Tetrahedron Vol 47, No 37, pp 7911-7924, 1991
Printed in Great Britain

0040-4020/91 $3 00+ 00

Synthesis and Reactivity of 2-(1,3-Dithian-2-yl)indoles. IV.[1] Influence of the *N,N*-Diethylcarbamoyl Indole Protecting Group

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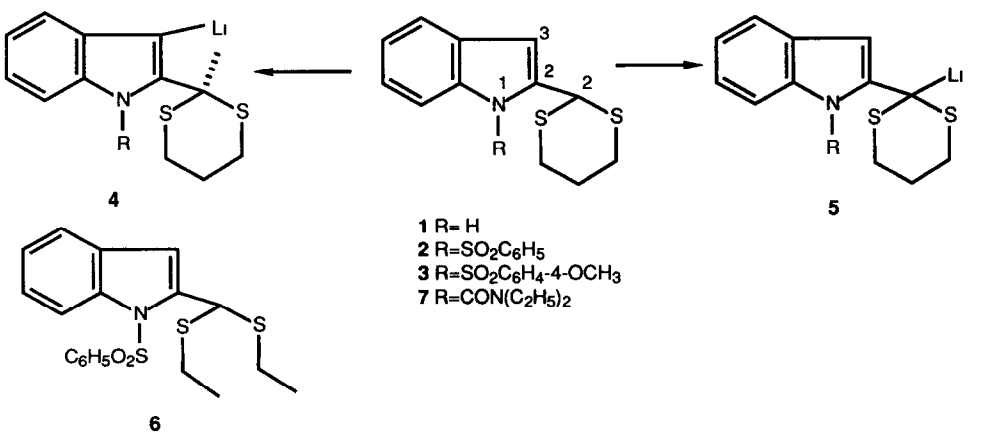
(*Received in UK* 3 *July* 1991)

Key words 2-(1,3-Dithian-2-yl)indoles, Indole, *N,N*-diethylcarbamoyl protecting group

Abstract- *The effect of the N,N-diethylcarbamoyl indole protecting group on the reactivity of 2-(1,3-dithian-2-yl)indole 7 in front of a series of electrophiles, as well as the potential synthetic usefulness of the resulting 2,2-disubstituted dithianes is reported*

Over the past several years we have explored the use of 2-(1,3-dithian-2-yl)indoles as intermediates in indole alkaloid synthesis [2-3] Fundamental to the success of this approach is the ability to selectively lithiate and functionalize the dithiane C-2′ center, and to direct subsequent ring closure reactions to the C-3 position of the indole ring In this regard, studies using the dianion of **1** showed that, whereas regioselective reaction of a range of electrophiles at C-2 is observed, ring closure of the resultant products occurs preferentially at N_1 The results obtained for the latter transformation demonstrate the necessity to block the indole nitrogen in **1** by a group which is readily introduced and removed, and whose presence will not interfere with the dithiane anion formation



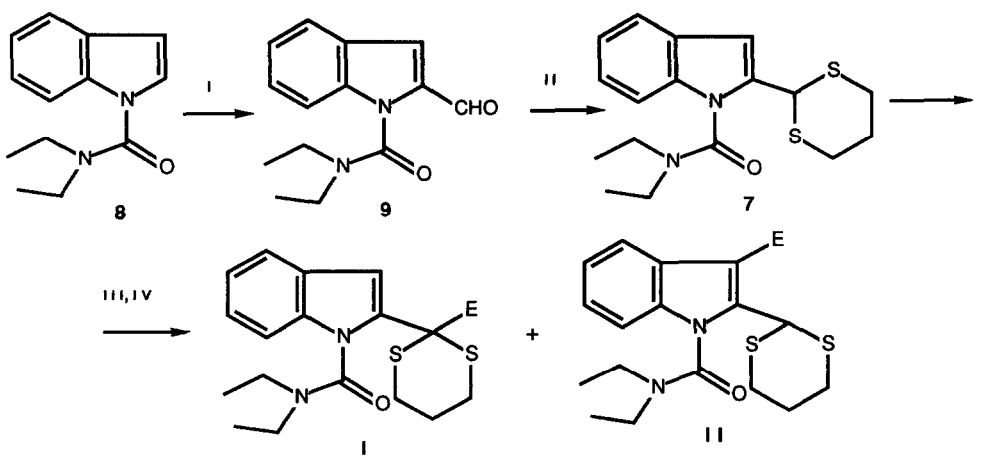
1 R= H
2 R=$SO_2C_6H_5$
3 R=$SO_2C_6H_4$-4-OCH_3
7 R=$CON(C_2H_5)_2$

Scheme 1

Following this line of investigation, we have described in previous reports[1,4] the influence of the phenylsulfonyl[5] and *p*-methoxyphenylsulfonyl[6] protecting groups on the reactivity of the indole dithiane system [7,8] It was found that the reaction of dithiane **2** with *n*-BuLi did not lead to formation of the expected C-2 lithiated species but rather to anion **4** resulting from the loss of the proton at C-3 [9] This reaction, which ultimately leads to opening of the indole ring, is promoted by the presence of the highly electron withdrawing phenylsulfonyl group on the indole nitrogen and by the stabilization of the lithium cation through coordination to sulphur [12] However, the required C-2 substituted products were obtained using dithiane **3**, substituted at N_1 by the *p*-methoxyphenylsulfonyl group, and using the less rigid indole dithioacetal **6** [1]

In the present paper we describe our recent results on a study of the *N,N*-diethylcarbamoyl group, an indole protective group employed by Comins *et al* in the context of the synthesis of 3-substituted 1-(*N, N*-diethylcarbamoyl)indoles [13] The preparation of dithianylindole **7** was accomplished by initial regioselective formylation of **8** according to the Gribble procedure[14] followed by thioacetalization with 1,3-propanedithiol in the presence of *p*-toluenesulfonic acid The ^{1}H NMR spectrum of **7** displays two singlets at δ 5 58 and 6 85 for the dithiane C-2 and indole C-3 protons, respectively, and two broad signals at δ 1 00-1 40 and 2 90 corresponding to the methyls and methylenes of the ethyl chains of the indole protective group, as the most important signals In the ^{13}C NMR the signals at δ 153 1 and 40 7 were attributed to the carbonyl and the dithiane methine carbons The presence of a broad signal centered at δ 41 8 for the two methylene carbons of the protective group is also characteristic of compound **7**, as they are next to coalescence

Lithiation of dithiane **7** at the 2 position was achieved by treatment with *n*-BuLi in THF at -78°C Compounds **10-12** were produced by reaction with methyl iodide, and ethyl or benzyl bromide The 2,2-



Reagents i) LDA, DMF, THF, ii) $HSCH_2CH_2CH_2SH$, *p*-TsOH, benzene, iii) n-BuLi, THF, -78°C, 30 min, iv) electrophile, THF, -78°C to -45°C

Scheme 2

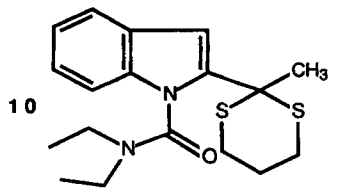
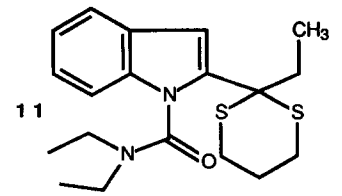
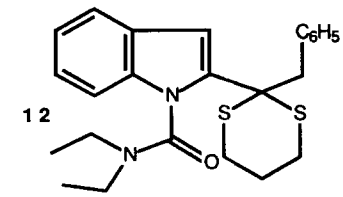
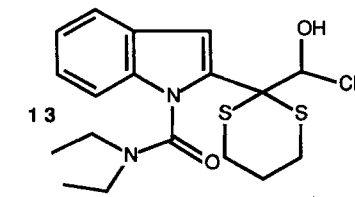
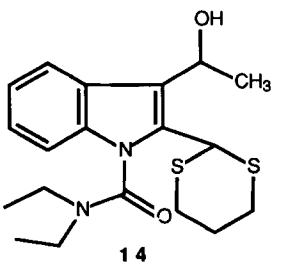
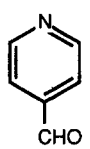
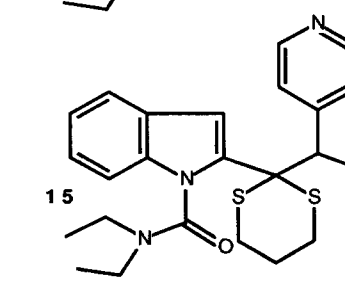
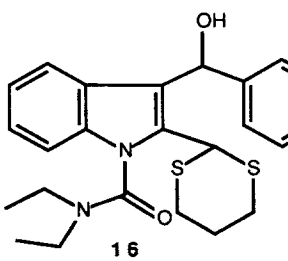
Electrophile	Product (I)	Yield (%)	Product (II)	Yield (%)
CH_3I	 **10**	92	———	
CH_3CH_2Br	 **11**	67	———	
$C_6H_5CH_2Br$	 **12**	65	———	
CH_3CHO	 **13**	46	 **14**	13
	 **15**	33	 **16**	35

Table 1

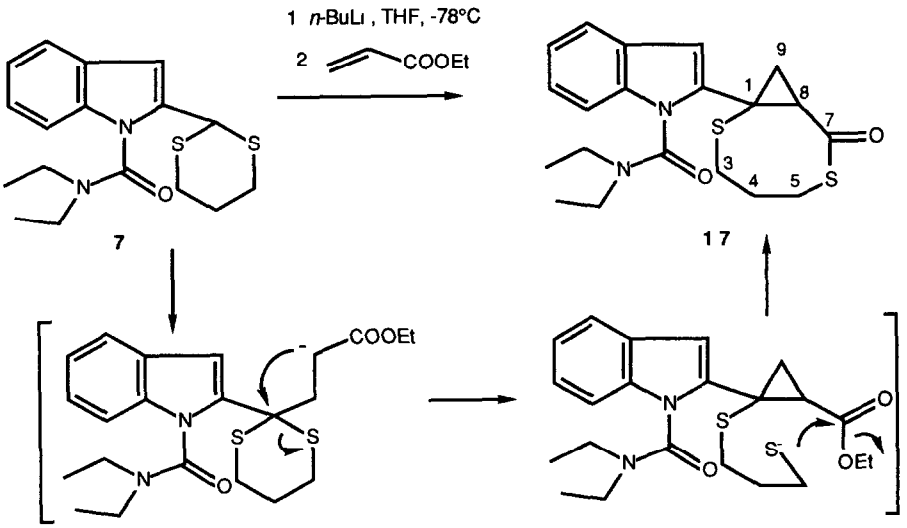
disubstituted dithiane products exhibit characteristic spectroscopic features Thus, in the ^1H NMR spectrum of **10-12** a typical singlet at δ ~7 0 for the indole C-3 proton and two triplets centered at δ 1 16 and 1 37 for the non-equivalent methyl groups were observed Also, signals at δ 11 7 and 13 1, and 39 8 and 43 0 corresponding to the methyl and methylene groups were present in the ^{13}C NMR spectrum

On the other hand, reaction of the lithium salt of **7** with acetaldehyde afforded a mixture of dithian C-2 alkylation and indole C-3 products (see Table 1) Formation of alcohol **13** was confirmed by the disappearance of the signal at δ 5 58 in the ^{1}H NMR spectrum and by the existence, in the ^{13}C NMR spectrum, of signals at δ 73 9 and 22 7 corresponding to the hydroxyethyl chain The structure of the regioisomeric dithiane **14** was clearly demonstrated by the presence of a signal at δ 5 52 and a doublet at δ 1 76 characteristic of the C-2 dithiane proton and α-hydroxymethyl group respectively, as well as by the absence of the signal corresponding to indole C-3 proton The ^{13}C NMR spectrum of this compound displayed a signal at δ 63 7 corresponding to the carbinol carbon and two broad signals due to the NCH_2CH_3 carbons (δ 13 0 and 42 6)

Similarly, reaction of the lithium derivative of dithiane **7** with pyridine-4-carbaldehyde afforded a 1 1 mixture of carbinols **15** and **16** The structure of **15** was confirmed by the presence in the ^{1}H NMR spectrum of two signals at δ 6 03 and 6 65 for the carbinol methine and indole C-3 protons, and for **16** by the presence of signals at δ 4 85 and 5 35 corresponding to the carbinol methine and C-2 dithiane protons

The formation of **14** and **16** indicates the competition between the lithiation on dithiane C-3 position, when the indole protecting group is *N,N*-diethylcarbamoyl which makes the acidity of indole C-3 proton similar to that of the dithiane C-2 Nevertheless, the indole C-3 alkylation products were only observed when aldehydes were used as the electrophiles, which is consistent with the major soft character of the reactives sites, compared to the reaction of alkyl halides with the dithiane anion [15]

Surprisingly, when the reaction was carried out using a Michael acceptor such as ethyl acrylate as the electrophile a new product **17** was obtained which showed a molecular peak at m/z 406 in the IC-MS indicating the

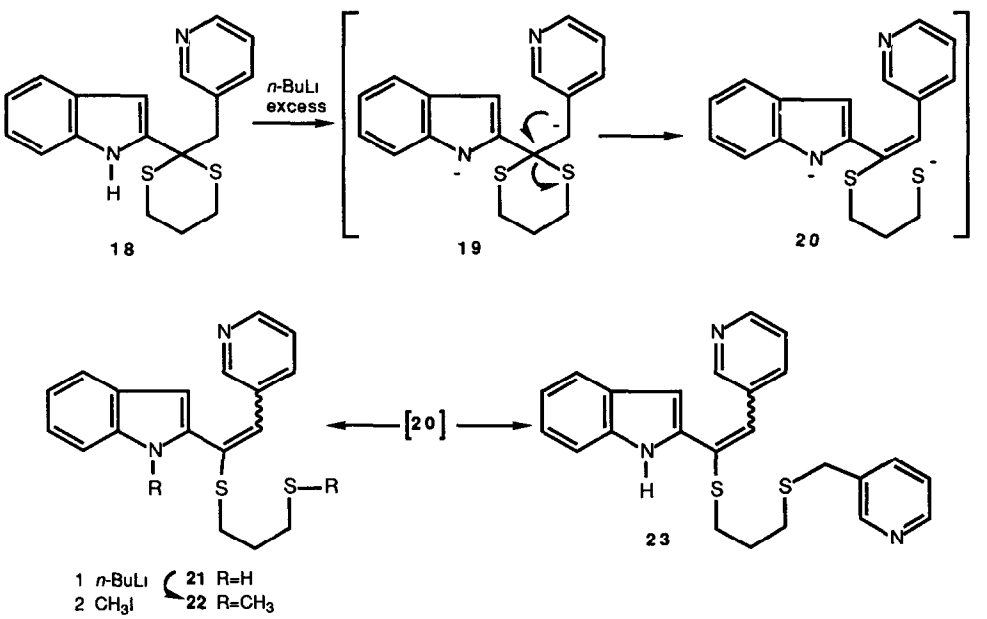


Scheme 3

loss of the ethoxy group The structure of **17** was inferred from its NMR data Two striking features were the presence of a signal for the indole C-3 proton (δ 6 99) and an unexpected doublet of doublets at δ 4 45, in the ^{1}H NMR spectrum [16]

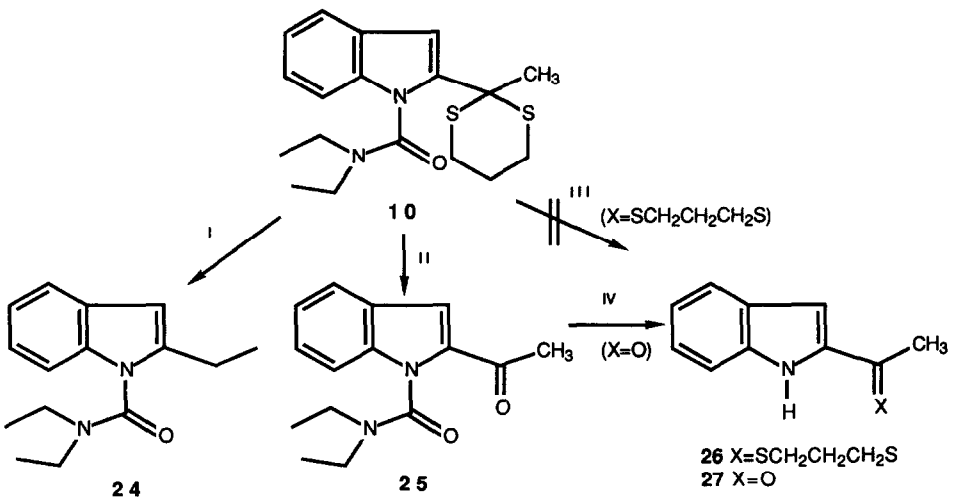
The analysis of the ^{13}C NMR data of **17** showed the existence of only two ethyl chains and a methine carbon at δ 45 3 Noteworthy chemical shift differences with respect to the expected product were observed, in particular for the aliphatic quaternary carbon (δ 45 7) and for the two carbonyl groups (δ 165 6 and 167 2) Thus, the structure of compound **17** was determined to be the cyclopropyl derivative shown in Scheme 3, formed by dithiane ring opening promoted by the attack of the α-anion carboxylate generated in the basic conditions from the expected 1,4-addition product followed by thiolactonization

Dithiane ring opening had also been observed in the alkylation reaction of dithiane **1** with 3-chloromethylpyridine using an excess of *n*-BuLi In that case the formation of dianion **19** from the initially formed indole anion of **18** is considered to occur A plausible mechanism to the rearrangement of **19** to the observed product **23** is depicted in Scheme 4 This transformation occurred by alkylation of the sulfide with chloromethylpyridine to give **23** as a by-product (11% yield) when the electrophile was added upon the dianion, and by protonation of **20** in the work-up to give **21** when the addition was reverse The structure of **21** was confirmed by its further *S*-alkylation (*n*-BuLi followed by methyl iodide) which furnished **22**



Scheme 4

Finally, the utility of 2-[1-(*N,N*-diethylcarbamoyl)indolyl]dithianes in indole alkaloid synthesis is shown using **10** as a model Thus, treatment of **10** using Raney nickel in refluxing ethanol afforded **24**, and treatment of **10** with bis(trifluoroacetoxy)iodobenzene in aqueous acetonitrile[17] gave 2-acylindole **25** in 41% yield without any modification of the indole protecting group When **10** was subsequently treated with sodium hydroxide, in the described standard conditions for carbamoyl deprotection, dithiane **26** was not detected However, treatment of 2-acylindole **25** with a base gave 2-acetylindole (**27**) [18]



Reagents (i) Ni-Raney, EtOH, Δ, 4 h, (ii) $(CF_3COO)_2IC_6H_5$, $CNCH_3$-H_2O (9 1), room temp (iii) 50% NaOH, EtOH, Δ (iv) 25% NaOH, EtOH, Δ

Scheme 5

EXPERIMENTAL

General Melting points were determined in a capillary tube on a Buchi apparatus and are uncorrected ^1H- 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 Quimica Orgànica Biològica, Barcelona

1-(Diethylcarbamoyl)indole-2-carbaldehyde (8) To a solution of indole (10 g, 85 mmol) and sodium hydride (3 15 g, 130 mmol) in anhydrous THF (200 ml) diethylaminocarbonyl chloride (10 7 ml, 85 mmol) was added After stirring for 7 h at room temperature the mixture was poured into aqueous sodium carbonate The organic layer was dried and evaporated to give 1-(diethylcarbamoyl)indole **8** (11 1 g, 60 %) after flash chromatography (hexane ether, 90 10), ^{1}H NMR 1 21 (t, J=7 Hz, 6H, CH_3), 3 45 (q, J=7 Hz, 4H, CH_2), 6 59 (d, J=4 Hz, In-3H), 7 17 (t, J=8 Hz,1H, In-5H), 7 27 (d, J=4 Hz, 1H, In-2H), 7 28 (t, J=8 Hz, 1H, In-6H), 7 40 (d, J=8 Hz, 1H, In-7H), 7 60 (d, J=8 Hz, 1H, In-4H), ^{13}C NMR 13 0 (CH_3), 42 1 (CH_2), 105 2 (In-C3), 112 1 (In-C7), 120 8, 121 4, and 123 3 (In-C4, In-C5, and In-C6), 125 8 (In-C2), 129 2 (In-C3a), 135 5 (In-C7a), 154 3 (C=O), MS (m/z,%) 216 (M^+, 32), 100 (100), 89 (10), and 72 (66)

To a solution of **8** (4 g, 18 5 mmol) in anhydrous THF (300 ml) cooled at -70°C *t*-butyllithium (1 7 M, 16 3 ml, 27 7 mmol) was added The solution was stirred at -70°C for 1h, and freshly distilled DMF (3 0 ml, 38 8 mmol) was added After stirring for 4-5 h at -70°C the reaction was quenched with aqueous ammonium chloride and extracted first with ether, then with CH_2Cl_2 The extracts were dried and evaporated to give **9** (4 4 g, 98%) as an unstable oil which was used without purification ^{1}H NMR 1 10-1 30 (br s, 6H, CH_3), 3 10-3 70 (br s, 4H, CH_2), 7 23 (t, J=8 Hz, 1H, In-5H), 7 30-7 50 (m, 3H, In-H), 7 73 (d, J=8 Hz, 1H, In-4H), 9 87 (s, 1H, CHO), ^{13}C NMR 12 9 (br s, CH_3), 42 3 (br, CH_2), 111 3 (In-C3), 117 6 (In-C7), 122 3 (In-C5), 123 6 (In-C4), 126 8 (In-C3a), 128 1 (In-C6), 136 0 (In-C7a), 138 5 (In-C2), 154 5 (NC=O), 181 2 (CHO), MS (m/z, %) 245 (M^+, 3), 244 (M^+-1, 20), 144 (12), 100 (100), 89 (36), 72 (75)

2-(1,3-Dithian-2-yl)-1-(diethylcarbamoyl)indole (7) A stirred solution of the aldehyde **9** (5 g, 20 5 mmol), *p*-toluenesulfonic acid (3 90 g, 20 5 mmol), and 1,3-propanedithiol (3 0 ml, 30 74 mmol), in anhydrous toluene (200 ml) was refluxed for 6 5 h with removal of water by a Dean-Stark trap The reaction mixture was poured into 5% aqueous sodium bicarbonate and extracted with ether The organic extracts were dried and evaporated to give dithiane **7** which was purified by flash chromatography using ether-hexane (30 70) as the eluent (2 8 g, 41 %), IR ($CHCl_3$) 1681 (CO), ^{1}H NMR 1 00-1 40 (br s, 6H, CH_3), 1 80-2 20 (m, 2H, SCH_2CH_2), 2 90 (br s, 4H, CH_2), 3 20-3 50 (m, 4H, SCH_2), 5 58 (s, 1H, SCHS), 6 85 (s, 1H, In-3H), 7 10-7 30 (m, 3H, In-H), 7 55 (d, J=8 Hz, 1H, In-4H), ^{13}C NMR 12 8 (CH_3), 25 2 ($SCCH_2$), 29 8 (SCH_2), 40 7 (SCHS), 41 0 (br s, CH_2), 106 5 (In-C3), 110 9 (In-C7), 121 2, 121 4, and 123 4 (In-C4, In-C5, and In-C6), 127 7 (In-C3a), 135 8 (In-C7a), 137 5 (In-C2), 153 1 (C=O), CIMS (m/z, %) 352 (M^++NH_3, 100), 335 (M^++1, 1) Anal Calcd for $C_{17}H_{22}N_2OS_2$ C, 61 04, H, 6 63, N, 8 37 Found C, 61 20, H, 6 79, N, 8 39

General Procedure for the Preparation of Compounds 10-13

n-Butyllithium (1 6 *M* in hexane, 1 2 eq) was slowly added *via* syringe to a cooled (-70°C) solution of **7** (1 eq) in dry THF (15 ml) under argon atmosphere The mixture was stirred for 15-30 min and the electrophile (1 5 eq) was added at -70°C The reaction temperature was raised to -30°C for 1 h, and to room temperature for 30 min The reaction mixture was quenched with aqueous ammonium chloride and extracted first with ether then with CH_2Cl_2

2-(2-Methyl-1,3-dithian-2-yl)-1-(diethylcarbamoyl)indole (10) Operating as above, from **7** (210 mg, 0 63 mmol), *n*-butyllithium (0 47 ml, 0 75 mmol), and methyl iodide (57 µl, 0 94 mmol), dithiane **10** (168 mg, 92 %) was obtained, after flash chromatography (ether-hexane, 25 75), IR ($CHCl_3$) 1680, ^{1}H NMR 1 16 (t, J=7 Hz, 3H,

CH_3), 1 37 (t, *J*=7 Hz, 3H, CH_3), 1 80-2 00 (m, 2H, $SCCH_2$), 2 10 (s, 3H, $SCCH_3$), 2 50-2 70 (m, 3H, SCHa and SCHe), 3 10-3 40 (m, 3H, NCH2 and SCHe), 3 50-3 70 (m, 2H, NCH_2), 7 01 (s, 1H, In-3H), 7 10-7 30 (m, 3H, InH), 7 55 (d, *J*=6 Hz, 1H, In-4H), ^{13}C NMR 11 7 and 13 1 (CH_2CH_3), 24 2 ($SCCH_2$), 28 5 (SCH_2), 30 8 ($SCCH_3$), 39 8 (NCH_2), 43 0 (NCH_2), 48 9 (SCS), 109 3 (In-3H), 110 8 (In-7H), 120 8 , 121 2, and 123 1 (In-C4, In-C5 and In-C6), 127 5 (In-C3a), 137 3 (In-C7a), 142 4 (In-C2), 154 1 (C=O), MS (m/z, %) 348 (M^+, 8), 242 (47), 213 (8), 100 (100), 72 (51) Anal Calcd for $C_{18}H_{24}N_2OS_2 H_2O$ C, 58 98, H, 7 64, N, 7 15 Found C, 58 65, H, 7 50, N, 7 06

2-(2-Ethyl-1,3-dithian-2-yl)-1-(diethylcarbamoyl)indole (11) Operating as above, from **7** (200 mg, 0 6 mmol), *n*-butyllithium (0 45 ml, 0 72 mmol), and ethyl bromide (67 µl, 0 9 mmol), dithiane **11** (96 2 mg, 67 %) was obtained, after flash chromatography (ether-hexane, 15 85) mp 141-142°C (acetona), IR ($CHCl_3$) 1681, ^1H NMR 0 96 (t, *J*=7 Hz, 3H, CH_3), 1 16 and 1 35 (2t, *J*=7 Hz, 3H each, $NCCH_3$), 1 80-2 00 (m, 2H, SCCH2), 2 15 (m, 2H, CH_2CH_3), 2 50-2 80 (m, 3H, SCHa and SCHe), 3 15-3 35 (m, 3H, NCH_2 and SCHe), 3 50-3 57 (m, 2H, NCH_2), 6 99 (s, 1H, In-3H), 7 10-7 25 (m, 3H, InH), 7 65 (d, *J*=6Hz, 1H, In-4H), ^{13}C NMR 8 7 (CH_2CH_3), 11 7 and 13 1 ($NCCH_3$), 24 9 (SCH_2CH_2), 27 7 and 28 4 (SCH_2), 34 9 (CH_2CH_3), 39 9 and 43 1 (NCH_2), 54 4 (SCS), 110 7 (In-C3), 111 7 (In-C7), 120 7, 121 1, and 123 0 (In-C4, In-C5, and In-C6), 127 3 (In-C3a), 137 4 (In-C7a), 139 9 (In-C2), 153 9 (C=O), CIMS (m/z, %) 397 (M^++2NH_3, 6), 380 (M^++NH_3, 100), 363 (M^+, 50), 254 (16), 197 (7) Anal Calcd For $C_{19}H_{26}N_2OS_2$ C, 62 94, H, 7 23, N, 7 73, S, 17 69 Found C, 62 87, H, 7 28, N, 7 80, S, 17 78

2-(2-Benzyl-1,3-dithian-2-yl)-1-(diethylcarbamoyl)indole (12) Operating as above, from **7** (200 mg, 0 60 mmol), *n*-butyllithium (0 45 ml, 0 72 mmol), and benzyl bromide (107 µl, 0 90 mmol), dithiane **12** (154 mg, 65 %) was obtained, after flash chromatography (ether-hexane, 15 85) mp 181-182°C, IR ($CHCl_3$) 1677, ^1H NMR 1 16 and 1 42 (2t, *J*=7 Hz, 3H each, $NCCH_3$), 1 80-2 00 (m, 2H, SCH_2), 2 50-2 70 (m, 3H, SCH_2), 3 05 (ddd, *J*= 12, 8, and 2 Hz, 1H, SCHe), 3 20-3 40 (m, 2H, NCH_2), 3 37 (d, J_{AB}= 12 Hz, 1H, ArCH), 3 55-3 75 (m, 2H, NCH_2), 4 30 (d, J_{AB}= 12 Hz, 1H, ArCH), 6 56 (s, 1H, In-3H), 7 00-7 40 (m, 8H, Ar-H), 7 45 (d, *J*=6 Hz, 1H, In-4H), ^{13}C NMR 11 8 and 13 0 (CH_3), 24 5 ($SCCH_2$), 27 5 and 28 4 (SCH_2) , 39 9 and 43 1 (NCH_2), 47 1 ($ArCH_2$), 54 1 (SCS), 110 8 (In-C3), 112 3 (In-C7), 120 8, 121 1, and 123 2 (In-C4, In-C5, and In-C6), 126 7 (Ar-*para*), 127 2 (Ar-*meta*), 131 2 (Ar-*ortho*), 135 3 (In-C7a), 137 3 (Ar-*ipso*), 139 3 (In-C2), 154 3 (C=O) MS (m/z, %) 425 (M^+, 1), 333 (46), 262 (22), 217 (12), 100 (79), 72 (100) Anal Calcd for $C_{24}H_{28}N_2OS_2$ C, 67 89, H, 6 64, N, 6 64, S, 15 10 Found C, 67 67, H, 6 60, N, 6 67, S, 14 96

General Procedure for the Preparation of Compounds 13-16

n-Butyllithium (1 6 *M* in hexane, 1 2 eq) was slowly added *via* syringe to a cooled (-78°C) solution of **7** (1 eq) in dry THF (15 ml) under argon atmosphere The mixture was stirred for 15-30 min and the electrophile (1 2 eq) was added at -78°C After stirring for 45 min at -78°C and 45 min at -23°C, the reaction mixture was quenched with aqueous ammonium chloride and extracted first with ether then with CH_2Cl_2

1-(Diethylcarbamoyl)-2-[2-(1-hydroxyethyl)-1,3-dithian-2-yl]indole (13) and 1-(Diethylcarbamoyl)-2-(1,3-dithian-2-yl)-3-(1-hydroxyethyl)indole (14) Operating as above, from **7** (200 mg, 0 6 mmol), *n*-butyllithium (0 45 ml, 0 72 mmol) and acetaldehyde (0 10 ml, 1 79 mmol), a 3 5 1 mixture of

compounds **13** and **14** was obtained, which was separated by flash chromatography Dithiane **13** (higher Rf, 45 5 mg, 46 %) was obtained on elution with ether-hexane (3 1) mp 127-128°C, IR ($CHCl_3$) 3368 (OH), 1667 (CO), ^1H NMR 1 19, 1 23, and 1 26 (m, 3H each, CH_3), 1 80-2 00 (m, 2H, $SCCH_2$), 2 45-3 05 (m, 5H, SCH_2 and C*H*OH), 3 20-3 70 (m, 4H, CH_2), 4 30 (br, 1H, OH), 7 02 (s, 1H, In-3H), 7 10-7 25 (m, 3H, In-H), 7 50 (d, *J*=6 Hz, 1H, In-4H), ^{13}C NMR 11 9 and 13 0 (CH_3), 19 7 (CHOH*C*H_3), 24 8 (SC*C*H2), 27 5 and 28 2 (SCH2), 40 3 and 43 6 (NCH2), 61 1 (SCS), 74 0 (HOCH), 110 9 (In-C3), 114 7 (In-C7), 121 2, 121 8, and 123 8 (In-C4, In-C5, and In-C6), 127 8 (In-C3a), 137 4 (In-C7a), 139 5 (In-C2), 155 7 (C=O), CIMS (m/z, %) 396 (M^++NH_3, 100), 379 (M^+, 19), 257 (44), 240 (98), 197 (28) Anal Calcd for $C_{19}H_{26}N_2O_2S_2$ C, 60 29, H, 6 92, N, 7 40, S, 16 94 Found C, 59 92, H, 6 89, N, 7 42, S, 16 39

Dithiane **14** (lower Rf, 13 mg, 13 %) was obtained on elution with ether IR ($CHCl_3$) 3449 (OH), 1677 (CO), ^1H NMR 1 10-1 45 (m, 6H, $NCCH_3$), 1 77 (d, *J*=7 Hz, 3H, $HOCCH_3$), 1 80-2 2o (m, 4H, $SCCH_2$), 2 80-3 50 (m, 4H, NCH_2), 5 52 (s, SCHS), 6 12 (q, *J*=7 Hz, 1H, C*H*OH), 7 10-7 40 (m, 3H, InH), 8 00 (d, *J*=6 Hz, 1H, In-4H), ^{13}C NMR 13 0 (br s, NCH_2CH_3), 22 9 (SC*C*H_2), 24 8 and 24 9 (SCH_2), 42 1 and 42 9 (NCH_2), 32 7 (HOC*C*H_3), 63 7 (HOCH), 110 9 (In-C7), 113 8 (In-C3), 121 3, 121 9, and 123 7 (In-C4, In-C5, and In-C6), 129 3 (In-C3a), 132 5 (In-C2), 136 0 (In-C7a), 153 3 (C=O), MS (m/z, %) 360 (M^+-H_2O, 39), 334 (16), 100 (63), 72 (63), 29 (100)

1-(Diethylcarbamoyl)-2-[2-(1-hydroxy-4-pyridylmethyl)-1,3-dithian-2-yl]indole (15) and 1-(Diethylcarbamoyl)-2-(1,3-dithian-2-yl)-3-(1-hydroxy-4-pyridylmethyl)indole (16)

Operating as above, from **7** (200 mg, 0 59 mmol), *n*-butyllithium (0 45 ml, 0 72 mmol) and pyridine-4-carbaldehyde (67 µl, 0 72 mmol), a 1 1 mixture of compounds **15** and **16** was obtained, which was separated by flash chromatography (CH_2Cl_2-methanol, 98 2) Dithiane **15** (higher Rf, 49 mg, 33 %) mp 171-172 °C, IR ($CHCl_3$) 3432 (OH), 1703 (C=O), ^1H NMR 1 06 and 1 30 (2t, *J*=7 Hz, 3H each, $NCCH_3$), 1 80-2 00 (m, 2H, $SCCH_2$), 2 60-2 90 (4H, SCH_2), 3 10-3 60 (m, 4H, NCH_2), 6 03 (s, 1H, HOC*H*), 6 65 (d, *J*=2 Hz, 1H, In-3H), 6 85 (d, *J*= 5 Hz, 2H, Pyr-*meta*), 7 10 (td, *J*=7 and 2 Hz, 1H, In-5H), 7 20 (td, *J*=7 and 2 Hz, 1H, In-6H), 7 30 (d, *J*=7 Hz, 1H, In-7H), 7 55 (d, *J*=7 Hz, 1H, In-4H), 8 40 (d, *J*=5 Hz, 2H, Pyr-*ortho*), 8 55 (br s, 1H, OH), ^{13}C NMR 13 1 and 14 2 (CH_3), 24 3 ($SCCH_2$), 27 3 and 27 4 (SCH_2), 41 3 and 42 1 (NCH_2), 80 0 (HO*C*H), 106 8 (In-C3), 111 1 (In-C7), 120 0, 120 9, and 122 5 (In-C4, In-C5, and In-C6), 123 1 (Pyr-*meta*), 128 3 (In-C3a), 133 9 , 135 9, 144 6 (Pyr-*ipso*), 149 0 (Pyr-*ortho*), 154 2 (C=O), MS (m/z, %) 442 (M^+, 100), 152 (22), 135 (21) Anal Calcd for $C_{23}H_{27}N_3O_2S_2$ C, 62 55, H, 6 16, N, 9 51, S, 14 52 Found C, 62 21, H, 6 11, N, 9 19, S, 14 26

Dithiane **16** (lower Rf, 53 mg, 35 %) IR ($CHCl_3$) 3411 (OH), 1680 (C=O), ^1H NMR 1 0-1 30 (br s, 6H, CH_3), 2 15-2 25 (m, 2H, $SCCH_2$), 2 50-3 00 (m, 6H, SCH_2 and NCH_2), 3 40 (br s, 2H, NCH_2), 4 80 (br d, 1H, HOC*H*), 5 45 (s, 1H, SCHS), 6 40 (d, *J*=7 Hz, 1H, In-7H), 6 90 (t, *J*=7 Hz, 1H, In-5H), 6 95 (d, *J*=5 Hz, 2H, Pyr-*meta*), 7 12 (t, 1H, In-6H), 7 45 (d, *J*=7 Hz, 1H, In-4H), 8 30 (d, *J*=5 Hz, 2H, Pyr-*ortho*), ^{13}C NMR 13 1 (br s, CH_3), 25 6 ($SCCH_2$), 31 2 and 32 2 (SCH_2), 41 3 (br s, NCH_2), 54 2 (SCHS), 74 3 (HOCH), 108 9 (In-C7), 121 6, 122 5 126 5 (In-C4, In-C5, and In-C6), 126 9 (In-C3a), 128 7 (Pyr-*meta*), 148 4 (Pyr-*ortho*), 155 2 (C=O), MS (m/z, %) 442 (M^+, 4), 409 (8), 352 (55), 125 (100)

Reaction of lithium salt of 7 with ethyl acrylate Operating as above, from **7** (200 mg, 0 59 mmol), *n*-butyllithium (1 6 M, 0 45 ml, 0 72 mmol), and ethyl acrylate (78 µl, 0 72 mmol), **1-[1-(diethylcarbamoyl)-2-indolyl]-2,6-dithiabicyclo[6 1 0]nonan-7-one (17)** was obtained (72 4 mg, 69 %) after purification by flash chromatography (CH_2Cl_2) IR (CHCl3) 1633 (C=O), 1704 (C=O), ^1H NMR 1 15-1 35 (m, 3H, CH_3), 1 80-2 20

(m, 2H, 4-H), 2 85 (dddd, J=12, 12, 4 and 3 Hz, 1H, 9-H) , 2 95-3 10 (m, 4H, SCH_2), 3 28 (br t, J=12 Hz, 1H, 9-H), 3 30-3 45 (m, 2H, NCH_2), 3 55-3 80 (m, 2H, NCH_2), 4 45 (dd, J=12 and 4 Hz, 1H, 8-H), 6 99 (s, 1H, In-3H), 7 29 (t, J=7 Hz, 1H, In-5H), 7 32 (t, J=7 Hz, 1H, In-6H), 7 50 (d, J=7 Hz, 1H, In-7H), 7 84 (d, J=7 Hz, 1H, In-4H), ^{13}C NMR 12 8 and 14 7 ($NCCH_3$), 24 4 (C-4), 27 7 (C-3 and C-7), 36 8 (C-9), 40 9 and 42 6 (NCH_2), 45 3 (C-8), 45 7 (C-1), 109 3 (In-C7), 116 7 (In-C3), 121 7, 124 6, and 125 8 (In-C4, In-C5, and In-C6), 129 3 (In-C3a), 135 5 (In-C7a), 138 5 (In-C2), 165 6 (C=O), 167 2 (C=O), CIMS (m/z, %) 406 (M^++NH_3), 119 (100), 389 (17), 316 (9) Anal Calcd for $C_{20}H_{24}N_2O_2S_2$ C, 61 50, H, 6 70, N, 7 17, S, 16 50 Found C, 61 93, H, 6 44, N, 7 06, S, 16 32

2-[2-(3-Pyridylmethyl)-1,3-dithian-2-yl]indole (18) To a solution of 3-chloromethylpyridine, prepared from the corresponding commercial hydrochloride by the action of *n*-BuLi (1 3 eq) in THF (20 ml) at -78°C, the lithium salt of **1**, prepared from **1** (0 5 g, 2 13 mmol) and 1 3 eq of *n*-BuLi at -20°C, was transferred *via* cannula The reaction mixture was stirred for 15 min at -78°C and allowed to reach room temperature, and quenched with aqueous ammonium chloride 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 a 4 1 mixture of dithiane **18** and compound **23**, which was separated by flash chromatography Dithiane **18** (higher Rf, 366 mg, 54%) was separated using dichloromethane-methanol (96 4) mp 120-121°C (ether), ^1H NMR 1 80-2 05 (m, 2H, $SCCH_2$), 2 66 (dt, J= 12 and 3 Hz, 2H, SCHe), 2 84 (ddd, J=12, 11, and 3 Hz, 2H, SCHa), 2 32 (s, 2H, $ArCH_2$), 6 59 (d, J=1 5 Hz, 1H, In-3H), 6 95-7 20 (m, 4H, ArH), 7 33 (d, J=7 Hz, 1H, In-7H), 7 53 (d, J=7 Hz, 1H, In-4H), 8 20 (s, 1H, Pyr-C2), 8 40 (br s, 1H, Pyr-C6), 8 60 (br s, 1H, NH), ^{13}C NMR 24 4 (SCH_2CH_2), 27 6 (SCH_2), 47 6 ($Pyr\text{-}CH_2$), 52 5 (SCS), 105 0 (In-C3), 111 1 (In-C7), 120 0, 120 8, 122 3, and 122 8 (In-C4, In-C5, In-C6, and Pyr-C5), 127 0 (In), 128 5, 130 3 (Pyr-C3), 137 0, 138 4 (Pyr-C4), 148 2 (Pyr-C6), 150 9 (Pyr-C2), MS (m/z, %) 326 (M^+, 5), 251 (49), 234 (100), 160 (60), 92 (75) Anal Calcd for $C_{18}H_{18}N_2S_2$ C, 66 22, H, 5 56, N, 8 58 Found C, 66 18, H, 5 58, N, 8 26

Compound **23** (lower Rf, 96 mg, 11%) was separated on elution with dichloromethane-methanol (93 7) ^1H NMR 1 78 (t, J=7 Hz, 2H, $SCCH_2$), 2 46 (t, J= 7 Hz, 2H, SCH_2), 2 68 (t, J=7 Hz, 2H, SCH_2), 3 68 (s, 2H, $ArCH_2$), 6 64 (s, 1H, In-3H), 6 73 (s, 1H, =CH), 6 80-7 40 (m, 6H, Ar-H), 7 58 (d, 2H, Pyr-H), 8 30 (m, 2H, Pyr-H), 8 44 (br s, 2H, Pyr-H), 9 80 (br, 1H, NH), ^{13}C NMR 28 8, 30 0, 31 2, 33 2, 105 0, 111 2, 120 1, 120 9, 122 9, 123 0, 123 5, 124 9, 128 2, 131 8, 132 4, 132 5, 134 1, 135 0, 136 0, 136 6, 147 6, 148 2, 149 6, 149 8, MS (m/z, %) 417 (M^+, 3), 325 (5), 251 (30), 125 (11), 92 (100) Anal Calcd for $C_{24}H_{23}N_3S_2$ C, 69 03, H, 5 54, N, 10 06 Found C, 69 15, H, 5 44, N, 9 89

2-[1-(3-Mercaptopropylthio)-2-(3-pyridyl)vinyl]indole (21) Operating as above, from dithiane **1** (1 0 g, 4 25 mmol) , THF (50 ml), *n*-BuLi (4 eq, 10 6 ml, 17 mmol) and 3-chloromethylpyridine hydrochloride (1 0 g, 6 3 mmol), **2-[1-(3-mercaptopropylthio)-2-(3-pyridyl)-vinyl]indole (21)** (560 mg, 40 %) was obtained after flash chromatography ^1H NMR 1 98 (t, J=7 Hz, 2H, $SCCH_2$), 2 59 and 2 76 (2t, J=7 Hz, 2H each, SCH_2), 6 63 (d, J=1 5 Hz, 1H, In-3H), 6 75 (s, 1H, =CH), 6 80-7 35 (m, 6H, Ar-H), 7 58 (d, 1H, In-4H), 8 25 (m, 2H, Pyr-H), 9 55 (br, 1H, NH), ^{13}C NMR 22 8 (SCH_2CH_2), 30 4 and 32 8 (SCH_2), 104 8 (In-C3), 111 3 (In-C7), 119 9 (In-C5), 120 9 (In-C4), 122 7 (In-C6), 123 1 (Pyr-C5), 124 1 (=CH), 128 2 (In-C3a), 132 3 ,132 5 and 132 7 (In-C2, Pyr-C3, and =CS), 135 2 (Pyr-C4), 136 7 (In-C7a), 147 0 (Pyr-C2), 149 6 (Pyr-C6), MS (m/z, %) 326 (M^+, 4), 251 (5), 234 (34), 219 (10), 160 (24), 114 (6), 89 (58), 41 (100) Anal Calcd for $C_{18}H_{18}N_2S_2$ C, 66 22, H, 5 55, N, 8 58 Found C,66 34, H, 5 66, N, 8 56

2-[1-(3-Methylthiopropylthio)-2-(3-pyridyl)vinyl]-1-methylindole (22) A sample of **21** in THF was treated with *n*-BuLi (2 eq) at - 40 °C and then methyl iodide (2 2 eq) was added After the usual work-up compound 22 (85 %) was obtained ^{1}H NMR 1 86 (t, *J*=7 Hz, 2H, $SCCH_2$), 2 05 (s, 3H, SCH_3), 2 56 and 2 75 (2t, *J*=7 Hz, 2H each, SCH_2), 3 50 (s, 3H, NCH_3) , 6 57 (s, 1H, =CH), 6 90 (d, *J*=2 Hz, 1H, In-3H), 7 0-7 40 (m, 6H, Ar-H), 7 60 (d, *J*=6 Hz, 1H, In-4H), 8 35 (br s, 1H, Pyr-2H), ^{13}C NMR 15 4 (SCH3), 22 4 (SCH2CH2), 28 4 (NCH3), 30 8 and 32 8 (SCH2), 103 5 ((In-C3), 109 8 (In-C7), 120 4 In-C5), 121 1 (In-C4), 122 4 (In-C6), 123 3 (Pyr-C5), 126 1 (=CH), 132 3, 132 5, and 132 8 (In-C2, Pyr-C3, and =CS), 133 9 (Pyr-C4), 136 5 (In-C7a), 147 9 (Pyr-C2), 150 0 (Pyr-C6) Anal Calcd for $C_{20}H_{22}N_2S_2$ C, 67 76, H, 6 25, N, 7 90 Found C, 68 04, H, 6 33, N, 7 95

1-(Diethylcarbamoyl)-2-ethylindole (24) A suspension of dithiane **10** (80 mg, 0 23 mmol) and W-2 Raney nickel (*c a* 200 mg) in ethanol (20 ml) was refluxed for 4 h Filtration upon Celite of the Raney nickel afforded a filtrate which after evaporation and purification by flash chromatography (1 1 hexane-ether) gave **24** (26 mg, 46%), IR ($CHCl_3$) 1675 (C=O), ^{1}H NMR 1 27 (br t, 3H, CH_3), 1 37 (t, *J*=7 Hz, 6H, NCH_2CH_3), 4 35 (q, *J*=7 Hz, 4H, NCH_2), 6 34 (s, 1H, In-3H), 7 13-7 19 (m, 3H, In-4H), 7 45 (br, 1H, NH), ^{13}C NMR 13 4 and 13 9 (NCH_2CH_3), 22 3 (CH_3), 31 3 ($InCH_2$), 41 7 (br, NCH_2), 102 4 (In-C3), 110 4 (In-C7), 120 2 and 120 9 (In-C4 and In-C5), 122 0 (In-C6), 128 9 (In-C3a), 131 0 (In-C2), 136 0 (br, In-C7a), 152 0 (br, C=O) Anal Calcd for $C_{15}H_{20}N_2O$ C, 73 74, H, 8 24, N, 11 46 Found C, 73 64, H, 8 13, N, 11 22

1-(Diethylcarbamoyl)-2-acetylindole (25) To a solution of **10** (83 mg, 0 238 mmol) in 9 1 CH_3CN-H_2O (10 ml) stirred at room temperature, bis(trifluoroacetoxy)iodobenzene (Aldrich, 143 4 mg, 0 333 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 CH_2Cl_2 The organic layers were dried and the solvent was evaporated to give **25** (25 mg, 41%) after flash chromatography (6 4 hexane-ether), IR ($CHCl_3$) 1665 and 1688 (C=O), ^{1}H NMR 1 03 (t, *J*=7 Hz, 3H, NCH_2CH_3), 1 43 (t, *J*=7 Hz, 3H, NCH_2CH_3), 2 53 (s, 3H, $COCH_3$) 3 05 (q, *J*=7 Hz, 2H, NCH_2), 3 68 (q, *J*=7 Hz, 2H, NCH_2), 7 15-7 35 (m, 4H, InH), 7 73 (d, *J*=6 Hz, 1H, In-4H), ^{13}C NMR 12 0 and 13 3 (NCH_2CH_3), 26 2 ($COCH_3$), 41 2 and 43 0 (NCH_2) , 111 1 (In-C7), 112 9 (In-C3), 122 0 (In-C5), 123 3 (In-C4), 126 8 (In-C3a), 127 1 (In-C6), 135 7 (In-C2), 138 1 (In-C7a),152 9 (NCO), 189 6 (InCO) Anal Calcd for $C_{15}H_{18}N_2O_2$ C, 69 74, H, 7 02, N, 10 84 Found C, 69 76, H, 7 01, N, 10 90

Deprotection of 1-(Diethylcarbamoyl)-2-acetylindole (25) A solution of **25** (64 mg, 0 262 mmol), 25% aqueous sodium hydroxyde (5 ml) and ethanol (15 ml) was stirred at reflux for 16 h The solution mixture was evaporated and extracted with CH_2Cl_2 The solvent was dried and evaporated to gave 2-acetylindole **27** (27 mg, 65 %) after flash chromatography (ether) mp 155°C (hexane-ether) (lit [18] 154-155°C), IR 1653 ($CHCl_3$), ^{1}H NMR 2 55 (s, 3H, $COCH_3$), 7 10 (t, *J*=7 Hz, 1H, In-5H), 7 13 (s, 1H, In-3H), 7 30 (t, *J*=7 Hz, 1H, In-6H), 7 37 (d, *J*=7 Hz, 1H, In-7H), 7 63 (d, *J*=7 Hz, 1H, In-4H), 9 25 (br, 1H, NH) ^{13}C NMR 27 5 (CH_3), 109 9 (In-C3), 112 2 (In-C7), 120 9 (In-C5), 123 0 (In-C4), 126 4 (In-C6), 128 0 (In-C3a), 136 5 (In-C7a),137 5 (In-C2), 190 9 (C=O), MS (m/z, %) 258 (M^+, 19), 215 (2), 149 (12), 100 (100), 72 (82)

3-(1,3-Dithian-2-yl)-1-(phenylsulfonyl)indole (28) A stirred solution of 1-(phenylsulfonyl)indole-3-carbaldehyde[10] (2 g, 7 0 mmol), *p*-toluenesulfonic acid (1 33 g, 7 0 mmol), and 1,3-propanedithiol (0 84 ml, 8 4

mmol), in anhydrous toluene (200 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 **28** which was purified by flash chromatography using ether-hexane (1 1) as the eluent (1 81 g, 69 %), mp 159-161°C (ether-acetone), IR($CHCl_3$) 1435, 1365, and 1165, ^{1}H NMR 1 90-2 30 (m, 2H, SCH_2CH_2), 2 85-3 20 (m, 4H, SCH_2), 5 41 (s, 1H, SCHS), 7 20-7 60 (m, 5H, Ar-H), 7 72 (s, 1H, In-2H), 7 80-8 00 (m, 4H, Ar-H), ^{13}C NMR 25 8 (SCH_2CH_2), 32 1 (SCH_2), 42 5 (SCS), 114 4 (In-C7), 121 4 (In-C6), 124 0 (In-C4), 125 3 (In-C3), 125 4 (In-C5), 126 0 (C-*ortho*), 127 6 (In-C2), 130 0 (In-C3a), 131 2 (C-*meta*), 134 8 (C-*para*), 136 5 (In-C7a), 138 0 (C-*ipso*), MS (m/z, %) 375 (M^+, 7), 301 (14) 234 (7), 160 (14), 141 (18), 133 (14), 101 (10), 89 (24), 77 (100) Anal Calcd for $C_{18}H_{17}NO_2S_3$ C, 57 57, H, 4 56, N, 3 73 Found C, 57 47, H, 4 56, N, 3 73

3-(1,3-Dithian-2-yl)-2-methyl-1-(phenylsulfonyl)indole (29) To a solution of dithiane **28** (171 mg, 0 46 mmol) in anhydrous THF (15 ml) cooled at -30°C under argon atmosphere *n*-butyllithium (1 6*M*, 0 34 ml, 0 55 mmol) was slowly added After the mixture was stirred for 15 min, methyl iodide (57 µl, 0 92 mmol) was added The reaction mixture was stirred at -30°C for 45 min and at room temperature for 20 min, quenched with aqueous ammonium chloride, and extracted first with ether and then with CH_2Cl_2 The organic extracts were dried and evaporated to give **29** which was purified by flash chromatography (ether-hexane, 30 70, 132 mg, 74 %), IR ($CHCl_3$) 1450, 1380, and 1180, ^{1}H NMR ($CDCl_3$) 1 80-2 20 (m, 2H, CH_2CH_2S), 2 68 (s, 3H, CH_3), 2 80-2 95 (dt, *J*=12 and 4 Hz, 2H, SHeq), 3 05 (td, *J*=12 and 4 Hz, 2H, SCHax), 5 48 (s, 1H, SCHS), 7 25 (td, *J*=7 and 1 Hz, In-6H and In-5H), 7 37 (t, *J*=8 Hz, 2H, Ar-H), 7 45 (t, *J*=8 Hz, 1H, Ar-H), 7 74 (d, *J*=8 Hz, 2H, ArH), 7 90-8 00 (dd, *J*=7 and 1 Hz, 1H, In-4H), 8 10-8 20 (dd, *J*=7 and 1 Hz, 1H, In-7H), ^{13}C NMR 13 3 (In-CH_3), 24 9 (SCH_2CH_2), 32 2 (SCH_2), 42 9 (SCS), 114 5 (In-C7), 117 7 (In-C3), 120 7 , 123 3 and 124 5 (In-C4, In-C5, and In-C6), 126 4 (C-*ortho*), 128 2 (In-C3a), 129 5 (C-*meta*), 134 0 (C-*para*), 134 5 (In-C2), 136 5 (In-C7a), 138 5 (C-*ipso*) Anal Calcd for $C_{19}H_{19}NO_2S_3$ C, 58 58, H, 4 92, N, 3 60 Found C, 58 77, H, 4 95, N, 3 57

When an excess of *n*-BuLi (3 equivalents) was used a (1 2 5) mixture of dithiane **29** and 3-(1,3-dithian-2-yl)-2-methyl-1-[2-methyl(phenylsulfonyl)]indole (**30**) (94 mg, 51%) was obtained, IR ($CHCl_3$) 1440, 1350, and 1165 cm^{-1}, ^{1}H NMR 1 85-2 30 (m, 2H, SCH_2CH_2), 2 42 (s, 3H, Ar-CH_3), 2 55 (s, 3H, In-CH_3), 2 92 (dt, *J*=12 and 1 Hz, 2H, SCHeq), 3 10 (td, *J*=12 and 1 Hz, 2H, SCHax), 5 52 (s, 1H, SCHS), 7 15-7 30 (m, 4H, Ar-H), 7 35-7 50 (t, *J*=7 Hz, 2H, Ar-H), 8 00 (d, *J*=8 Hz, 1H, In-4H), 8 05 (d, *J*=7 Hz, 1H, In-7H), ^{13}C NMR 12 9 (CH_3), 19 7 (CH_3), 24 9 (SCH_2CH_2), 32 1 (SCH_2), 42 8 (SCS), 114 4 (In-C7), 117 0 (In-C3), 120 7, 122 9 and 124 3 (In-C4, In-C5, and In-C6), 126 5 (*ortho*), 127 5 (In-C3a), 127 9 (phenyl C-5), 133 0 (phenyl C-2), 133 6 (phenyl C-4), 134 0 (In-C2), 137 0 (phenyl C-3), 138 0 (In-C7a), 139 0 (*ipso*) Anal Calcd for $C_{20}H_{21}NO_2S_3$ C, 59 51, H, 5 24, N, 3 47 Found C, 59 83, H, 5 33 N, 3 13

ACKNOWLEDGEMENT This work was supported by the DGICYT (Spain) through Grant PB-88/0316 and by the Acción Integrada Hispano-Francesa N° 111/2 (1990) and HF-167 (1991)

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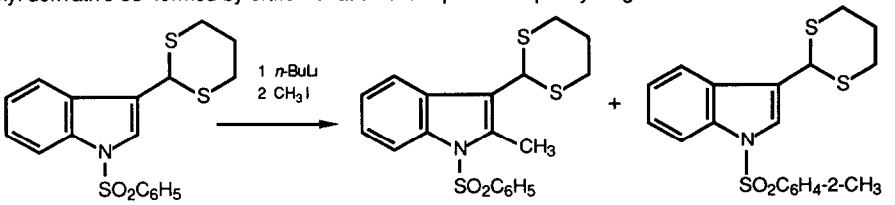
7 The synthetic usefulness of *N*-BOC-2-(1,3-dithian-2-yl)indole was dramatically decreased due to its instability and the low yield of its obtention [4]

8 For the synthesis and reactivity of *N*-methyl-2-(1,3-dithian-2-yl)indole, see (a) Bennasar, M -Ll , Torrens, A , Rubiralta, M , Bosch, J , Gnerson, D S , Husson, H -P *Heterocycles*, **1989**, *29*, 745-760 (b) Bennasar, M -Ll , Zulaica, E , Torrens, A , Perez, A , Bosch, J *Tetrahedron Lett* , **1990**, *31*, 1893-1896

9 Lithiation of 3-(1,3-dithian-2-yl)-*N*-phenylsulfonylindole (**28**), prepared by thioacetalization of the corresponding aldehyde[10] with 1,3-propanedithiol, with 1 2 equivalents of *n*-BuLi at -30°C followed by methyl iodide alkylation afforded only methylindole **29** resulting from the regioselective lithiation of indole 2-position (see Experimental Part) The use of an excess of *n*-BuLi furnished a 1 2 5 mixture of **29** and the dialkyl derivative **30** formed by *ortho* lithiation of the protective phenyl ring [11]



28 **29** **30**

10 Saulnier, M G , Gribble, G W *Tetrahedron Lett* , **1983**, *24*, 5435-5438

11 Sundberg, R J , Broome, R , Powers Walters, C , Schnur, D *J Heterocycl Chem* , **1981**, *18*, 807-809

12 (a) Gribble, G W , Saulnier, M G *J Org Chem* , **1983**, *48*, 607- 609, (b) Johnson, D A , Gribble, G W *Heterocycles*, **1986**, *24*, 2127-2131

13 Comins, D L , Stroud, E D *Tetrahedron Lett* , **1986**, *27*, 1869-1872

14 Saulnier, M G , Gribble, G W *J Org Chem* , **1982**, *47*, 757-761

15 Ho, T -L *Tetrahedron*, **1985**, *41*, 1-86

16 Spin decoupling experiments established that the doublet of doublets corresponding to H-8 (δ 4 45) was coupled with the C-9 diastereotopic methylene protons, whose signals appear at δ 2 85 and 3 28 Otherwise, when irradiating at δ 2 85 the doublet of doublets at δ 4 45 (H-8) was simplified to a doublet (*J*=12 Hz), while irradiation at δ 3 28 transforms it into a broad signal

17 Stork, G , Zhao, K *Tetrahedron Lett* , **1989**, *30*, 287-290

18 Sundberg, R J *J Org Chem* , **1965**, *30*, 3604-3610