SYNTHESIS AND REACTIVITY OF 2-(1,3-DITHIAN-2-YL)INDOLES. III[1]. INFLUENCE OF THE INDOLE PROTECTIVE *N*-PHENYLSULFONYL GROUP

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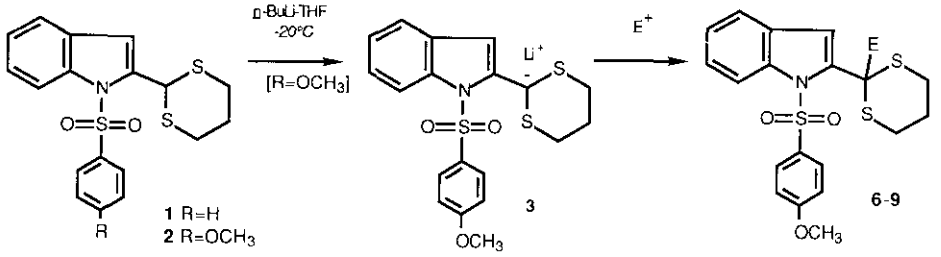
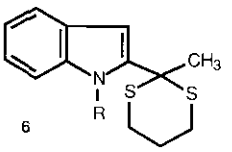
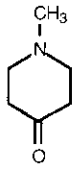
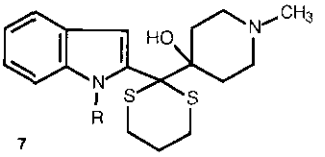
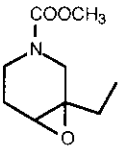
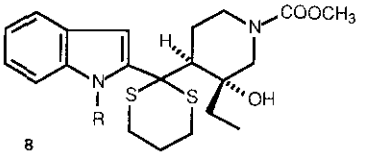
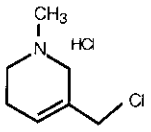
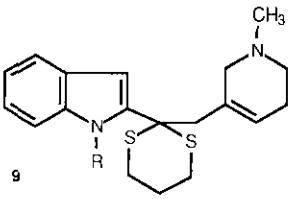
Abstract– Formation of the anion of 2-(1,3-dithian-2-yl)indoles was shown to be possible when the indole nitrogen is protected by a p-methoxyphenylsulfonyl group. In contrast to the corresponding N-phenylsulfonylindole dithiane **1**, the anion of dithiane **2** reacts efficiently with electrophiles.The influence of the indole protective group on the metallation of 2-bis(ethylthio)-methyl-1-(phenylsulfonyl)indole (**14**) and the corresponding sulfoxide **24** with n-butyllithium is also reported.

In previous papers[1,2] we have reported results on the reactivity of the anions derived from the 2-(1,3-dithian-2-yl)indole and 2-(1,3-dithian-2-yl)-1-methylindole towards a series of electrophiles, and the application of this chemistry to the preparation of tetracyclic 2-acylindole analogues of the indole alkaloid dasycarpidone .[3,4] Thus, 1-methyl-20-hydroxydasycarpidone and 1-methyl-15-hydroxydeethyldasycarpidone were obtained for the first time. Nevertheless, protection of the indole NH was necessary in these synthesis in order to direct the key cyclization step to the indole C-3 position. A priori, phenylsulfonyl was the most appropriate protective group;[5] however, it was found that treatment of the 2-(1,3-dithian-2-yl)-1-phenylsulfonylindole **1** with n-butyllithium led to the fragmentation of the indole B-ring and not to the desired anion.[2]

In this paper we report that metallation at the dithiane center with n-butyllithium is readily achieved when a p-methoxyphenylsulfonyl group[6] is employed on the N_a (indole) as the protective group. Moreover, the unusual reactivity of 2-bis(ethylthio)methyl-1-(phenylsulfonyl)indole (**14**), an analogue of the indolyl dithianes, and its corresponding S-oxide **24** to n-butyllithium are also reported.

Dithioacetals **2** and **14** (Schemes 1 and 3) were prepared by our usual method, i.e. by protection with an appropriate thiol of the corresponding indole-2-carbaldehydes which are in turn obtained by the Gribble procedure[7] from 1-(p-methoxyphenylsulfonyl)- and 1-(phenylsulfonyl)indoles, respectively.



Electrophile	Product	Yield (%)
CH_3I	 6	70
 7		74
 4	 8	52
 5	 9	68

R= p-(OCH3)C6H4SO2

Scheme 1

When indole dithiane **2** was treated with n-butyllithium (1.2 eq., THF, -20°C, 30 min) followed by addition of methyl iodide (1 eq.), the condensation product **6** was obtained in 70% yield (Scheme 1). Formation of **6** was confirmed by the presence of a singlet at δ 1.86 in the ^{1}H-nmr spectrum corresponding to the methyl group, as well as the absence of the methine proton (δ 6.29) characteristic of the initial dithiane **2**. Similarly, reaction of anion **2** with 1-methyl-4-piperidone gave piperidinol **7** in 74% yield. These results are in marked

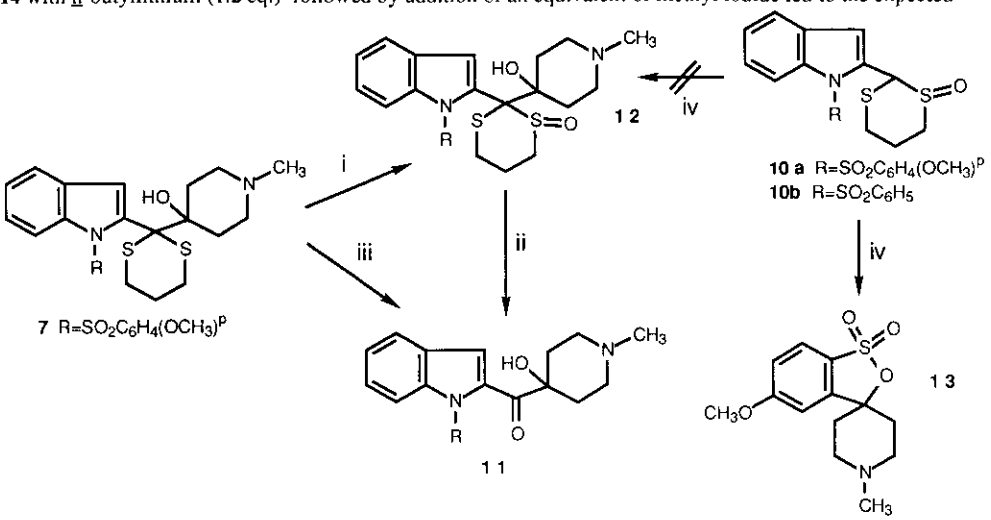
contrast with the negative ones obtained in the reaction of the demethoxylated analogue **1** with the same electrophiles,[2] which led to an acetylene derivative by metallation of indole C-3 position followed by ring opening.[8] The important contribution of the use of this protective group in the dithiane anion reactions was evidenced by the results obtained with more elaborated piperidine electrophiles. Thus, when anion **3** was treated with 1-methoxycarbonyl-3-ethyl-3,4-epoxypiperidine (**4**), prepared by epoxidation of 3-ethyl-1-methoxycarbonyl-1,2,5,6-tetrahydropyridine,[9] 3-piperidinol **8** was obtained in 52% yield. In this case, the anion reacted only with the epoxy function and no reaction product resulting from the attack on the urethane function was observed. The formation of **8** was confirmed from both spectroscopic and microanalytical data. Furthermore, condensation of anion **3** with 3-chloromethyltetrahydropyridine hydrochloride **5**, provided indolyl derivative **9** in 68% yield. Compound **9** showed characteristic signals in its ^{1}H-nmr spectrum at δ 7.69 and 5.85 assigned to C-3 proton of indole ring and vinyl protons, respectively, and at δ 3.09 for the methylene exocyclic protons.

Transformation of dithiane **7** into 2-acylindole **11** by our procedure (scheme 2),[1,2] involving reaction of **7** with 85% MCPBA and subsequent acid treatment of the resultant sulfoxide, proved to be inefficient. Moreover, when sulfoxide **10a**, obtained by oxidation of dithiane **2** with 85% MCPBA, was reacted sequentially with 1 equivalent of n-butyllithium and N-methyl-4-piperidone at -20°C, only sultone **13** was isolated in 21 % yield, the expected piperidinol **12** not being detected from the reaction mixture.

Formation of compound **13** can be rationalized in terms of a competitive aromatic metallation of the p-methoxyphenylsulfonyl substituent, condensation with N-mehyl-4-piperidone, and indole deprotection. Similar competitive reaction of N-(phenylsulfonyl)indole derivatives has been described.[10] Under the same reaction conditions the related sulfoxide **10b** did not yield the condensation product **12**, nor sultone **13**, the starting material being recovered to a significant extent.

However, treatment of **7** with bis(trifluoroacetoxy)iodobenzene[11] in aqueous acetonitrile gave the desired ketone **11** in 49% yield. Ketone **11** was characterized by the presence of absorptions at 1675 and 3330 cm^{-1} in the ir spectrum corresponding to carbonyl and hydroxy groups, respectively. The molecular peak at m/z 428 in its mass spectrum, and the observed downfield shift of the C-3 proton in the ^{1}H-nmr spectrum (δ 7.25 in **7**; δ 7.60 in **11**), are also in accordance with the proposed structure. When deprotection of dithiane **7** was carried out in methanol-water (9:1), dimethyl acetal of ketone **11** was obtained in agreement with described results.[11] The absence of a carbonyl absorption in the ir spectrum of this product and a new signal at δ 3.40 for the two OCH_3 groups in the ^{1}H-nmr spectrum confirmed the acetal formation. Finally, treatment of dimethyl acetal of **11** with 10% hydrochloric acid-methanol led to ketone **11**.

In order to check the effect of the dithiane ring on the metallation reaction of 2-(1,3-dithian-2-yl)-1-phenylsulfonylindole,[2] we studied the analogous diethyldithioacetal **14** (Scheme 3). Surprisingly, reaction of **14** with n-butyllithium (1.2 eq.) followed by addition of an equivalent of methyl iodide led to the expected



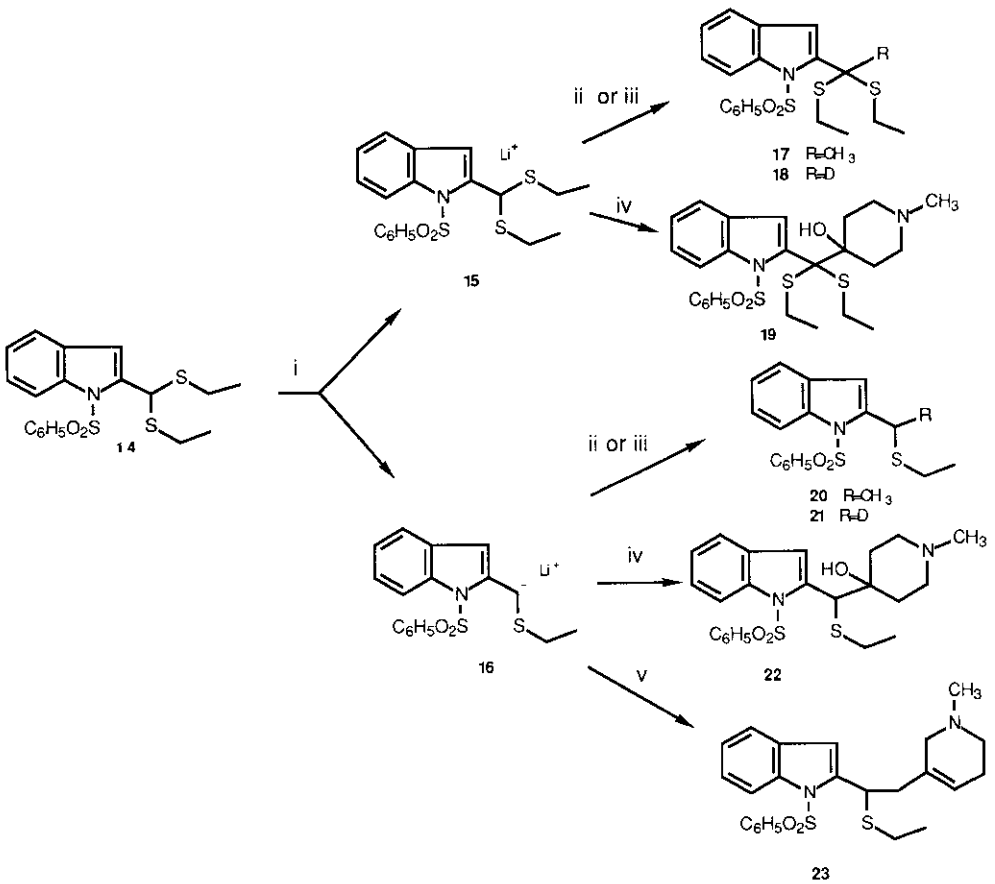
Reagents and Conditions: (i) 85% MCPBA, CH_2Cl_2-H_2O (80:1), -20°C, 6 h or 1. C_2H_5OH-HCl, 2. $NaIO_4$, C_2H_5OH, room temp , 12 h; (ii) THF-HCl (9:1), reflux, 3 h or 50% AcOH (23% yield); (iii) $(CF_3CO_2)_2IC_6H_5$, CH_3CN-H_2O (9:1), room temp (49% yield); (iv) 1. n-C_4H_9Li, THF, -20°C, 20 min; 2. 1-methyl-4-piperidone (21% yield).

Scheme 2

compound **17** (44% yield) together with **20** (56% yield), resulting from anion **16** generated by loss of an ethylthio chain. This behaviour was also observed when N-methyl-4-piperidone was used as the electrophile, leading to **19** and **22** in 16% and 39% yield, respectively. The most characteristic signals in the ^{1}H-nmr spectra were the singlet due to the methine proton at δ 4.85 for **20** and 4.88 for **22**.

When the reaction of the anion generated from **14** by treatment with n-butyllithium (1.4 eq.) was carried out upon 3-chloromethyltetrahydropyridine **5**, only compound **23** was obtained in 64% yield. Compound **23** presents a characteristic triplet at δ 5.05 for the methine proton α to the sulfur atom and two singlets at δ 6.97 and 5.70 for the C-3 indole and vinyl protons, respectively.

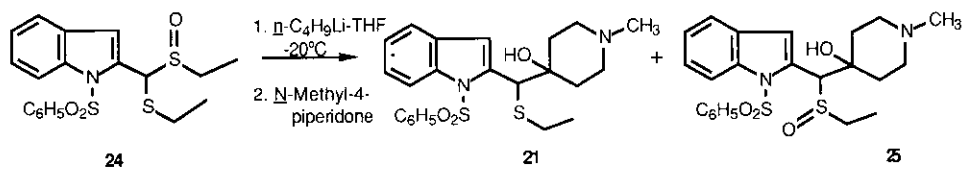
The temperature effect in these reactions was unimportant. Thus, reaction of **14** with 1.2 equivalents of n-butyllithium at -20°C for 1.5 h followed by quenching with deuterium oxide afforded a 3:2 mixture of **18** and **21** formed from anions **15** and **16**, respectively. When the reaction was carried out at -78°C no significant change was observed in the ratio of products **18** and **21**. These observations suggested that n-butyllithium acts as a nucleophile[12] promoting the cleavage of the sulfur bond.



Reagents and Conditions. (i) n-C_4H_9Li, THF, -20°C, 1 h; (ii) D_2O, -20°C; (iii) CH_3I, -20°C, 1 h; (iv) 1-methyl-4-piperidone, -20°C, 1 h; (v) 3-chloromethyl-1-methyl-1,2,5,6-tetrahydropyridine.

Scheme 3

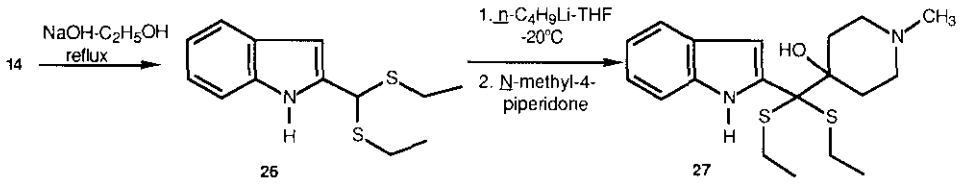
On the other hand, we studied the reactivity of sulfoxide **24** (Scheme 4), prepared by oxidaton of **14** with 85% MCPBA, towards 1-methyl-4-piperidone, under identical experimental conditions. In this case, an



Scheme 4

equimolecular mixture of **21** and **25** was obtained resulting from the loss of ethyl thio or ethyl sulfoxide chain.

In order to determine the role of the phenylsulfonyl group, diethyldithioacetal **26** was prepared by refluxing **14** with 10% aqueous sodium hydroxide in ethanol. When dithioacetal **26** was treated with 2 equivalents of n-butyllithium followed by N-methyl-4-piperidone the only product obtained was **27** in 50% yield. The latter result suggests that the benzenesulfonyl group exerts a certain influence on the loss of an ethyl thio or ethyl sulfoxide chain.



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 XL-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 the workup of reactions was performed over anhydrous sodium sulfate. Microanalyses were performed on a Carlo-Erba 1106 analyzer by Departament de Química Orgànica Biològica, Barcelona.

2-(1,3-Dithian-2-yl)-1-(4-methoxyphenylsulfonyl)indole (**2**). To a solution of indole (11 g, 93 mmol) and tetrabutylammonium hydrogensulfate (742 mg, 2.18 mmol) in benzene (300 ml) a 50% aqueous solution of sodium hydroxide (100 ml) was added. The two phase mixture was strongly stirred and p-methoxybenzenesulfonyl chloride (25 g, 120 mmol) was added. After stirring for 16 h at room temperature the mixture was poured into an aqueous sodium carbonate solution. The organic layer was dried and evaporated to give N-(4-methoxyphenylsulfonyl)indole (27 g) which was purified by crystallization from ether (22.6 g, 83%); mp 112-114 °C (ether); ir (KBr) 1360, 1165; ^{1}H-nmr 3.76 (s, 3H, OCH_3), 6.64 (dd, J=4 and 1 Hz, 1H, In-3H), 6.84 (d, J=8.5 Hz, 2H, Ar-3H), 7.20 (td, J=7 and 1 Hz, 1H, In-6H), 7.30 (td, J=7 and 1 Hz, 1H, In-2H), 7.51 (ddd, J=7.7, 1.4 and 1 Hz, 1H, In-5H), 7.55 (d, J=4 Hz, 1H, In-4H), 7.81 (d, J= 8.5 Hz, 2H, Ar-2H), 7.98 (dq, J=7.7 and 1 Hz, 1H, In-7H); ^{13}C-nmr 55.6 (OCH_3), 108.9 (In-C2), 113.4 (In-C3), 114.4 (In-C7), 121.3 (In-C6), 123.2 (In-C4), 124.4 (In-C5), 126.3 (C-ortho), 129.0 (C-meta), 129.6 (C-ipso), 130.7 (In-C3a), 134.7 (In-C7a), 163.7 (C-para); ms (m/z,%) 287 (M^+, 32), 170 (100), 122 (29), 115 (30), 106

(53), 89 (45), 77 (55). Anal. Calcd for $C_{15}H_{13}NO_3S$: C, 62.70; H, 4.50; N, 4.89; S, 11.16. Found:C, 62.83; H, 4.55; N, 4.87; S, 11.18.

To a solution of diisopropylamine (6.51 ml, 46 mmol) in anhydrous THF (10 ml) cooled at -70°C n-butyllithium (1.6 M, 31.3 ml, 50.1 mmol) was added . The solution was stirred at -70°C for 1 h, slowly warmed to 0°C, and then 1-(4-methoxyphenylsulfonyl)indole (12 g, 41.78 mmol) in anhydrous THF (30 ml) was quickly added. The reaction mixture was stirred for 30 min at 0°C and cooled to -70°C. Freshly distilled DMF (7.1 ml, 41.8 mmol) was added to the resulting solution. After stirring at room temperature for 5 h, the reaction mixture was poured into aqueous ammonium chloride and extracted with ether. The extracts were dried and evaporated to give 1-(4-methoxyphenylsulfonyl)indole-2-carbaldehyde (12 g, 90%): mp 131-133 °C (ether-acetone); ir (KBr) 1665 (C=O); ^{1}H-nmr 3.73 (s, 3H, OCH_3), 6.80 (d, J=8.5 Hz, 2H, Ar-H), 7.29 (ddd, J=7.5, 7, and 0.8 Hz, 1H, In-6H), 7.44 (d, J=0.8 Hz, 1H, In-3H), 7.51 (ddd, J=7.5, 7, and 1.2 Hz, 1H, In-5H), 7.60 (ddd, J=7, 1.2, and 0.8 Hz, 1H, In-4H), 7.70 (d, J=8.5 Hz, 2H, Ar-H), 8.21 (dq, J=7.5 and 0.8 Hz, 1H, In-7H), 10.52 (br s, 1H, CHO); ^{13}C-nmr 55.8 (OCH_3), 114.8 (In-C3), 115.7 (In-C7), 119.1 (In-C6), 124.0 (In-C4), 125.1 (In-C5), 128.5 (C-ortho), 129.2 (C-meta), 129.3 (C-ipso), 138.1 (In-C3a), 138.8 (In-C7a), 164.5 (C-para), 183.9 (C=O); ms (m/z, %) 287 (M^+, 32), 170 (100), 122 (29), 115 (30), 106 (53), 89 (45), 77 (55), 63 (45). Anal. Calcd for $C_{16}H_{13}NO_4S$: C, 60.94; H, 4.16; N, 4.40. Found; C, 61.40; H, 4.14; N, 4.42.

A stirred solution of the aldehyde (12 g, 38.1 mmol), p-toluenesulfonic acid (21.7 g, 1.14 mmol), and 1,3-propanedithiol (1.6 ml, 60.96 mmol), in anhydrous toluene (300 ml) was refluxed for 15 h with removal of water by a Dean-Stark trap. The reaction mixture was poured into 10% aqueous sodium carbonate, dried and evaporated to give dithiane **2** which was purified by flash chromatography using dichloromethane as the eluent (14.9 g, 95%); mp 133-135 °C (ether-acetone); ir (KBr) 1160, 1350; ^{1}H-nmr 1.95 (m, 1H, 5-Hax), 2.19 (m, 1H, 5-Heq), 2.93 (ddd, J=14.5, 5, and 3.3 Hz, 2H, 4-Heq and 6-Heq), 3.17 (ddd, J= 14.5, 11.6, and 2.5 Hz, 2H, 4-Hax and 6-Hax), 3.73 (s, 3H, OCH_3), 6.29 (s, 1H, 2-H), 6.82 (d, J=8.5 Hz, 1H, Ar-H), 7.00 (td, J=7.5 and 1 Hz, 1H, In-5H), 7.28 (td, J=7.5 and 1.5 Hz, 1H, In-6H), 7.44 (ddd, J=7.5, 1.5, and 1 Hz, 1H, In-4H), 7.86 (d, J=8.5 Hz, 1H, Ar-H), 8.07 (dq, J=7.5 and 1 Hz, 1H, In-7H); ^{13}C-nmr 25.3 ($SCH_2\underline{C}H_2$), 32.7 ($S\underline{C}H_2CH_2$), 42.5 (SCHS), 55.7 (OCH_3), 109.1 (In-C2), 113.5 (In-C7), 115.0 (In-C3), 121.4 (In-C6), 124.1 (In-C4), 125.5 (In-C5), 129.4 (C-ipso), 129.4 (In-C3a), 129.6 (C-ortho), 139.1 (In-C7a), 164.1 (C-para); ms (m/z, %) 405 (M^+, 7), 266 (7), 234 (62), 188 (8), 171 (33), 160 (25), 107 (48), 92 (76), 77 (100), 64 (57), 45 (67). Anal. Calcd for $C_{19}H_{19}NO_3S_3$: C, 56.29; H, 4.69; N, 3.41; S, 23.73. Found: C, 56.54; H, 4.76; N, 3.42; S, 23.68.

3-Ethyl-1-(methoxycarbonyl)-3,4-epoxypiperidine (**4**). To a solution of 3-ethyl-1-methoxycarbonyl-1,2,5,6-tetrahydropyridine[9] (9.0 g, 53.2 mmol) in 50% THF-H_2O (140 ml) N-bromosuccinimide (10.4 g, 58.5 mmol) was slowly added. The reaction mixture was stirred for 20 h and then the organic solvent was evaporated. The aqueous residue was extracted with ether, dried and evaporated to give 4-bromo-3-ethyl-1-methoxycarbonyl-3-piperidinol (12.6 g, 89%): mp 125-126°C (ether) ; ir (NaCl) 3300-3500 (OH), 1690 (CO); ^{1}H-nmr 0.97 (t, J=7 Hz, 3H, $CH_2C\underline{H}_3$), 1.40-1.80 (m, 2H, $C\underline{H}_2CH_3$), 3.70 (s, 3H, OCH_3), 4.20 (t, J=4 Hz, 1H, OCH); ^{13}C-nmr 6.1 ($CH_2\underline{C}H_3$), 26.1 ($\underline{C}H_2CH_3$), 30.9 (C-5), 40.8 (C-6), 48.9 (C-2), 52.9 (OCH_3), 71.7 (C-3), 74.6 (C-4), 156.0 (C=O); ms (m/z, %) 267 (M^++1, 10), 265 (7), 250 (5), 186 (31), 168 (28), 154 (100), 118 (46), 88 (80), 57 (96). Anal. calcd for $C_9H_{16}BrNO_3$: C, 40.61; H, 6.06; N, 5.26. Found: C, 41.01; H, 6.17; N, 5.03. A solution of potassium hydroxide (5.27 g, 79.8 mmol) in methanol (140 ml) was added to 3-piperidinol (12.6 g, 47.5 mmol). The reaction mixture was stirred for 1 h at room temperature, evaporated, diluted with water (100 ml) and extracted with ether. The organic layer was dried and evaporated to give epoxide

4 (5.5 g, 59%) after purification by flash chromatography (3:7 hexane-ether); ir ($CHCl_3$) 1690 (C=O); ^{1}H-nmr 0.97 (t, J=7 Hz, 3H, $CH_2\underline{C}H_3$), 1.65 (q, J=7 Hz, 2H, $\underline{C}H_2CH_3$), 3.13 (t, J=2 Hz, 1H, 4-H), 3.68 (s, 3H, OCH_3); ^{13}C-nmr 8.5 ($CH_2\underline{C}H_3$), 24.1 ($\underline{C}H_2CH_3$), 27.9 (C-5), 37.7 (C-6), 45.2 (C-2), 52.8 (OCH_3), 56.3 (C-4), 59.8 (C-3), 156.2 (C=O); ms (m/z, %) 185 (M^+, 13), 168 (79), 156 (58), 101 (100), 88 (61), 59 (74), 42 (76). Anal. Calcd for $C_9H_{15}NO_3.H_2O$: C, 53.19; H, 8.43; N, 6.89. Found: C, 53.65; H, 8.30; N, 6.74.

3-Chloromethyl-1-methyl-1,2,5,6-tetrahydropyridine Hydrochloride (**5**). To a solution of 3-hydroxymethyl-pyridine (25 ml, 0.26 mol) in dry toluene (200 ml), freshly distilled methyl iodide (32.4 ml, 0.35 mol) was slowly added. The mixture was refluxed for 1 h, filtered and the resulting solid was washed with dry toluene to obtain 3-hydroxymethyl-1-methylpyridinium iodide (64 g, 98%); mp 81-83°C (methanol); ^{1}H-nmr (CD_3OD) 4.28 (s, 3H, NCH_3), 4.60 (s, 2H, OCH_2), 7.70 (t, J=9 Hz, 1H, Pyr-5H), 8.16 (d, J=9 Hz, 1H, Pyr-4H), 8.46 (d, J=9 Hz, 1H, Pyr-6H), 8.50 (s, 1H, Pyr-2H). Anal. Calcd for $C_7H_{10}INO$: C, 33.46; H, 4.01; N, 5.58. Found: C, 33.01; H, 4.45; N, 6.05.

A solution of the pyridinium salt (18.9 g, 0.75 mmol) in methanol (200 ml) cooled to 0°C was treated with sodium borohydride (18.9 g, 0.5 mol) for 3 h. The residue after evaporation was dissolved in water and extracted with dichloromethane to afford 3-hydroxymethyl-1-methyl-1,2,5,6-tetrahydropyridine (6.21 g, 65%); ir (NaCl) 3500-3100 (OH), 1590, and 1575 ; ^{1}H-nmr (60 MHz) 2.00-2.60 (m, 4H, 2-H and 3-H), 2.23 (s, 3H, NCH_3), 2.80 (br s, 2H, 6-H), 3.76 (br s, 2H, CH_2OH), 5.50 (dd, J=10 and 3 Hz, 1H, =CH); ^{13}C-nmr 25.0 (C-3), 45.2 (NCH_3), 51.4 (C-2), 54.2 (C-6), 64.0 (CH_2OH), 119.1 (C-4), 136.4 (C-5); ms (m/z,%) 127 (M^+, 80), 110 (76), 96 (100), 94 (63), 81 (27), 72 (31), 55 (49), 42 (69). Anal. Calcd for $C_7H_{13}NO$: C, 66.10; H, 10.30; N, 11.01. Found: C, 65.61; H, 10.69; N, 11.06.

To a solution of crude tetrahydropyridine (14 g, 0.11 mol) in anhydrous THF (150 ml) cooled at -15°C, thionyl chloride (26.2 g, 0.22 mol) was added. The reaction mixture was stirred at room temperature for 2 h, and the resulting precipitate filtered. The white solid was washed with dry toluene and dried to give hydrochloride **5** (15.87 g, 79%): mp 162-164 °C (methanol); ^{1}H-nmr (CD_3OD) 2.98 (s, 3H, NCH_3), 2.53 (s, 2H, 5-H), 3.30 (s, 2H, 6-H), 3.90-4.00 (m, 2H, CH_2Cl), 4.19 (s, 2H, 2-H), 6.14 (s, 1H, =CH); ^{13}C-nmr (CD_3OD) 23.3 (C-3), 43.1 (NCH_3), 46.6 (CH_2Cl), 50.8 (C-2), 52.9 (C-6), 125.8 (C-4), 129.4 (C-5); ms (m/z,%) 148 (23), 146 (M^+, 63), 132 (10), 128 (16), 110 (13), 91 (10), 85 (8), 73 (10), 57 (100). Anal. Calcd for $C_7H_{13}NCl_2.1/2CH_3OH$: C, 45.04; H, 7.63; N, 7.07. Found: C, 45.07; H, 7.64; N, 7.24.

2-(2-Methyl-1,3-dithian-2-yl)-1-(4-methoxyphenylsulfonyl)indole (**6**). To a solution of dithiane **2** (0.42 g, 1.03 mmol) in anhydrous THF (25 ml) cooled at -40 °C under argon atmosphere n-butyllithium (1.6M, 0.78 ml, 1.25 mmol) was slowly added. After the mixture was stirred for 15 min, methyl iodide (0.8 ml, 2 mmol) was added at -40°C. The reaction mixtre was stirred at -40°C for 45 min, quenched at this temperature with aqueous ammonium chloride, and extracted with ether. The organic extracts were dried and evaporated to give **6** as an oil which was purified by flash chromatography (99:1 ether-diethylamine) (0.3 g, 70%); ir ($CHCl_3$) 1155, 1340; ^{1}H-nmr 1.86 (s, 3H, CCH_3), 1.70-2.00 (m, 1H, 5-Hax), 2.10-2.30 (m, 1H, 5-Heq), 2.84 (ddd, J=14, 3.5, and 2.5 Hz, 2H, 4-Heq and 6-Heq), 3.25 (ddd, J=14, 12, and 2.5 Hz, 2H, 4-Hax and 6-Hax), 3.80 (s, 3H, OCH_3), 6.85 (d, J=8.8 Hz, 2H, Ar-3H), 7.01 (ddd, J=7.5, 7, and 1 Hz, 1H, In-5H), 7.11 (s, 1H, In-3H), 7.23 (ddd, J=7.5, 1.5, and 1 Hz, 1H, In-4H), 7.32 (ddd, J=7.5, 1.5, and 1 Hz, 1H, In-6H), 7.59 (br d, J=7.5 Hz, 1H, In-7H), 7.73 (d, J=8.8 Hz, 2H, Ar-2H); ^{13}C-nmr 15.3 (CH_3), 24.7 ($SCH_2\underline{C}H_2$), 29.3 (SCH_2), 55.6 (OCH_3), 65.8 (SCS), 97.5 (In-C2), 113.4 (In-C7), 114.2 (C-meta), 119.5 (In-C5), 124.4 (In-C4), 129.2 (In-C3a), 129.4 (C-ortho), 129.7 (In-C6), 130.6 (C-ipso), 132.1 (In-C3), 137.9 (In-C7a), 163.2

(C-para); ms (m/z, %) 419 (M^+, 0.2), 248 (62), 201 (36), 175 (53), 170 (53), 154 (100), 107 (45), 92 (43), 77 (65). Anal. Calcd for $C_{20}H_{21}NO_3S_3$: C, 57.25; H, 5.04; N, 3.33. Found: C, 57.13 ; H, 4.96; N, 3.48.

1-Methyl-4-[2-[1-(4-methoxyphenylsulfonyl)-2-indolyl]-1,3-dithian-2-yl]-4-piperidinol (**7**). Operating as above from dithiane **2** (1.75 g, 4.31 mmol), anhydrous THF (150 ml), n-butyllithium (1.6M, 3.2 ml, 5.12 mmol), and N-methyl-4-piperidone (0.6 ml, 5.16 mmol), alcohol **7** (1.7 g, 74%) was obtained after purification by flash chromatography (ether): mp 84-86°C (ether-acetone); ^{1}H-nmr 1.75-2.00 (m, 1H, SCH_2CHax), 1.98 (br d, J=12 Hz, 2H, 3-Heq and 5-Heq), 2.06-2.18 (m, 1H, SCH_2CHeq), 2.22 (td, J=12 and 4.5 Hz, 2H, 3-Hax and 5-Hax), 2.35 (td, J=12 and 1.8 Hz, 2H, 2-Hax and 6-Hax), 2.76 (br d, J=12 Hz, 2-Heq and 6-Heq), 2.93 (dt, J=13.5 and 3.5 Hz, 2H, SCHeq), 3.28 (ddd, J=13.5, 12, and 3.5 Hz, 2H, SCHax), 3.79 (s, 3H, OCH_3), 6.83 (d, J=9.5 Hz, 2H, Ar-H), 6.98 (td, J=9.5 and 7.5 Hz, 1H, In-5H), 7.24 (ddd, J=9.5, 7.5, and 1.5 Hz, 1H, In-6H), 7.25 (s, 1H, In-3H), 7.32 (dd, J=7.5 and 1.2 Hz, 1H, In-4H), 7.58 (dd, J=9.5 and 1.2 Hz, 1H, In-7H), 7.77 (d, J=9.5 Hz, 2H, Ar-H); ^{13}C-nmr 25.3 (SCH_2CH_2), 28.8 (NCH_2CH_2), 32.7 (SCH_2), 45.9 (NCH_3), 51.1 (NCH_2), 55.5 (OCH_3), 58.7 (SCS), 74.9 (COH), 94.3 (In-C2), 113.4 (In-C7), 114.0 (C-meta), 119.4 (In-C5), 123.7 (In-C4), 128.8 (In-C3a), 129.4 (C-ortho), 129.8 (In-C6), 131.0 (C-ipso), 132.1 (In-C3), 139.0 (In-C7a), 163.0 (C-para); ms (m/z, %) 518 (M^+, 1), 485 (2), 404 (4), 329 (4), 234 (100), 171 (15), 160 (13), 112 (60), 77 (45). Anal. Calcd for $C_{25}H_{30}N_2O_4S_3$: C, 57.88; H, 5.83; N, 5.40. Found; C, 57.31; H, 5.89; N, 5.10.

3-Ethyl-1-methoxycarbonyl-4-[2-[1-(4-methoxyyphenylsulfonyl)-2-indolyl]-1,3-dithian-2-yl]-3-piperidinol (**8**). To a solution of **2** (2.22 g, 5.51 mmol) in anhydrous THF (120 ml) cooled at -35°C under argon atmosphere, n-butyllithium (1.6M, 3.79 ml, 6.06 mmol) was added via syringe. The mixture was stirred for 15 min and epoxide **4** (1.02 g, 5.51 mmol) was added at -35°C. The reaction mixture was stirred for 1 h at the same temperature and allowed to reach room temperature. The mixture was poured into 5% aqueous sodium bicarbonate and extracted with ether. The organic layer, dried and evaporated yielded urethane **8** as a pale oil (1.74 g, 54%) after purification by flash chromatography (dichloromethane to 9:1 dichloromethane-methanol); ir (NaCl) 3380-3240 (OH), 1690, 1640 (C=O); ^{1}H-nmr 0.97 (t, J=7 Hz, CH_2CH_3), 3.70 (s, 3H, OCH_3), 3.80 and 3.81 (2s, 3H, $COOCH_3$), 5.80 (m, 1H, 2-Heq), 6.80-7.90 (m, 9H, Ar-H); ^{13}C-nmr 8.4 (CH_2CH_3), 23.9 (CH_2CH_3), 28.2 (SCH_2CH_2), 29.4 (C-5), 32.7 (SCH_2), 37.5 (C-6), 45.0 (C-2), 52.6 ($COOCH_3$), 55.6 (OCH_3), 56.1 (C-4), 59.8 (SCS), 81.9 (C-3), 94.5 (In-C2), 114.2 (C-meta), 114.4 (In-C7), 119.9 (In-C5), 123.5 (In-C4), 124.6 (In-C6), 129.0 (In-C3a), 129.5 (C-ortho), 130.2 (C-ipso), 132.2 (In-C3), 138.0 (In-C7a), 163.1 (C=O), 163.8 (C-para); ms (m/z, %) 590 (M^+, 0.1), 531 (1), 456 (6), 361 (6), 327 (23), 283 (27), 265 (34), 233 (17), 172 (40), 130 (82), 77 (87), 41 (100). Anal. Calcd for $C_{28}H_{34}N_2O_6S_3$: C, 56.92; H, 5.80; N, 4.74. Found: C, 57.08; H, 5.81; N, 4.25.

2-[2-(1-Methyl-1,2,5,6-tetrahydro-3-pyridylmethyl)-1,3-dithian-2-yl]-1-(4-methoxyphenylsulfonyl)indole (**9**).To a solution of dithiane **2** (0.78 g, 2 mmol) in anhydrous THF (25 ml) cooled at -40°C under argon atmosphere n-butyllithium (1.6M, 1.75 ml, 2.8 mmol) was slowly added. After the mixture was stirred for 15 min, a solution of 3-chloromethyl-1-methyl-1,2,5,6-tetrahydropyridine (1 mmol), prepared by treatment of hydrochloride **5** (0.182 g, 1 mmol) with n-butyllithium (0.62 ml, 1 mmol) at -40°C in dry THF (2 ml), was slowly transferred via syringe. The reaction mixture was stirred for 1 h at -40°C, quenched with aqueous ammonium chloride and the reaction mixture was poured into 5% hydrochloric acid and extracted with ether. The aqueous phase was basified with potassium carbonate and extracted with ether. The organic extracts

were dried and evaporated to give **9** as an oil (0.35 g, 68 %) after purification by flash chromatography (97:3 dichloromethane-methanol); ir ($CHCl_3$) 1600 (C=C); ^{1}H-nmr 2.83 (s, 3H, NCH_3),·3.09 (br s, 2H, $SCCH_2C$=), 3.77 (s, 3H, OCH_3), 5.85 (br s, 1H, =CH), 6.82 (d, J=8.5 Hz, 2H, Ar-H), 6.90-7.15 (m, 2H, In-H), 7.20-7.40 (m, 2H, In-H), 7.70 (d, J=8.5 Hz, 2H, Ar-H), 7.69 (s, 1H, In-3H); ^{13}C-nmr 24.9 ($SCH_2\underline{C}H_2$), 25.5 (C-5), 28.8 (SCH_2), 45.4 (NCH_3), 46.5 ($SC\underline{C}H_2C$=), 51.3 (C-6), 55.3 (OCH_3), 58.1 (SCS and C-2), 94.0 (In-C2), 113.9 (C-meta and In-C7), 123.1 (In-C4), 124.6 (=CH), 126.1 (In-C6), 129.3 (C-ortho), 129.6 (In-C5), 129.7 (C-ipso),129.8 (In-C3a), 132.0 (=C), 133.0 (In-C3), 138.0 (In-C7a), 163.0 (C-para); ms ic (m/z, %) 515 (M^++1, 100), 411 (3), 345 (16), 295 (5), 239 (14), 236 (10), 207 (22), 190 (71), 155 (32). Anal. Calcd for $C_{26}H_{30}N_2S_3O_3$: C, 60.67; H, 5.87; N, 5.44. Found: C, 60. 51; H, 5.95 ; N, 5.80.

1-(4-Methoxyphenylsulfonyl)-2-(1-oxide-1,3-dithian-2-yl)indole (**10a**). A solution of dithiane **2** (0.48 g, 1.19 mmol) and 85% MCPBA (0.27 g, 1.5 mmol) in dichloromethane (80 ml) and water (1 ml) was stirred at 0°C for 4 h. The reaction mixture was poured into aqueous sodium bicarbonate and extracted with dichloromethane. The organic layers were washed with water, dried, and evaporated to give a 4:1 diastereomeric mixture of sulfoxides **10a** as a yellow foam (0.43 g, 87%). The major sulfoxide (S=O equatorial; higher Rf) (0.29 g) was separated by flash chromatography (96:4 dichloromethane-methanol): mp 174-176 °C (acetone); ir (NaCl) 1370 , 1160; ^{1}H-nmr 2.30-2.60 (m, 2H, $SCH_2C\underline{H}_2$), 2.70 (br d, J=13 Hz, SCHeq), 2.98 (td, J=13 and 3.2 Hz, 1H, SCHax), 3.05 (td, J=13 and 3.2 Hz, 1H, SOCHax), 3.65 (br d, J=13 Hz, 1H, SOCHeq), 3.74 (s, 3H, OCH_3), 6.14 (s, 1H, SCHS), 6.85 (d, J=8.5 Hz, 2H, Ar-H), 6.97 (s, 1H, In-3H), 7.19 (td, J=7 and 1 Hz, 1H, In-6H), 7.29 (td, J=7 and 1 Hz, 1H, In-5H), 7.48 (dd, J=7 and 1 Hz, 1H, In-4H), 7.97 (d, J=8.5 Hz, 1H, Ar-H), 7.98 (d, 1H, In-7H); ^{13}C-nmr 29.9 ($SCH_2\underline{C}H_2$), 32.4 (SCH_2), 55.8 ($SOCH_2$), 61.2 (SOCHS), 113.4 (In-C3), 114.6 (C-meta), 115.3 (In-C7), 121.8 (In-C5), 124.3 (In-C4), 125.8 (In-C6), 129.4 (In-C3a), 130.1 (C-ortho), 134.0 (In-C2), 137.0 (In-C7a), 164.3 (C-para); ms (m/z, %) 421 (M^+, 14), 315 (6), 201 (12), 173 (12) 171 (74), 123 (23), 77 (100), 64 (55), 45 (40). Anal. Calcd for $C_{19}H_{19}NO_4S_3$: C, 54.13; H, 4.54; N, 3.32. Found: C, 53.69; H, 4.46; N, 3.29.

2-(1-Oxide-1,3-dithian-2-yl)-1-(phenylsulfonyl)indole (**10b**). Operating as above from 2-(1,3-dithian-2-yl)-1-(phenylsulfonyl)indole (1 g, 2.68 mmol) and 85% MCPBA (0.54 g, 3.13 mmol) in dichloromethane (98 ml) and water (2 ml), sulfoxide **10b** was obtained (0.83 g, 85%) after crystallization: mp 144-147°C (methanol); ir (KBr) 1445, 1360, 1050; ^{1}H-nmr 2.30-2.70 (m, 2H, $SCH_2C\underline{H}_2$), 2.42 (br d, J= 13 Hz, 1H, SCHeq), 2.94 (td, J=13 and 3 Hz, 1H, SCHax), 3.00 (td, J=13 and 3 Hz, 1H, SOCHax), 3.64 (br d, J=13 Hz, 1H, SOCHeq), 6.10 (s, 1H, SCHS), 6.98 (s, 1H, In-3H), 7.20-7.50 (m, 8H), 7.85-7.90 (m, 1H, In-7H); ^{13}C-nmr 29.9 ($SCH_2\underline{C}H_2$), 32.3 (SCH_2), 55.7 ($SOCH_2$), 61.1 ($SOCH_2$), 113.3 (In-C3), 115.0 (In-C7), 121.5 (In-C5), 124.1 and 125.6 (In-C4 and In-C6), 127.3 (C-ortho), 129.1 (C-meta), 129.3 (In-C3a), 134.0 (C-para), 134.1 and 134.2 (In-C2 and In-C7a), 137.7 (C-ipso); ms (m/z, %) 391 (M^+, 10), 236 (8), 160 (14), 130 (13) 89 (26), 77 (100), 51 (24). Anal. Calcd for $C_{18}H_{16}NO_3S_3.CH_3OH$: C, 54.01; H, 4.77; N, 3.31. Found: C, 54.18; H, 4.81; N, 3.36.

1-(4-Methoxyphenylsulfonyl)-2-indolyl 1-Methyl-4-hydroxy-4-piperidyl Ketone (**11**) (a) To a solution of **7** (0.2 g, 0.385 mmol) in 9:1 CH_3CN-H_2O (10 ml) stirred at room temperature, bis(trifluoroacetoxy)iodobenzene (Aldrich, 248 mg, 0.577 mmol) was added. The reaction mixture was stirred for 45 min and the solution was poured into saturated aqueous sodium bicarbonate (10 ml) and extracted with ether (3 x 10 ml). The organic layers were dried and the solvent was evaporated to give **11** (80 mg, 49%) as a

yellow oil after purification by flash chromatography (95:5 dichloromethane-methanol); ir ($CHCl_3$) 3300 (OH), 1675 (CO); ^{1}H-nmr 2.46 (s, 3H, NCH_3), 2.30-3.50 (m, 8H), 3.63 (s, 3H, OCH_3), 5.60 (br, 1H, OH), 6.56 (d, J=8 Hz, 2H, Ar-H), 7.00 (s, 1H, In-3H), 6.95-7.20 (m, 4H, In-H), 7.46 (d, J=8 Hz, 2H, Ar-H); ^{13}C-nmr 31.7 ($NCH_2\underline{C}H_2$), 46.0 (NCH_3), 51.2 (NCH_2), 55.7 (OCH_3), 88.6 (COH), 102.2 ((In-C7), 114.3 (C-meta), 199.0 (In-C2), 121.9 (In-C5), 124.7 (In-C4), 129.3 (C-ortho), 130.5 (In-C6), 130.6 (C-ipso), 133.5 (In-C3), 133.5 (In-C3a), 136.4 (In-C7a), 163.4 (C-para), 182.9 (C=O); ms (m/z, %) 428 (M^+, 2), 426 (7), 343 (2), 275 (2), 255 (15), 210 (11), 171 (23), 123 (20), 107 (34), 92 (36), 70 (100), 42 (65). Anal. Calcd for $C_{22}H_{24}N_2O_5S$: C, 61.67; H, 5.64; N, 6.53. Found: C, 61.72; H, 5.88; N, 6.89.

(b) Operating as above from **7** (0.29 g, 0.56 mmol) in 9:1 CH_3OH-H_2O (20 ml), bis(trifluoroacetoxy)-iodobenzene (350 mg. 0.8 mmol), **11**. dimethylacetal (197 mg, 74%) was obtained after purification by flash chromatography (dichloromethane to 95:5 dichloromethane-methanol); ir ($CHCl_3$) 3100-3400 , 1595, 1490, 1255, 1150; ^{1}H-nmr 1.75 (br d, J=12 Hz, 2H, 3- and 5-Heq), 2.16 (td, J=12 and 3 Hz, 2H, 3-H and 5-Hax), 2.39 (s, 3H, NCH_3), 2.50 (t, J= 12 Hz, 2H, 2- and 6-Hax), 2.90 (br d, J=12 Hz, 2- and 6-Heq), 3.52 (s, 6H, OCH_3), 3.76 (s, 3H, OCH_3), 5.10 (br, 1H, OH), 6.83 (d, J=8 Hz, 2H, Ar-H), 6.96 (t, J=8 Hz, 1H, In-5H), 7.24 (td, J=7 and 1 Hz, 1H, In-6H), 7.33 (d, J=7 Hz, 1H, In-4H), 7.40 (s, 1H, In-3H), 7.45 (d, J=8 Hz, 1H, In-7H), 7.78 (d, J=8 Hz, 2H, Ar-H); ^{13}C-nmr 30.4 ($NCH_2\underline{C}H_2$), 45.3 (NCH_3), 50.7 (NCH_2), 54.5 (OCH_3), 55.4 (OCH_3), 75.0 (COH), 86.0 ($COCH_3$), 104.0 (In-C2), 114.1 (C-meta and In-C7), 120.3 (In-C5) 124.0 (In-C4), 129.4 (C-ortho), 129.7 (In-C3a), 130.3 (In-C6), 131.6 (C-ipso), 132.2 (In-C3), 139.9 (In-C-7a), 163.1 (C-para). Anal. Calcd for $C_{24}H_{30}N_2O_6S$: C, 60.74; H, 6.37; N, 5.90. Found: C, 61.12; H, 6.77; N, 6.18. A solution of the acetal (197 mg) and 1:1 CH_3OH-10% HCl (30 ml) was refluxed for 6 h and the resulting mixture was basified with aqueous potassium carbonate and extracted with ether. The organic layer was dried and evaporated to give **11** (150 mg, 85 %) after purification by flash chromatography .

(c) A solution of **7** (0.428 g, 0.825 mmol) and 85% MCPBA (0.180 g, 0.99 mmol) in dichloromethane (100 ml) and water (1 ml) was stirred at -20°C under nitrogen atmosphere for 6 h. The reaction mixture was poured into aqueous sodium bicarbonate and extracted with dichloromethane. The organic layer was washed with water, dried, and evaporated to give sulfoxide **12** (185 mg, 42%) which was stirred at 65°C overnight with 50% acetic acid (60 ml). The reaction mixture was poured into aqueous potassium carbonate and extracted with ether. Drying and evaporation of the organic extracts followed by flash chromatography (95:5 dichloromethane-methanol) afforded ketone **11** (35 mg, 23%).

5-Methoxybenzo[c][1,2]oxathiolane-3-spiro-4′-(N-methylpiperidine) 2,2-Dioxide (**13**) Operating as in the preparation of **7**, from sulfoxide **10a** (500 mg, 1.18 mmol), n-butyllithium (1.6M, 1 ml, 1.6 mmol), N-methyl-4-piperidone (0.16 ml, 1.41 mmol) and dry THF (50 ml), sultone **13** was obtained as a pale foam (70 mg, 21%) after purification by flash chromatography (80:20 CH_2Cl_2-MeOH); ir ($CHCl_3$) 1340 ; ^{1}H-nmr (60 MHz) 2.30 (s, 3H, NCH_3), 3.80 (s, 3H, OCH_3), 6.53 (d, J=2 Hz, 1H, Ar-3H), 6.80 (dd, J=8 and 2 Hz, 1H, Ar-5H), 7.40 (d, J=8 Hz, 1H, Ar-6H); ms (m/z,%) 283 (M^+, 57), 282 (36), 257 (2), 204 (2), 176 (2), 159 (12), 115 (11), 95 (10) 70 (22), 57 (100), 42 (80). Anal. Calcd for $C_{13}H_{17}NO_4S$: C, 55.10; H, 6.04; N, 4.94. Found: C, 54.91; H, 6.43; N, 4.97.

2-Bis(ethylthiomethyl)-1-phenylsulfonylindole (**14**). A solution of 1-phenylsulfonyl-2-carbaldehyde[7] (2.8 g, 8.8 mmol), p-toluenesulfonic acid (1.6 g, 8.8 mmol), ethanethiol (2.3 ml, 30.8 mmol), and toluene (300 ml) was stirred at room temperature for 15 h. The reaction mixture was poured into 10% aqueous sodium bicarbonate and extracted with toluene. The organic extracts were washed several times with water, dried, and

evaporated to give dithioacetal **14** (2.4 g, 70%) after purification by flash chromatography (CH_2Cl_2): mp 74- 76 °C (ether-hexane); ir ($CHCl_3$) 1170, 1370; ^{1}H-nmr 1.24 (t, J=7 Hz, 6H, CH_2CH_3), 2.63 (q, J=7 Hz, 4H, CH_2CH_3), 6.05 (s, 1H, SCHS), 7.02 (s, 1H, In-3H), 7.10-8.10 (m, 8H, Ar-H); ^{13}C-nmr 13.2 (CH_2CH_3), 25.0 (CH_2CH_3), 43.5 (SCHS), 111.4 (In-C3), 114.5 (In-C7), 120.4 (In-C5), 123.3 (In-C4), 124.4 (In-C6), 126.0 (C-ortho), 128.3 (In-C3a), 128.5 (C-meta), 133.3 (C-para), 136.6 (In-C7a), 138.1 (C-ipso), 139.4 (In-C2). Anal. Calcd for $C_{19}H_{21}NO_2S_3$: C, 58.28; H, 5.41; N, 3.58; S, 24.56. Found: C, 58.44; H, 5.33; N, 3.52; S, 24.84.

2-[1,1-Bis(ethylthio)ethyl]-1-(phenylsulfonyl)indole (**17**). Operating as in the preparation of **6** from dithioacetal **14** (0.84 g, 2.15 mmol), anhydrous THF (75 ml), n-butyllithium (1.6M, 1.6 ml, 2.6 mmol), and methyl iodide (0.18 ml, 2.8 mmol), a 2:3 mixture of compound **17** and 1-(benzenesulfonyl)-2-(1-ethylthio) ethylindole (**20**) was obtained after purification by flash chromatography (40:60 hexane-ether). **17** (0.21 g, 44%): Ir (NaCl) 3450-3100 (OH); ^{1}H-nmr (60 MHz) 1.15 (t, J=7 Hz, 6H, CH_2CH_3), 1.83 (s, 3H, CH_3), 2.70 (q, J=7 Hz, 4H, CH_2CH_3), 6.65 (s, 1H, In-3H), 6.70-7.30 (m, 9H). Anal. Calcd for $C_{20}H_{23}NO_2S_3$: C, 59.22; H, 5.71; N, 3.45. Found: C, 59.60; H, 5.76; N, 3.17. **20** (0.27 g, 56%): Ir ($CHCl_3$) 1370, 1440; ^{1}H-nmr 1.11 (t, J=7 Hz, 3H, CH_2CH_3), 1.62 (d, J=7 Hz, 3H, $SCHCH_3$), 2.40 (q, J=7 Hz, 2H, SCH_2), 4.85 (q, J=7 Hz, 1H, SCH), 6.70 (s, 1H, In-3H), 6.7-7.6 (m, 7H), 7.85 (d, J=7.5 Hz, 1H, In-4H), 8.15 (d, J=7.5 Hz, 1H, In-7H); ^{13}C-nmr 13.4 (SCH_2CH_3), 22.0 (In-CCH_3), 24.1 (SCH_2), 35.3 (SCH), 109.2 (In-C3), 114.5 (In-C7), 120.1 (In-C5), 123.2 (In-C4), 123.9 (In-C6), 125.7 (C-ortho), 128.5 (C-meta), 128.6 (In-C3a), 133.2 (C-para), 137.1 (In-C7a), 138.0 (C-ipso), 144.0 (In-C2); ms (m/z, %) 345 (M^+, 7), 284 (47), 270 (7), 206 (11), 143 (71), 115 (44), 89 (27), 77 (100), 51 (27). Anal. Calcd for $C_{18}H_{19}NO_2S_2$: C, 62.58; H, 5.54; N, 4.05. Found: C, 62.73; H, 5.48; N, 3.95.

4-[1,1-Bis(ethylthio)-1-(1-phenylsulfonyl-2-indolyl)methyl]-1-methyl-4-piperidinol (**19**). Operating as in the preparation of **6** from dithioacetal **14** (1 g, 2.55 mmol), anhydrous THF (100 ml), n-butyllithium (1.6M, 1.92 ml, 3 mmol), and N-methyl-4-piperidone (0.36 ml, 2.55 mmol), a mixture of two compounds was obtained which were separated and purified by flash chromatography. On elution with 97:3 dichloromethane-methanol piperidinol **19** was obtained as an oil (0.2 g, 16 %); ir ($CHCl_3$) 3450-3100 (OH); ^{1}H-nmr 1.30 (t, J=6 Hz, 6H, CH_2CH_3), 2.03 (d, J=10 Hz, 2H, β-CHeq), 2.38 (s, 3H, NCH3), 2.84 (q, J=6 Hz, 4H, SCH_2), 4.60 (br, 1H, OH), 7.01 (td, J=7 and 1.2 Hz, 1H, In-5H), 7.47 (s, 1H, In-3H), 7.20-7.60 (m, 7H, Ar-H), 7.90 (dd, J=7 and 1 Hz, 1H, In-7H); ^{13}C-nmr 14.8 (CH_2CH_3), 28.1 and 28.4 (CH_2CH_3), 33.4 and 34.8 (NCH_2CH_2), 46.1 (NCH_3), 51.6 (NCH_2), 72.5 (COH), 72.8 (SCS), 113.5 (In-C3), 115.9 (In-C7), 121.5 (In-C5), 124.6 (In-C4), 125.3 (In-C6), 126.9 (C-ortho), 129.8 (In-C3a), 129.9 (C-meta), 134.5 (C-para), 138.0 (In-C7a), 140.0 (C-ipso), 140.2 (In-C2); ms (m/z, %) 504 (M^+, 1), 330 (25), 283 (24), 232 (34), 189 (29), 114 (60), 77 (100), 70 (94), 44 (60), 43 (91). Anal. Calcd for $C_{25}H_{32}N_2O_3S_3$ HCl: C, 55.48; H, 6.15; N, 5.18. Found: C, 55.80; H, 6.19; N, 5.37. On elution with 90:10 dichloromethane-methanol 4-[1-ethylthio-1-(1-phenyl sulfonyl-2-indolyl)methyl]-1-methyl-4-piperidinol (**22**) (0.43 g, 38%) was obtained as an oil; ir ($CHCl_3$) 3450-3100 (OH); ^{1}H-nmr 1.10 (t, J=7 Hz, 3H, CH_2CH_3), 1.50-2.00 (m, 6H), 2.32 (s, 3H, NCH_3), 3.59 (q, J=7 Hz, 2H, SCH2), 4.88 (s, 1H, SCH), 7.01 (s, 1H, In-3H), 7.26 (td, J=7 and 1 Hz, 1H, In-5H), 7.51 (td, J=7 and 1 Hz, 1H, In-6H), 7.73 (dd, J=7 and 1 Hz, 1H, In-4H), 8.20 (br d, J=7 Hz, 1H, In-7H); ^{13}C-nmr 13.8 (CH_2CH_3), 23.3 ($SCHCH_3$), 35.5 and 36.0 (NCH_2CH_2), 46.2 (NCH_3), 50.8 and 50.9 (NCH_2), 53.3 (SCH), 73.6 (COH), 113.5 (In-C3), 115.9 (In-C7), 121.6 (In-C5), 124.6 (In-C4), 125.3 (In-C6), 126.8 (C-ortho), 129.2 (C-meta), 129.3 (In-C3a), 134.5 (C-para), 138.0 (In-C7a), 140.0 (C--ipso),

141.0 (In-C2); ms (m/z, %) 444 (M^+, 1), 383 (8), 331 (3), 270 (5), 242 (5), 190 (33), 114 (100), 77 (50), 43 (42). Anal. Calcd for $C_{23}H_{28}N_2O_3S_2$: C, 62.13; H, 6.34; N, 6.30. Found: C, 62.45 ; H, 6.57; N, 6.69.

2-[Ethylthiol$^2H_1$]methyl]-1-(phenylsulfonyl)indole (**21**).To a solution of **14** (175 mg, 0.43 mmol) in anhydrous THF (30 ml) n-butyllithium (1.6M, 0.32 ml, 0.51 mmol) was added at -20°C under argon atmosphere. After stirring for 15 min the reaction mixture was quenched with deuterium oxide (2 ml) and extracted with ether. The organic layers were dried and evaporated to afford a 3:2 mixture of oils **18** (78 mg, 48%) and **21** (45 mg, 31%) after purification by flash chromatography (99:1 ether-diethylamine). **18**: The ^{1}H-nmr data are the same of than those of dithioacetal **14** except the absence of the signal corresponding to SCHS. **21**: Ir (NaCl) 1165, 1370; ^{1}H-nmr 1.25 (t, J=7 Hz, 3H, CH_3), 2.54 (q, J=7 Hz, 2H, SCH_2CH_3), 4.17 (s, 1H, SCHD), 6.68 (s, 1H, In-3H), 7.20-7.60 (m, 7H), 7.87 (d, J=8 Hz, 1H, In-4H), 8.12 (d, J=8 Hz, 1H, In-7H); ^{13}C-*nmr* 14.1 (SCH_2CH_3), 25.7 (SCH_2CH_3), 29.1 (InCS), 111.2 (In-C3), 114.8 (In-C7), 120.6 (In-C5), 123.7 (In-C4), 124.6 (In-C6), 126.7 (C-ortho), 129.2 (C-meta), 129.3 (In-C3a), 133.9 (C-para), 138.0 and 138.9 (In-C7a and C-ipso).

3-[2-Ethylthio-2-(1-phenylsulfonyl)indolyl)ethyl]-1-methyl-1,2,5,6-tetrahydropyridine (**23**). To a solution of dithioacetal **14** (0.78 mg, 2 mmol) in anhydrous THF (25 ml) cooled at -40°C under argon atmosphere n-butyllithium (1.6 M, 1.75 ml , 2.8 mmol) was added . After stirring for 20 min at the same temperature, a solution of 3-chloromethyl-1-methyl-1,2,5,6-tetrahydropyridine **5**(2.03 mmol) , prepared by treatment of hydrochloride **5** (370 mg, 2.03 mmol) with n-butyllithium (1.6 M, 1.4 ml, 2.2 mmol) at -40°C , in anhydrous THF (20 ml), was slowly transferred via syringe. The reaction mixture was stirred for 1h at -40°C, quenched with aqueous ammonium chloride, poured into 5% hydrochloric acid and extracted with ether. The aqueous phase was basified with solid potassium carbonate and extracted with ether. The organic extracts were dried and evaporated to give tetrahydropyridine **23** as an oil after purification by flash chromatography 99:1 dichloromethane-methanol) (699 mg , 68%); ^{1}H-nmr 1.59 (t, J=7 Hz, 3H, CH_2CH_3), 2.42 (s, 3H, NCH_3), 2.15-2.60 (m, 6H), 2.70-2.90 (m, 2H, $=CCH_2N$), 3.03 (br s, 2H, $SCHCH_2$), 5.05 (t, J=7 Hz, 1H, SCH), 5.70 (br, 1H, =CH), 6.97 (s, 1H, In-3H), 7.30-8.00 (m, 8H), 8.19 (d, J=7 Hz, 1H, In-7H); ^{13}C-nmr 15.0 (SCH_2CH_3), 26.0 and 26.3 ($S-CH_2$ and C-5), 42.1 (SCH), 43.4 ($SCHCH_2$), 45.6 (NCH_3), 52.3 (C6), 57.9 (C-2), 112.1 (In-C3), 116.3 (In-C7), 122.1 (In-C5), 123.6 (In-C4), 125.2 (In-C3a), 125.9 (=CH), 127.7 (C-ortho), 130.7 (C-meta), 134.0 (C-para), 135.5 (=C), 135.2 (In-C7a), 139.0 (C-ipso) ,144.0 (In-C2); ms (m/z, %) 440 (M^+, 0.5), 330 (3), 299 (11), 237 (30), 194 (21), 110 (100), 77 (18), 42 (3). Anal. Calcd for $C_{24}H_{28}N_2O_2S_2$: C, 65.42; H, 6.40; N, 6.35. Found: C, 65.31; H, 6.80; N, 6.20.

2-[S-Oxide-1,1-bis(ethylthio)methyl]-1-(phenylsulfonyl)indole (**24**). To a solution of **14** (0.5 g, 1.28 mmol) *in dichloromethane (40 ml) and water (1 ml)* 85% MCPBA (0.278 g, 1.6 mmol) was added. The reaction mixture was stirred for 5 h at 0°C, poured into aqueous sodium bicarbonate and extracted with dichloromethane. The organic layers were dried and evaporated to give **24** (437 mg, 84%) after purification by flash chromatography (95:5 dichloromethane-methanol); ir ($CHCl_3$) 1170, 1370 (SO_2); ^{1}H-nmr 1.20 (t, J=7 Hz, 3H, SCH_2CH_3), 1.25 (t, J=7 Hz, 3H, $SOCH_2CH_3$), 2.50 (q, J=7 Hz, 2H, SCH_2CH_3), 2.80 (q, J=7 Hz, 2H, $SOCH_2CH_3$), 5.73 and 5.86 (2 s, 1H, 2-H), 6.60 and 6.80 (2 s, 1H, In-3H), 6.90-7.40 (m, 7H, In-H), 7.40-8.00 (m, 2H, In-4H and In-7H); ms (m/z,%) 407 (M^+, 0.1), 346 (35), 330 (100), 285 (71), 156 (28), 145 (23), 144 (440, 130 (25), 116 (42), 77 (99). Anal. Calcd for $C_{19}H_{21}NO_3S_3$: C, 55.98; H, 5.19; N, 3.43; S, 23.60. Found: C, 55.61; H, 5.34; N 3.53; S, 24.05.

4-[1,1-Bis(ethylthio)-1-(2-indolyl)methyl]-1-methyl-4-piperidinol (**27**). A solution of **14** (2 g, 5.1 mmol) in ethanol (100 ml) and 10% aqueous sodium hydroxide (50 ml) was refluxed for 15 h. Ethanol was removed and the residue, solved in dichloromethane, was washed with water. The organic phase, dried and evaporated, was purified by flash chromatography (70:30 hexane-ether) to give 2-bis(ethylthio)methylindole (**26**) as a pale oil (600 mg, 47%); ir (NaCl) 3400 (NH); ^{1}H-nmr 1.10 (t, J=7 Hz, 6H, CH_2CH_3), 2.43 (q, J=7 Hz, 4H, CH_2CH_3), 4.88 (s, 1H, SCHS), 6.20 (s, 1H, In-3H), 6.60-7.70 (m, 4H), 8.15 (br s, 1H, NH); ^{13}C-nmr 13.8 (CH_3), 25.6 (CH_2), 44.1 (SCHS), 102.1 (In-C3), 112.1 (In-C7), 120.5 (In-C4), 121.0 (In-C5), 122.8 (In-C6), 127.5 (In-C3a), 135.5 (In-C2), 141.5 (In-C7a); ms (m/z,%) 251 (M^+, 21), 190 (41), 160 (32), 130 (30), 117 (22), 77 (100), 43 (62). Anal. Calcd for $C_{13}H_{17}NS_2$: C, 56.14; H, 17.13; N, 21.01. Found: C, 56.44; H, 17.34; N, 21.33.

Operating by the general method from **26** (300 mg, 1.19 mmmol), n-butyllithium (1.6M, 1.63 ml, 2.6 mmol), N-methyl-4-piperidone (0.14 ml, 1.19 mmol) and dry THF (40 ml), compound **27** was obtained as an oil (210 mg, 50%) which was purified by flash chromatography (ether-diethylamine 98:2); ir (NaCl) 3500-3100 (OH); ^{1}H-nmr 1.59 (t, J=7 Hz, 6H, CH_2CH_3), 1.73 (d, J=12 Hz, 2H, NCH_2CHeq), 2.44 (s, 3H, NCH_3), 2.30-3.00 (m, 10H), 6.77 (d, J=1 Hz, 1H, In-3H), 7.06 (td, J=7 and 1 Hz, 1H, In-5H), 7.15 (td, J=7 and 1 Hz, 1H, In-6H), 7.37 (br d, J=7 Hz, 1H, In-7H), 7.58 (br d, J=7 Hz, 1H, In-4H), 9.50 (br, 1H, NH); ^{13}C-nmr 13.6 (CH_2CH_3), 26.2 (CH_3CH_2), 31.7 (NCH_2CH_2), 44.5 (NCH_3), 51.0 (NCH_2), 71.6 (SCS), 77.1 (COH), 105.6 (In-C3), 111.3 (In-C7), 120.0 (In-C4), 120.7 (In-C5), 122.4 (In-C6), 127.1 (In-C3a), 136.2 (In-C7a), 136.6 (In-C2); ms (m/z, %) 364 (M^+, 0.6), 331 (1), 252 (12), 251 (61), 222 (24), 160 (62), 114 (100), 70 (39), 44 (60). Anal. Calcd for $C_{19}H_{28}N_2OS_2$: C, 62.59; H, 7.74; N, 7.68. Found: C, 62.79; H, 7.88; N, 7.26.

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