.77 mmol) in dry THF (30 ml) was added freshly sublimed *t*-C_4H_9OK (215 mg, 1.92 mmol) under N_2. After being stirred at 0°C for 3 h $NaBH_4$ (87 mg, 2.30 mmol) was added. The reaction mixture was refluxed for 12 h and then poured into an aqueous NH_4Cl solution and extracted with CH_2Cl_2. Evaporation of the dried organic extract gave **15** (67 mg, 31%) after flash chromatography (95:5, CH_2Cl_2-C_2H_5OH); crystal form, mp 82-83 °C (ether-acetone); ir ($CHCl_3$) 2900-3400 (NH); ^1H nmr 1.82 (t, *J*=8 Hz, 4H, CH_2), 2.33 (s, 3H, Ind.-CH_3), 2.50-2.90 (m, 8H, NCH_2 and Ind.-CH_2), 3.95 (s, 4H OCH_2), 7.00 (m, 2H, Ind.-5H and Ind.-6H), 7.15 (d, *J*=7 Hz, 1H, Ind.-7H), 7.25 (d, *J*=7 Hz, 1H, Ind.-4H), 7.90 (br, 1H, NH); ^{13}C nmr 11.3 (CH_3), 21.7 (InCH$_2$), 34.4 (C-3) 51.2 (NCH_2), 58.6 (C-2), 64.2 (OCH_2), 107.1 (C-4), 110.3 (Ind.-C7), 117.9 (Ind.-C5), 119.2 (Ind.-C4), 121.0 (Ind.-C6), 128.5 (Ind.-C3a), 131.4 (Ind.-C2), 135.1 (Ind.-C7a); ci ms (*m/z*, %) 301 (M^++1, 100), 272 (3), 197 (7). Anal. Calcd for $C_{18}H_{24}N_2O_2.1/2H_2O$: C, 69.87; H, 8.14; N, 9.05. Found: C, 69.77; H, 7.82; N, 8.63.

***N*-[2-(2-Methyl-3-indolyl)ethyl]-2,3-dihydro-1*H*-pyridin-4-one (16).** To a solution of piperidine(**4**) (250 mg, 0.54 mmol) in dry THF (30 ml) was added freshly sublimed *t*-C_4H_9OK (135 mg, 1.2 mmol) under N_2. After being stirred at 0°C for 3 h, 4*N* HCl (25 ml) and methanol (25 ml) were added after evaporation of THF. The resulting mixture was refluxed for 3h, cooled, basified (Na_2CO_3) and extracted with CH_2Cl_2 to provide enaminone (**16**)(32 mg, 23%) as an oil after flash chromatography (95:5, CH_2Cl_2-CH_3OH); ir (KBr) 3200 (NH), 1580-1600; ^1H nmr 2.39 (t, *J*= 8 Hz, 2H, 3-H), 2.98 (t, *J*=7 Hz, 2H, Ind.-CH_2), 3.46 (t, *J*=8 Hz, 2H, 2-H), 3.47 (s, 3H, Ind.-CH_3), 3.52 (t, *J*=7 Hz, 2H, Ind.-CH_2CH_2), 4.80 (d, *J*=7 Hz, 1H, 5-H), 6.65 (d, *J*=7 Hz, 1H, 6-H), 7.00-7.15 (m, 2H, Ind.-5H and Ind.-6H), 7.30 (d, *J*=7 Hz, 1H, Ind.-7H), 7.45 (d, *J*=7 Hz, 1H, 4H), 8.50 (br, 1H, NH); ^{13}C nmr 11.4 (CH_3), 23.9 (Ind.-CH_2), 35.3 (C-3), 47.2 (C-2), 56.0 (Ind.-CH2*C*H2N), 97.1 (C-5), 107.0 (Ind.-C2), 110.7 (Ind.-C7), 117.3 (Ind.-C5), 119.5 (Ind.-C4), 121.5 (Ind.-C6), 127.9 (Ind.-C3a), 132.5 (Ind.-C7a), 154.4 (C-6), 191.6 (CO); ci ms (m/z, %) 272

(M^++NH_3), 255 (M^++1, 100). Anal. Calcd for $C_{16}H_{18}N_2O$: C, 75.56; H, 7.13; N, 11.01. Found: C, 75.70; H, 7.09; N, 10.88.

1-Acetyl-3-[2-(4,4-ethylenedioxy-2-oxo-1-piperidylethyl]-2-methylindole (19). To a solution of spiroindolenine(3) prepared as above from **4** (350 mg, 0.77 mmol) and *t*-C_4H_9OK (215 mg, 1.92 mmol), in THF (30 ml) was added *n*-C_4H_9Li (1.6 *M*, 0.58 ml, 0.92 mmol) at -20°C. After stirring for 10 min at -20 °C, acetyl chloride (60 µl, 0.847 mmol) was added. The reaction mixture was stirred for 1 h at -20 °C, quenched with aqueous ammonium chloride, and extracted with CH_2Cl_2. The organic layers were dried and evaporated to give 2-piperidone(**19**)(93 mg, 34%) as an oil after flash chromatography (95:5, CH_2Cl_2-CH_3OH); ^{1}H nmr 1.60 (s, 3H, $COCH_3$), 1.65-1.80 (m, 2H, 5-H), 2.05 and 2.28 (2 d, J_{AB}=12 Hz, 1 H each, 3-H), 2.55 (s, 3H, Ind.-CH_3); 3.00-3.20 (m, 2H, NCH_2), 3.70-4.00 (m, 6H, 6-H and OCH_2), 7.10-7.30 (m, 2H, Ind.-5H and Ind.-6H), 7.85 (d, *J*=7 Hz, 1H, Ind.-4H), 8.45 (d, *J*=7 Hz, 1H, Ind.-7H); ^{13}C nmr 23.9 (CH_3), 26.5 (CH_3), 34.7 (Ind.-CH_2), 39.2 (C-5), 44.0 (C-3), 53.3 (C-6), 55.4 (NCH_2), 64.0 and 64.3 (OCH_2), 107.1 (C-4) , 110.5 (Ind.-C3), 116.9 (Ind.-C7), 121.1 (Ind.-C4), 123.3 (Ind.-C5), 125.0 (Ind.-C6), 126.0 (Ind.-C2), 128.1 (Ind.-C3a), 136.7 (Ind.-C7a), 160.1 (CO); ms (m/z, %) 357 (M^+, 3), 332 (6), 315 (M^+-$COCH_3$). Anal. calcd for $C_{20}H_{24}N_2O_4$: C, 67.39; H, 6.79, N, 7.85. Found: C, 67.19; H, 6.47; N, 7.55.

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