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# SYNTHESIS AND REACTIVITY OF 2-(1',3'-DITHIAN-2'-YL)INDOLES

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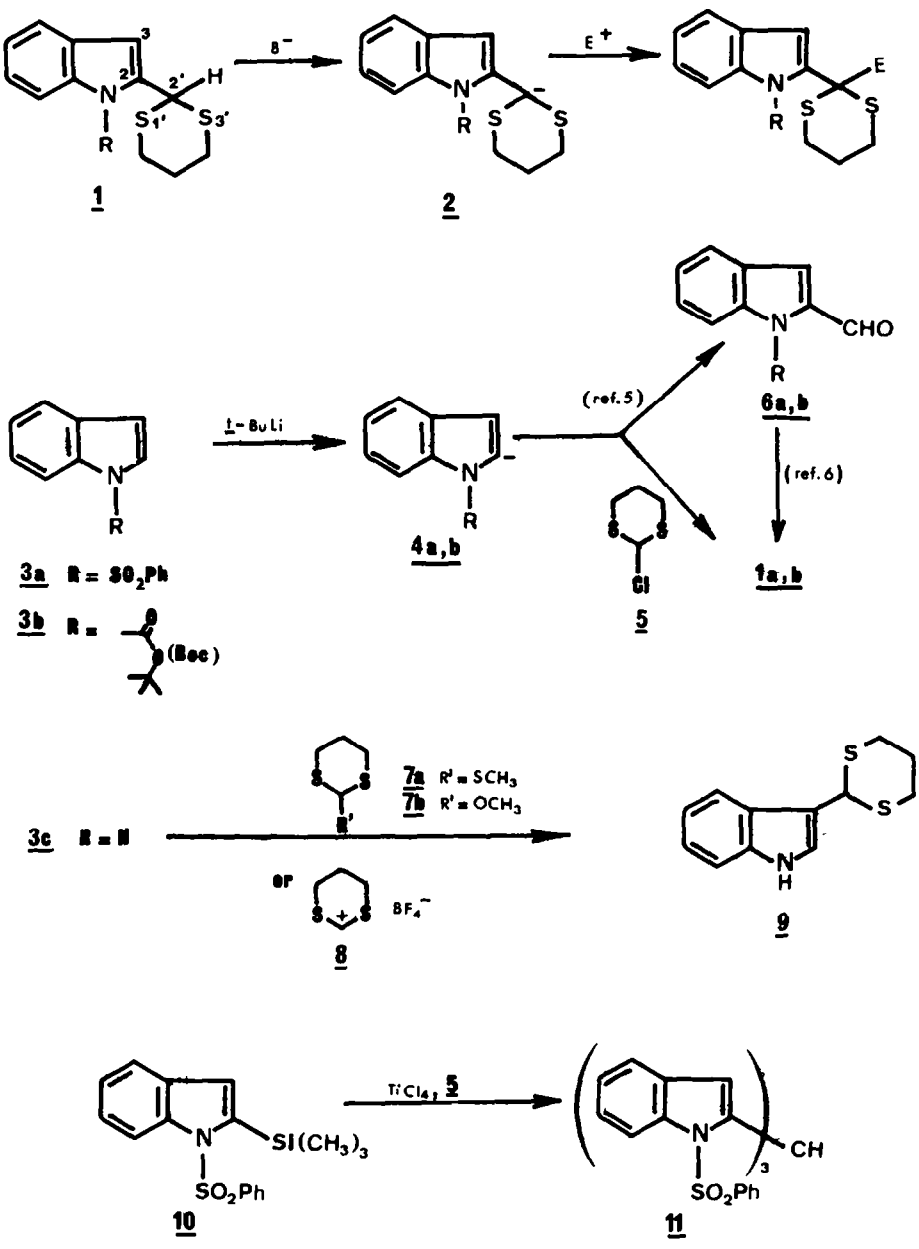
*Abstract : The 2-(1',3'-dithian-2'-yl)indoles 1a,b were prepared in a single operation involving reaction of the anions of the N-protected indoles 3a,b with 2-chloro-1,3-dithiane. Subsequent reaction of 1a with excess n-BuLi followed by an electrophile (1-methyl-4-piperidone) led to formation of the ring opened acetylene derivative 13 and not to the expected product 19 (N-SO$_2$Ø). When t-BuLi was employed as the base the dithiane ring opened product 14 was obtained. Successful functionalization of the dithiane C-2' carbon was achieved giving compounds 16-20 on reaction of the dianion derived from 1c and n-BuLi (2 equiv.) with an electrophile (Table 1 ; yields : 70-90%).*

The "formal" reaction[1] between the C-2 position of the indole ring and a carbonyl containing component has often been employed as a key operation in the synthesis of indole alkaloids.[2] Considering this bond connection problem from a different viewpoint we are currently investigating the possibility that a wide variety of indole compounds can be prepared through reaction of the anion 2, derived from the C-2 indole substituted dithiane 1, with an appropriately functionalized electrophile ($E^+$) (Scheme 1). In this paper we report our results concerning the preparation of the indole dithianes 1a-c and the study of the reactivity of their respective anions towards a series of electrophiles.

The method chosen for the preparation of compounds 1a,b involves the reaction of the N-protected (deactivated) indole anion 4a,b with 2-chloro-1,3-dithiane (5).[3,4] There are several reasons for this choice. Firstly, this route is more direct than the classical approach involving preparation of aldehyde 6[5a] followed by dithiane formation,[6] and secondly, the reaction of indole 3c itself with the dithiane derivatives 7a,b,[7] or the carbocation 8,[8] leads to selective formation of the C-3 substituted indole derivative 9 and not to compound 1c.

The chlorodithiane 5 was prepared by the reaction of 1,3-dithiane with either N-chlorosuccinimide in anhydrous benzene[3a,b] or sulfuryl chloride.[3c] The latter procedure generally gave a cleaner product. The subsequent reaction of 5 with the anion 4a of phenylsulfonylindole 3a (t-BuLi, -10°C),[5] gave the desired product 1a in 60-65% yield (gram scale). In a similar manner the anion 4b of N-tert-butoxycarbonylindole 3b was generated at -10°C and reacted with 5. However, in this instance compound 1b was isolated in only 35% yield together with 2,2-bis-1,3-dithiane (15%)[3c] and starting material. Significant in the nmr spectra



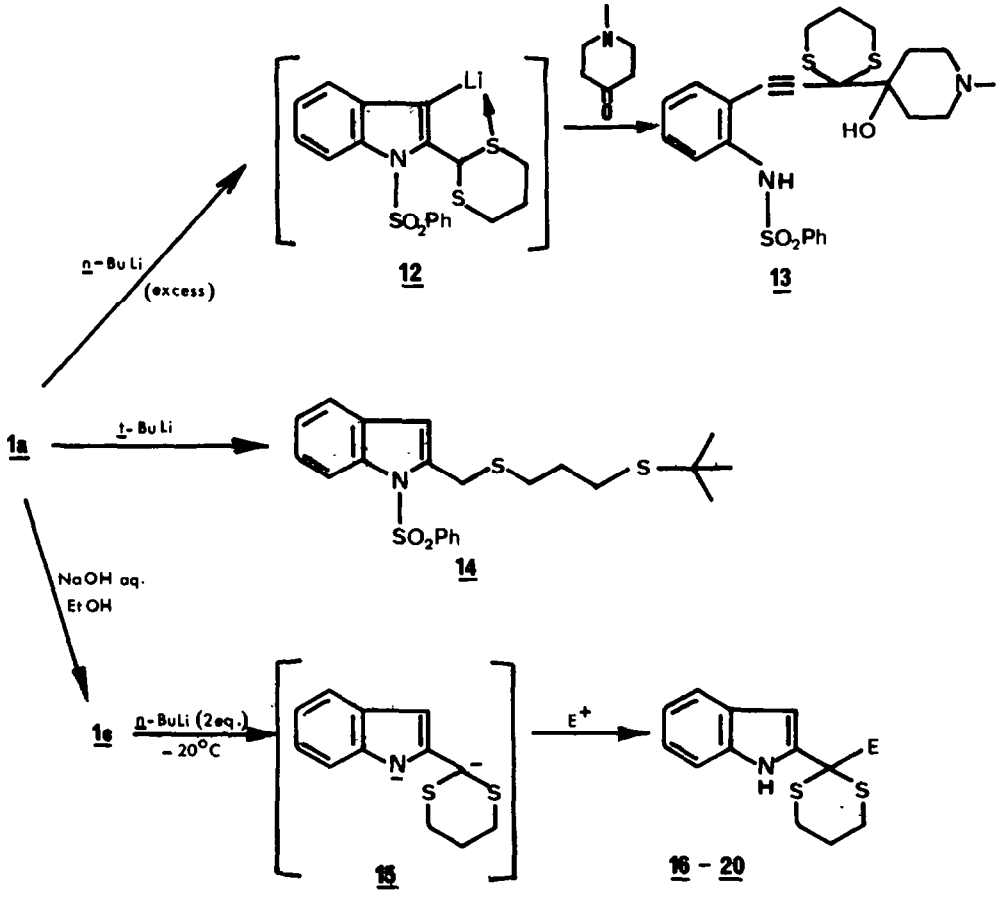

**Scheme 1**

for compounds 1a and 1b was the presence of singlet resonances at δ 7.0 (1a,b) and δ 6.26 (1a), 6,12 (1b) for the indole proton at C-3 and dithiane methine proton, respectively, and a peak at δ 42.4 for the methine carbons. Important also was the absence of a doublet peak at ∿ δ 7.50 in the $^1$H nmr spectra characteristic for the C-2 protons of the starting materials.

Attempts to prepare 1a by reaction of 2-chloro-1,3-dithiane (5) with 2-trimethylsilyl-1-(phenylsulfonyl)indole (10), obtained by reaction of 4a with trimethylsilyl chloride in THF (75% yield), in the presence of $TiCl_4$ proved to be unsuccessful. The only product isolated from the reaction was tris-1-(phenylsulfonyl)indolylmethane (11) resulting from attack of two indole

units onto the initially formed product 1a.[10] The structure of compound 11 was readily determined from the NMR data (δ 5.5 (s, CH) ; δ 31.0 (CH)) and from its mass spectrum in which prominent fragments were observed at m/z 640, 498, and 358 corresponding to successive loss of the three phenylsulfonyl groups. Under milder conditions mixtures of starting material 10 and phenylsulfonylindole 3a were obtained.

When dithiane 1a was reacted with n-butyllithium (1 eq) at -20°C in THF followed by addition of $D_2O$ only 30-40% deuterium incorporation was observed. Moreover, when the reaction was carried out with other electrophiles such as 1-methyl-4-piperidone the addition product was not detected and starting material was recovered unchanged. The use of an excess of n-butyllithium (4 eq) followed by reaction with 1-methyl-4-piperidone afforded the acetylenic derivative 13 in 31% yield (Scheme 2). Amongst other things, the opening of the indole ring was deduced from the disappearance of the signals at δ 6.26 and 7.03, corresponding to the protons of dithiane ring 2'-position and indole ring 3-position in the $^1H$ nmr spectrum. Furthermore, in the $^{13}C$ nmr, signals at δ 83.4 and 91.1, characteristic of a substituted alkyne system, where observed. Formation of 13 apparently results from a facile opening of the indole ring via the 3-lithio intermediate 12 followed by deprotonation and alkylation of the dithiane system. That the initial reaction of 1a with n-BuLi involves loss of the indole ring proton is probably the result of a stabilizing coordination of the lithium cation of 12 with sulfur. An analogous result was observed by Gribble et al[11] for the reaction of 1-phenylsulfonyl-2-(2'-pyridinyl)indole with alkyllithium bases.

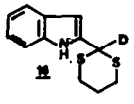
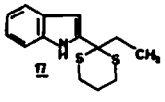
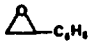
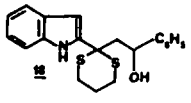
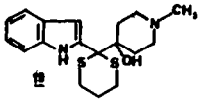
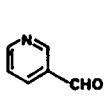
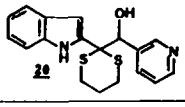



Scheme 2

Finally, treatment of 1a with tert-butyllithium (1 eq) at -30°C in THF produces the opening of the dithiane ring with formation of 2-(3-tert-butylthiopropylthiomethyl)-1-phenylsulfonylindole 14 in 43% yield. In the $^1$H nmr spectrum of this product two singlets were observed at δ 1.26 and 4.03 for the methyl protons of the t-butyl groups and the hydrogens of the methylene group adjacent to the indole ring. The aliphatic signals in the $^{13}$C nmr spectrum are in agreement with the proposed structure.

It was felt that these problems could be overcome by working with the dianion of 1c. Furthermore, this dianion should be highly reactive to electrophiles. The indole dithiane 1a was thus deprotected giving 1c (88%) by treatment with 10% aqueous NaOH in ethanol. Milder conditions (KO$^t$Bu, THF, 0°)[12] unfortunately gave 1c in much lower yields. Treatment of 1c with n-butyllithium (2 eq) at -20°C resulted in a rapid formation of the intermediate dianion 15 which on treatment with $D_2O$ affords the deuterated product 16 (E = D) in quantitative yield. Use of ethyl bromide (1 eq) as the electrophile resulted in regiospecific formation of dithiane 17 (E = $C_2H_5$). No N-alkylation products were detected. In the $^1$H nmr spectrum of this product a doublet (J = 1Hz) was observed at δ 6.90 for the indole proton at C-3 and a broad signal at δ 8.8 for the NH confirming its structure. This result, as well as the high yield of the reaction prompted us to try other electrophiles (Table I) in order to generalize the process. When the dithiane 1c was reacted with styrene oxide, alcohol 18 resulting from attack of anion of 15 at the less substituted carbon was obtained.

Table I

| Substrate | Electrophile | Product | Yield (%) |
|---|---|---|---|
| 1c | $D_2O$ |  16 | quantitative |
| 1c | $BrCH_2CH_3$ |  17 | 88 |
| 1c |  |  18 | 93 |
| 1c |  |  19 | 73 |
| 1c |  |  20 | 86 |

In contrast with the results observed for 1a, reaction of 1c with N-methyl-4-piperidone also proved to be efficient. Finally, reaction of dianion of 1c with nicotinaldehyde gave a satisfactorily yield of the corresponding alcohol 20. In all cases the structures of the condensation products were corroborated by elemental analyses and from the spectroscopic data.

In conclusion the method described in this paper presents the advantage that 2-(2'-substituted-2'3'-dithian-2'-yl) indoles, or potentially 2-acylindoles via dethioketalation, are readily prepared in three steps from 1-phenylsulfonyl indole.

## EXPERIMENTAL

Melting points were taken on a Reichert Hot Stage apparatus and are uncorrected. $^1H$ nmr spectra were recorded in a Brucker WP 80 (80 MHz), Brucker WP 200 (200 MHz) or Brucker WP 400 (400 MHz) spectrometer. $^{13}C$ nmr spectra were recorded in $CDCl_3$ on a Brucker WP 200 instrument. Chemical shifts ($\delta$) are in ppm downfield from tetramethylsilane as internal standard. Mass spectrometry was performed on an AEI MS 50 spectrometer by the Mass Spectrometry Service of the ICSN at Gif. Microanalyses were carried out at the ICSN at Gif. Chloroform and methylene chloride, when used as reaction solvents, were distilled from phosphorus pentoxide under an argon atmosphere. Tetrahydrofuran and ether were distilled from sodium-benzophenone under an argon atmosphere. In reactions requiring anhydrous conditions the apparatus and transfer equipment were dried at 100-110°C for at least 2 h and cooled to 25°C under an argon atmosphere before use. Flash chromatography refers to the medium pressure technique described by W.C. Still[13].

2-(1',3'-Dithianyl-2'-yl)-1-(phenylsulfonyl)indole (1a).

Commercial tert-butyllithium (13.0 mmol) was added via syringe to a solution of 1-(phenylsulfonyl)indole (3a) (3.0 g, 11.6 mmol) in dry THF (50 ml) cooled to -10°C under an argon atmosphere. After stirring for 45 min at -10°C a solution of 2-chloro-1,3-dithiane, prepared from 1,3-dithiane (1.40 g, 11.6 mmol) and N-chlorosuccinimide (1.7 g, 13.0 mmol) in anhydrous benzene (30 ml), was added slowly. The resulting reaction mixture was stirred at -10°C for 2 h and then diluted by addition saturated aqueous $NaHCO_3$ and extracted with ether. The ether layer was then washed with saturated brine, dried over $MgSO_4$ and concentrated. The crude product mixture was separated by flash chromatography on silica gel (hexane-ether ; 80-20). Compound 1a was obtained as a white solid (2.60 g, 63 %) : m.p. 137-138°C (acetone-hexane). $^1H$ nmr (400 MHz) : $\delta$ 1.98 (qt, J = 14 and 1.5 Hz, H-5'ax), 2.20 (br.d, J = 14 Hz, H-5'eq), 2.94 (dt, J = 14 and 4 Hz, H-4'éq and H-6'éq), 3.18 (td, J = 14 and 1.5 Hz, H-4'ax and H-6'ax), 6.26 (s, H-2'ax), 7.03 (s, H-3), 7.21 (t, J = 8 Hz, H-5), 7.30 (t, J = 8 Hz, H-6), 7.40 (t, J = 8 Hz, Ar-H), 7.45 (d, J = 8 Hz, indole-H), 7.50 (t, J = 8 Hz, Ar-H), 7.91 (dd, J = 8 and 1 Hz, indole-H), 8.08 (d, J = 8 Hz, 2H, Ar-H). $^{13}C$ nmr : $\delta$ 25.2, 32.4, 42.4, 113.4, 115.2, 121.1, 124.0, 125.2, 126.8, 129.0, 129.3, 133.8, 136.6, 138.1, 139.0. MS m/z (rel. intensity) : 375 ($M^{+\cdot}$, 42), 236(30), 234(100), 233(47), 116(17), 89(17), 77(27), 73(15), 45(13). Found : C, 57.37 ; H, 4.55 ; N, 3.68. Calcd. for $C_{18}H_{17}NO_2S_3$ : C, 57.57 , H, 4.56 ; N, 3.72.

1-(Phenylsulfonyl)-2-trimethylsilylindole (10)

Commercial tert-butyllithium (10 mmol) was added via syringe to a solution of 1-(phenylsulfonyl)indole (3a) (2.5 g, 9.7 mmol) in dry THF (50 ml) cooled to -10°C and under an argon atmosphere. The mixture was stirred for 45 min at -10°C and then treated with chlorotrimethylsilane (6.2 ml, 48.4 mmol) in dry THF (5 ml) keeping the temperature at -20°C. After stirring for an additional 2 h at -20°C the cold bath was removed and the reaction was warmed to room temperature, poured into 5 % aqueous $NaHCO_3$ and extracted with ether. The ether extract was then washed with water, dried ($MgSO_4$), and concentrated in vacuo affording an oil which was purified by flash chromatography on silica gel (hexane-ether ; 95-5). Compound 10 was obtained as a colourless solid : m.p. 65-67°C (hexane-acetone). $^1H$ nmr (80 MHz) : $\delta$ 0.45 (s, 9H, $CH_3$), 6.9 (s, H-3), 7.0-8.0 (m, 9H, Ar-H). $^{13}C$ nmr : $\delta$ 0.63, 114.1, 121.1, 121.9, 123.4, 125.0, 129.0, 130.9, 133.3, 138.8, 139.5, 143.1. MS m/z (rel. intensity) : 329 ($M^{+\cdot}$, 28), 314(100), 250(6), 189 ($M^{+\cdot}$-$SO_2C_6H_5$), 173(11), 158(7), 77(10), 51(7), 43(7). Found : C, 61.92 ; H, 5.74 ; N, 4.27. Calcd. for $C_{17}H_{19}NSO_2Si$ : C, 61.88 ; N, 5.81 ; N, 4.25.

Reaction of 1-(Phenylsulfonyl)-2-trimethylsilylindole (10) with 2-chloro-1,3-dithiane

Freshly distilled titanium tetrachloride (0.2 ml, 1.8 mmol) and 2-chloro-1,3-dithiane (0.63 mmol) prepared from 1.3-dithiane (76 mg, 0.63 mmol) and N-chlorosuccinimide (90 mg, 0.69 mmol) in $CH_2Cl_2$ (10 ml) according to ref. 3a,b) was added via syringe to a cooled (0°C) (solution of 1-(phenylsulfonyl)-2-trimethylsilylindole (10) (0.2 g, 0.53 mmol) in $CH_2Cl_2$ (10 ml) and the resulting mixture was stirred at 0°C for 30 min, at reflux for 4 h, and finally overnight at room temperature. The mixture was then poured into aqueous 5 % $NaHCO_3$ and extracted with $CH_2Cl_2$. The organic extract was dried ($MgSO_4$) and concentrated to give an oil which was purified by flash chromatography on silica gel (hexane-ether ; 70-30). Compound 11 was obtained as a colourless oil (90 mg, 65 %). $^1H$ nmr (80 MHz) : $\delta$ 5.5 (s, CH), 7.3 (s, H-3), 7.8 (d, J = 8Hz, 3H, indole-H). $^{13}C$ nmr : $\delta$ 31.0, 114.5, 121.9, 123.2, 123.6, 125.3, 125.5, 126.6, 129.4, 129.8, 134.0, 136.2, 138.1. MS m/z (rel. intensity) : 642(8), 641(17), 640(18), 525(6), 499(12), 498(16), 359(48), 358(100), 244(10), 242(38), 241(35), 77(74). Found : C, 66.32 ; H, 4.08 ; N, 5.42. Calcd. for $C_{43}H_{31}N_3S_3O_6$ : C, 66.05 ; H, 3.90 ; N, 5.37.

N-tert-Butoxycarbonyl-2-(1',3'-dithian-2'-yl)indole (1b)

Commercial tert-butyllithium (5.1 mmol) was added to a cooled (-10°C) solution of N-tert-butoxycarbonylindole (3b)[14,15] (1.0 g, 4.6 mmol) in dry THF (30 ml) and the resulting mixture was stirred at -10°C for 45 min. A solution of 2-chloro-1,3-dithiane (5.1 mmol), prepared as above, in benzene (30 ml) was then added keeping the temperature at -50°C. Stirring was continued for 3 h at this temperature, then at room temperature overnight. Usual

work-up and chromatography gave a 2:1:1 mixture of compound 1b, bis-1,3-dithiane, and the protected indole 3b. On elution with hexane-ether (90-10) compound 1b (0.54 g, 35 %) was obtained. $^1$H nmr (200 MHz) : δ 1.73 (s, 9H, $CH_3$), 1.85-2.05 (m, 2H, H-5'), 2.99 (m, 4H, H-4' and H-6'), 6.12 (s, H-2'), 7.02 (s, H-3), 7.27 (td, J = 8 and 1 Hz, H-5), 7.35 (td, J = 8 and 1 Hz, H-6), 7.59 (dd, J = 8 and 1 H, H-4), 8.16 (dd, J = 8 and 1 Hz, H-7). $^{13}$C nmr : δ 25.5, 28.2, 30.6, 42.4, 84.4, 110.7, 115.6, 120.6, 122.8, 124.6, 128.5, 136.8, 138.3, 149.9. MS m/z (rel. intensity) : 335(19), 278(32), 161(100), 58(93). Found : C, 60.80 ; H, 6.10 ; N, 4.20. Calcd. for $C_{17}H_{21}NS_2O_2$ : C, 60.87 ; H, 6.30 ; N, 4.20.

2-(1',3'-Dithian-2'-yl)indole (1c)

Compound 1a (2.0 g, 5.3 mmol) was dissolved in ethanol (200 ml) containing 10 % aqueous NaOH(30 ml) and refluxed until the solid went into solution. After subsequent cooling at 0°C for 2 h a precipitate formed which was collected by suction filtration and dissolved in $CH_2Cl_2$. The aqueous filtrate was further extracted with $CH_2Cl_2$. The combined organic layers were then dried ($Na_2SO_4$) and concentrated to give 1c (1.1 g, 88 %) as a colourless solid : m.p 197-198°C (ether-hexane). $^1$H nmr (80 MHz) : δ 1.7-2.1 (m, 2H, H-5'), 2.6-3.0 (m, 4H, H-4' and H-6'), 5.11 (br.s, H-2'), 6.27 (br.s, H-3), 6.6-7.25 (m, 4H, indole-H), 8.95 (br.s, NH). $^{13}$C nmr (DMSO-d6) : δ 26.6 (C-5'), 31.9 (C-4' and C-6'), 44.5 (C-2'), 101.7 (C-3), 112.4 (C-7), 120.6 and 121.3 (C-4 and C-5), 122.9 (C-6), 130.2 (C-3a), 134.2 (C-2), 137.5 (C-7a). MS m/z (rel. intensity) : 235 ($M^{+\cdot}$, 58), 202 (5), 170 (12), 161 (InC $S^{+\cdot}$, 100), 160(27), 156(9), 130(16), 117(12), 116(14), 89(14), 77(6), 45(8). Found : C, 60.99 ; H, 5.58 ; N, 5.87. Calcd. for $C_{12}H_{13}NS_2$ : C, 61.23 ; H, 5.56 ; N, 5.95.

2'(3'-tert-Butylthiopropylthiomethyl)-1-(phenylsulfonyl)indole (14)

Commercial tert-butyllithium (0.58 mmol) was added to a solution of 1a (200 mg, 0.53 mmol) in dry THF (5 ml) which was cooled to -30°C under an atmosphere of argon. After stirring for 10 min $D_2O$ (1 ml) was added and the resulting mixture was stirred for an additional 10 min before extraction with ether. The dried ($Na_2SO_4$) ether layers were evaporated to give an oil which was purified by flash chromatography on silica gel (hexane-ether ; 80-20). Compound 14 (100 mg, 43 %) was obtained as a colourless oil. $^1$H nmr (60 MHz) : δ 1.26 (s, 9H, $CH_3$), 1.80 (m, 2H, $SCH_2CH_2$), 2.56 (br.t, 4H, $SCH_2$), 4.03 (s, 2H, $InCH_2S$), 6.50 (s, H-3), 6.95-7.4 and 7.9-8.0 (m, Indole-H). $^{13}$C nmr : δ 27.3 ($SCH_2CH_2$), 29.6 and 29.8 ($SCH_2$), 31.1 ($CH_3$), 31.5 ($InCH_2$), 42.1 ($SC(CH_3)_3$), 111.3, 114.8, 120.7, 123.7, 124.6, 126.6, 129.2, 133.7, 137.5, 138.1, 139.2. Found : C, 60.75 ; H, 6.12 ; N, 3.25. Calcd. for $C_{22}H_{27}NS_3O_2$ : C, 60.93 ; H, 6.23 ; N, 3.23.

4-Hydroxy-4-[2-(phenylsulfonylamidophenylethynyl)-1',3'-dithian-2'-yl)]-1-methylpiperidine (13)

Commercial n-butyllithium (4.0 mmol) was added to a solution of 1a (0.37 g, 1.0 mmol) in dry THF (30 ml) which was cooled to -20°C under an atmosphere of argon. The anion solution was stirred for 5 h before slow addition of 1-methyl-4-piperidone was made. The resulting mixture was stirred at -20°C for 4 h and overnight at room temperature. The reaction was then stopped by the addition of $H_2O$, transferred to a separatory funnel containing 5 % aqueous $NaHCO_3$, and extracted with ether. The combined organic layers were washed with brine, dried over $Na_2SO_4$, and concentrated. The crude mixture was separated by flash chromatography on silica gel ($CH_2Cl_2$-$CH_3OH$ ; 99-1). Compound 13 was obtained as a very insoluble crystalline precipitate (0.15 g, 31 %) : m.p. 205-207°C ($CH_3OH$). IR (KBr) : 3100-3400 (OH), 3340 (NH) $cm^{-1}$. $^1$H nmr (200 MHz, DMSO-d6) : δ 1.6-2.7 (m, 10H, $CH_2$), 2.50 (s, $NCH_3$), 2.9-3.1 (m, 4H, H-4'(6')), 4.0 (br.s, OH), 7.30 (t, 1H, Ar-H), 7.5-7.9 (m, 7H, Ar-H), 8.2 (d, J = 8 Hz, 1H, Ar-H). $^{13}$C nmr : δ 23.8 ($SCH_2CH_2$), 26.7 ($SCH_2$), 30.2 ($NCH_2CH_2$), 43.8 ($NCH_3$), 49.4 ($NCH_2$), 57.2 (SCS), 72.1 (COH), 83.4 (SCC ), 91.1 (ArC ), 115.4, 120.9, 122.6, 125.3, 127.2, 127.4, 130.6, 131.3, 137.3, 139.1. MS m/z (rel. intensity) : 488 ($M^{+\cdot}$, 8), 470(3), 376(46), 330(27), 237(40), 236(28), 235(100), 124(39), 163(25), 162(26), 161(21), 129(26), 115(28). Found : C, 59.25 ; H, 5.86 ; N, 5.93. Calcd. for $C_{24}H_{28}N_2S_3O_3$ : C, 58.99 ; H, 5.77 ; N, 5.73.

General procedure for the preparation of compounds 16-20

To a solution of 1c (1 eq) in dry THF cooled at -20°C under an argon atmosphere, n-butyllithium 1.6M (2 eq) was slowly added via syringe. The mixture was stirred for 10 min and the electrophile (1 eq) was added at -20°C. The reaction mixture was stirred for 30 min and it was allowed to warm slowly to room temperature. The mixture was poured into 5% aqueous $NaHCO_3$ solution and extracted with ether. The organic extract was dried ($Na_2SO_4$) and evaporated to dryness in vacuo.

2-(2'-Ethyl-1',3'-dithian-2'-yl) indole (17)

Operating as above, from 1c (0.23 g, 1.0 mmol), THF (6 ml), n-butyllithium (2.0 mmol), and ethylbromide (0.1 g, 1.0 mmol), the dithiane 17 (0.21 g, 80 %) was obtained after purification by flash chromatography on silica gel (hexane-ether ; 60-40). $^1$H nmr (200 MHz) : δ 0.93 (t, $CH_3$), 1.75-2.0 (m, 2H, H-5'), 2.06 (q, $CH_2CH_3$) 2.66 (dt, J = 14 and 4 Hz, 2H, H-4'(6')eq), 2.85 (ddd, J = 14, 11 and 4 Hz, 2H, H-4'(6')ax), 6.83 (d, J = 2 Hz, H-3), 7.16 and 7.23 (2t, J = 7 Hz, 1H each, H-5 and H-6), 7.40 (d, J = 7 Hz, 1H, H-5), 7.66 (d, J = 7 Hz, H-7), 8.63 (br.s, NH). $^{13}$C nmr : δ 8.7 ($CH_3$), 25.1 ($CH_2CH_3$), 27.9 (C-4'), 37.5 (C-5'), 54.7 (C-2'), 104.2 (C-3), 110.9 (C-7), 119.8, 120.4, 121.8, 128.8, 136.0, 138.7. MS m/z (rel.

intensity) : 263 ($M^{+\cdot}$, 58), 234(42), 189(100), 160(30), 156(50), 130(22), 117(28). Found : C, 63.74 ; H, 6.43 ; N, 5.30. Calcd. for $C_{14}H_{17}NS_2$ : C, 63.83 ; H, 6.50 ; N, 5.31.

2-[2'-(2"-hydroxy-1"-phenyl)ethyl-1',3'-dithian-2'-yl] indole (18)

Operating as above, from 1c (0.23 g, 1.0 mmol), THF (6 ml), n-butyllithium (2 mmol) and styrene oxide (0,12 g, 1.0 mmol), the dithiane 18 (0.33 g, 93 %) was obtained after purification by flash chromatography on silica gel (hexane-ether, 40-60) : m.p. 123-124°C (hexane-ether). $^1$H nmr (200 MHz) : δ 1.8-2.0 (m, 2H, H-5'), 2.66 (br.d, J = 14 Hz, 2 H, H-4éq'), 2.90 (ddd, J = 14, 10 and 5 Hz, 2H, H-4ax), 5.01 (d, J = 9 Hz, CHOH), 6.90 (d, J = 1 Hz, H-3), 7.16 and 7.23 (2 t, J = 8 Hz each, H-5 and H-6), 7.26-7.33 (m, 5 H, Ar-H), 7.36 (d, J = 8 Hz, H-5), 7.63 (d, J = 8 Hz, H-7), 8.8 (br.s, NH). $^{13}$C nmr : δ 24.5 (C-5), 27.8 and 28.1 (C-4' and C-6'), 52.6 (C-2'), 53.7 ($CH_2COH$), 70.7 (Ar-CH), 104.1 (C-3), 111.2 (C-7) 120.0, 120.6, 122.2, 125.6, 127.3, 128.3, 128.5, 136.3, 139.6, 143.4. MS m/z (rel. intensity) : 355 ($M^{+\cdot}$, 58), 281(12), 248(60), 234(30), 235(72), 176(40), 160(28), 142(100), 130(24), 115(52), 105(68), 79(88), 77(80). Found : C, 67.76 ; H, 6.18 ; N, 3.64. Calcd. for $C_{20}H_{21}NOS_2$ : C, 67.57 ; H, 5.95 ; N, 3.94.

2-[2'-(4-Hydroxy-1-methyl-4-piperidyl)-1',3'-dithian-2'-yl] indole (19)

Operating as above, from 1c (1.0 g, 4.2 mmol), THF (60 ml), n-butyllithium (8.4 mmol), and N-methyl-4-piperidone, the product 19 (1.06 g, 73 %) was obtained. In this case the reaction mixture was poured into 5 % aqueous HCl and extracted with ether. The aqueous phase was then basified with potassium carbonate and extracted with $CH_2Cl_2$. Compound 19 was obtained as a colourless solid after flash chromatography on silica gel ($CH_2Cl_2$-$CH_3OH$ ; 99-1) : m.p. 255-257°C (acetone-ether). IR (NaCl) 3100-3600 cm$^{-1}$ (OH). $^1$H nmr (200 MHz) : δ 1.7-2.0 (m, 4H), 2.47 (s, $NCH_3$), 2.4-2.7 (m, 2H), 2.75-3.0 (m, 8H, $NCH_2$ and $SCH_2$), 7.13 (s, H-3), 7.3-7.5 (m, 2H, H-5 and H-6), 7.71 (d, J = 7 Hz, H-4), 7.91 (d, J = 7 Hz, H-7), 9.36 (br.s. NH). $^{13}$C nmr : δ 24.6 (C-5'), 28.0 ($NCH_2CH_2$), 32.5 (C-4' and C-6'), 45.7 ($NCH_3$), 51.1 ($NCH_2$), 65.1 (C-2'), 74.7 (COH), 106.4 (C-3), 110.8 (C-7), 119.6, 120.3, 121.8, 128.3, 135.8, 136.0. MS m/z (rel. intensity) : 348 ($M^{+\cdot}$, 4), 235(61), 234(12), 113(100), 43(98). Found : C, 56.34 ; H, 6.98 ; N, 7.13. Calcd. for $C_{18}H_{24}N_2OS_2 \cdot 2H_2O$ : C, 56.22 ; H, 7.33 ; N, 7.29.

2-[2'-(Hydroxy(3-pyridyl)methyl)-1',3'-dithian-2'-yl] indole (20)

Operating as above, from 1c (0.5 g, 2.1 mmol), THF (60 ml), n-butyllithium (4.2 mmol), and nicotinaldehyde (0.22 g, 2.1 mmol), dithiane 20 (0.62 g, 86 %) was obtained after flash chromatography on silica gel ($CH_2Cl_2$-$CH_3OH$ ; 99-1) : m.p. 199-200°C (acetone). $^1$H nmr (200 MHz) : δ 1.7-2.0 (m, 2H, H-5'), 2.56-3.0 (m, 4H, H-4' and H-6'), 5.08 (s, H-2 pyr), 8.50 (d, J = 6 Hz, H-6 pyr), 8.7 (br.s, NH). $^{13}$C nmr : δ 28.3 and 28.5 (C-4' and C-6'), 61.0 (C-2'), 79.5 (CHOH), 106.9 (C-3), 112.3 (C-7), 120.3, 121.1, 122.7, 123.8 (C-5 pyr), 128.7, 136.5, 137.1, 137.8 (C-4 pyr), 139.3 (C-3 pyr), 148.9 and 149.3 (C-2 pyr and C-6 pyr). MS m/z (rel. intensity) : 342 ($M^{+\cdot}$, 4), 235(72), 234(100), 161(36), 160(94). Found : C, 63.14 ; H, 5.32 ; N, 7.93. Calcd. for $C_{18}H_{18}N_2OS_2$ : C, 63.13 ; H, 5.29 ; N, 8.18.

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15. $^{13}C$ nmr of N-(tert-butoxycarbonyl)indole : 27.6 (q), 82.9 (s), 106.9 (d), 114.9 (d), 120.6 (d), 122.3 (d), 123.8 (d), 125.4 (d), 130.4 (s), 135.1 (s), 149.2 (s).