Convenient route for the synthesis of 3-substituted and 3,4-disubstituted pyrrole-2,5-dicarbaldehydes

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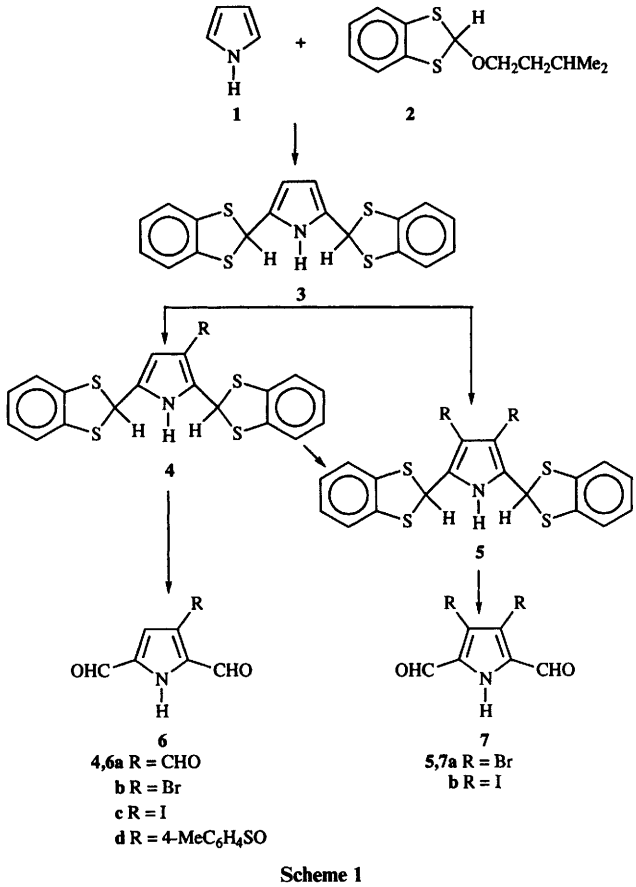
3-Substituted and 3,4-disubstituted pyrrole-2,5-dicarbaldehydes have been obtained by hydrolysis with HgO–35% aq. HBF_4–DMSO of the intermediates 4 and 5 prepared by electrophilic substitution reactions on 2,5-bis(1,3-benzodithiol-2-yl)pyrrole. The overall yields starting from pyrrole ranged from 41–88%.

Pyrrole-2,5-dicarbaldehyde and its derivatives, the 3-substituted **6** and the 3,4-disubstituted **7**, have become, especially in recent years, sought-after synthesis intermediates in various fields.[1,2] Our first efficient approach to the synthesis of these compounds was carried out by using 2-isopentyloxy-1,3-benzodithiole **2** as a formyl cation equivalent. The two formyl groups were introduced in a masked form at positions 2 and 5 of β-substituted pyrrole derivatives and then freed in good overall yield.[1] It must be kept in mind that not all β-substituted pyrrole derivatives are accessible[3] and that several, such as the mono- and di-bromopyrroles, are notoriously unstable,[3c,4] and cannot be manipulated under ordinary conditions without decomposition. In this work, conceived by us as being complementary to our previous research,[1] we sought to synthesise 3-substituted and 3,4-disubstituted pyrrole-2,5-dicarbaldehydes **6** and **7** by a reversal of the previously reported synthetic route, as illustrated in Scheme 1.

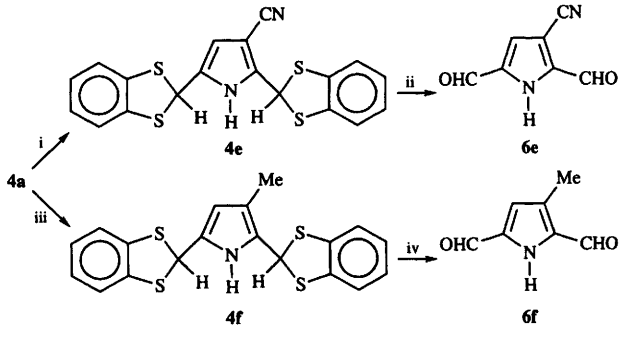
Thus 2,5-bis(1,3-benzodithiol-2-yl)pyrrole **3** was first prepared using a known procedure.[1,5] Then, using various electrophilic agents, attempts were made to carry out mono- and di-substitution at the free β positions. Finally the pyrrole-2,5-dicarbaldehydes **6** and **7** were obtained, after deprotection of the formyl groups, from monosubstituted products **4** and disubstituted products **5**. Yields of both the steps are reported in Table 1.

Among the many reactions with electrophilic carbon reagents, one very successful result was the formylation of **3**, carried out using the reaction of Vilsmeyer–Haack, which gave rise to a quantitative yield of 2,5-bis(1,3-benzodithiol-2-yl)-3-formylpyrrole **4a** (entry 1). Hydrolysis of this last product led to the projected pyrrole-2,3,5-tricarbaldehyde **6a** (entry 11). The same intermediate **4a** is also accessible *via* the previously described procedure,[1] however, even in the most favourable conditions[1] the preparation of pyrrole-3-carbaldehyde, the starting material needed to obtain **4a**, requires a greater number of steps and the overall yield starting from pyrrole is only 69%. Thus the new procedure is, without any doubt, more advantageous than the previous one.

It should be noted that **4a** can also be a useful synthesis intermediate. In the presence of protected formyl groups situated in positions 2 and 5, the free formyl group in position 3 can be converted using conventional procedures into different carbon functional groups, before the deprotection of the masked formyl groups. Thus, in a simple example, **4a** was initially converted into the corresponding 2,5-bis(1,3-benzodithiol-2-yl)-3-cyanopyrrole **4e** *via* a hydroxylamine derivative (entry 5) and then hydrolysed to give 3-cyanopyrrole-2,5-dicarbaldehyde **6e** (entry 15) in good overall yield (Scheme 2). In a second example, **4a** was converted to 2,5-bis(1,3-



Scheme 1



Scheme 2 *Reagents and conditions:* i, $HONH_3^+Cl^-$, DMF, $ClCH_2CH_2Cl$, 40 °C; Ac_2O, 80 °C; ii, 35% aq. HBF_4–DMSO, 60 °C; iii, $LiAlH_4$, THF, 40 °C; iv, 35% aq. HBF_4–DMSO, 0 to 60 °C

Table 1 Yields of products **4–7**

R	Entry	Product 4, 5	Yield (%)[a] from 3	Entry	Product 6, 7	Yield (%)[a] from 4, 5
CHO	1	**4a**	100	11	**6a**	60
Br	2	**4b**	96	12	**6b**	90
I	3	**4c**	43	13	**6c**	41[b]
4-MeC$_6$H$_4$SO	4	**4d**	95	14	**6d**	93
CN	5	**4e**	76[c]	15	**6e**	91
Me	6	**4f**	77[c]	16	**6f**	86[d]
Br	7	**5a**	50	17	**7a**	81
				18	**7a**	47[b]
Br	8	**5a**	60[e]			
I	9	**5b**	47	19	**7b**	44[b]
I	10	**5b**	55[f]			

[a] Yields of pure products. [b] From crude reaction mixture (see Experimental section). [c] From **4a**. [d] Reported overall yields from 5-chloro-3-methylpent-3-en-1-yne [ref. 7(*a*)], pyrrole-2-carbaldehyde [ref. 8(*a*,*b*)] and 3-methylpyrrole [ref. 7(*b*)] are 25, 20 and 41 and 6%, respectively. [e] From **4b**. [f] From **4c**.

benzodithiol-2-yl)-3-methylpyrrole **4f** by reduction with lithium aluminium hydride (entry 6), and then hydrolysed to 3-methylpyrrole-2,5-dicarbaldehyde **6f** (entry 16).

Among the halogenation reactions numerous unsuccessful attempts were made to obtain, using a range of chlorinating reagents, *i.e.* chlorine, *N*-chlorosuccinimide and sulfuryl chloride, the 3-chloro and 3,4-dichloro derivatives of **3** (see Experimental section). On the other hand, and demonstrating the complementary nature of the new synthetic route to the previous one, the 2,5-bis(1,3-benzodithiol-2-yl)-3,4-dichloropyrrole and corresponding 3,4-dichloropyrrole-2,5-dicarbaldehyde were obtained *via* the previously reported procedure.[1] Syntheses of 2,5-bis(1,3-benzodithiol-2-yl)-3-bromopyrrole **4b** and 2,5-bis(1,3-benzodithiol-2-yl)-3-iodopyrrole **4c** were successful, using as halogenating agents of **3**, respectively, *N*-bromosuccinimide in THF at −78 to −45 °C (entry 2) and *N*-iodosuccinimide in DMF at 0–5 °C (entry 3). Positive results were also obtained for the preparation of 2,5-bis(1,3-benzodithiol-2-yl)-3,4-dibromopyrrole **5a**, obtained by treating **3** or **4b** with bromine and pyridine in dichloromethane–acetic acid at −15 °C (entries 7 and 8), and 2,5-bis(1,3-benzodithiol-2-yl)-3,4-diiodopyrrole **5b**, obtained by the reaction of **3** or **4c** with iodine and pyridine in dichloromethane at 0–5 °C (entries 9 and 10).

Furthermore it was possible to realize the mono-toluene-*p*-sulfinylation of **3** (entry 4) whereas attempts to synthesise the disulfinyl product failed.

Finally the deprotection reactions of the formyl groups were achieved with HgO and 35% aq. HBF_4 in DMSO at 60 °C following the previously described procedure;[1] no particular difficulty was encountered and the yields ranged from good to excellent (Table 1).

In conclusion, the proposed synthetic route for the preparation of 3-substituted and 3,4-disubstituted pyrrole-2,5-dicarbaldehydes is efficient and fully complementary to the previously reported procedure.[1] Furthermore, it is noteworthy that these aldehydes are sought-after compounds and to date no alternative routes have been reported for most of them.

Experimental

^{1}H and ^{13}C NMR spectra were recorded on a Bruker WP 80 SY spectrometer for solutions in deuteriochloroform and in [$^2H_6$]DMSO, respectively, unless otherwise noted. The chemical shifts (δ) are expressed in ppm relative to internal tetramethylsilane and *J* values are given in Hz. Mass spectra were recorded on a quadrupole MS Engine HP 5989 B instrument, operating with a direct-inlet system at 70 eV for compounds **4a–f** and **5a,b**, and on an HP 5970 B mass selective detector connected to an HP 5890 GC, cross-linked methyl silicone capillary column (70 eV), for the other compounds. IR spectra were recorded on a Perkin-Elmer 599 B spectrophotometer for solutions in chloroform. Column chromatography and TLC were performed on Merck silica gel 60 (70–230 mesh ASTM) and GF 254, respectively. Light petroleum refers to the fraction boiling in the range 40–70 °C and is abbreviated as LP.

Reactions requiring anhydrous conditions were performed in oven-dried glassware under an atmosphere of nitrogen. Anhydrous *N*,*N*-dimethylformamide (DMF), pyridine, THF, dichloromethane and 1,2-dichloroethane, *N*-bromosuccinimide (NBS), *N*-chlorosuccinimide (NCS) and *N*-iodosuccinimide (NIS) were purchased from Aldrich; NBS, NCS and NIS were dried under reduced pressure in the presence of phosphorus pentoxide for 12 h before use.

Toluene-*p*-sulfinyl chloride[6] and 2,5-bis(1,3-benzodithiol-2-yl)pyrrole **3**[1,5] were prepared according to literature methods.

2,5-Bis(1,3-benzodithiol-2-yl)-3-formylpyrrole 4a

Anhydrous DMF (2.92 g, 40 mmol) was cooled at 0–5 °C in an ice-bath, with stirring. Phosphorous oxychloride (6.08 g, 40 mmol) was added dropwise, over a period of 15 min, cooling being maintained. After the addition was complete, the mixture was left to warm to room temperature and stirring was continued for a further 15 min. A solution of 2,5-bis(1,3-benzodithiol-2-yl)pyrrole **3** (3.71 g, 10 mmol) in DMF (15 cm^3) was added in one portion: an exothermic reaction occurred. Stirring was continued for 4 h, until monitoring (TLC: LP–$CHCl_3$, 7:3) indicated that all the starting compound **3** had disappeared. Then the reaction mixture was poured into cold aq. NaOH (5%; 200 cm^3). After stirring for 1 h, the resulting white precipitate was collected by filtration and washed successively with water (2 × 100 cm^3) and then with small amounts of EtOH (5 cm^3). After drying under reduced pressure, essentially pure (TLC, NMR) title compound **4a** (3.99 g) was obtained; mp 200–201 °C (from EtOH) (lit.,[1] mp 200–201 °C); *m*/*z* 399 (M^+).

2,5-Bis(1,3-benzodithiol-2-yl)-3-bromopyrrole 4b

A solution of compound **3** (3.71 g, 10 mmol; dried under reduced pressure in the presence of P_2O_5 for 12 h before use) in anhydrous THF (30 cm^3) was cooled to −78 °C in a N_2 atmosphere. A solution of NBS (recrystallized from benzene;[3c] 2.23 g, 12.5 mmol) in the same solvent (20 cm^3) was added dropwise over 30 min, with cooling being maintained. After the addition was complete, the temperature was allowed to rise to −45 °C over a period of about 2 h and was maintained until completion of the reaction (1.5 h; TLC: LP–$CHCl_3$, 7:3). A crystalline compound began to precipitate. To complete precipitation, the reaction mixture was poured into cold aq. $NaHCO_3$ (5%; 60 cm^3). The resulting precipitate was collected by filtration and washed with aq. $Na_2S_2O_3$ (5%; 20 cm^3) and then with small amounts of cold acetone (2 cm^3). After drying under reduced pressure, essentially pure (TLC, NMR) title compound **4b** was obtained (4.32 g); mp 155–156 °C (from CCl_4–LP) (Found: C, 48.1; H, 2.6; N, 3.1; S, 28.5; M^+, 449. $C_{18}H_{12}{}^{79}BrNS_4$ requires C, 48.00; H, 2.69; N, 3.11; S, 28.47%; *M*, 449); δ_H 6.22 (1 H, d, *J* 3.00, 4-H), 6.10 and 6.35 (2 H, 2 s, 1:1, 2 × SCHS), 6.97–7.24 (8 H, m, ArH) and 8.90 (1 H, br s, NH); δ_C 46.90 and 47.61 (d, *J* 155, SCHS), 95.18 (s, 3-C), 109.66 (d, *J* 181, 4-C), 121.79, 122.22 and 125.77 (d, *J* 163, ArCH), 126.01 and 133.41 (s, 2-C and 5-C) and 136.51 (s, ArCS); *m*/*z* 449 (M^+).

When the reaction was carried out with commercial NBS, a small amount of 2,5-bis(1,3-benzodithiol-2-yl)-3,4-dibromopyrrole **5a** was also obtained (0.32 g, 6%).

2,5-Bis(1,3-benzodithiol-2-yl)-3-iodopyrrole 4c

A solution of compound **3** (3.71 g, 10 mmol; dried before use as described above) in anhydrous DMF (25 cm^3) was cooled to 0–

5 °C in an ice-bath. A solution of NIS (recrystallized from CCl_4; 2.95 g, 1.31 mmol) in the same solvent (15 cm^3) was added dropwise over 30 min and the resulting mixture was stirred at *ca.* 0 °C until monitoring (TLC: LP–$CHCl_3$, 7:3) indicated that all the starting compound **3** had disappeared (1.5 h). The reaction mixture was poured into cold aq. $NaHCO_3$ (5%; 50 cm^3). The resulting precipitate was collected by filtration and then dissolved in CH_2Cl_2 (200 cm^3), which was washed successively with aq. $Na_2S_2O_3$ (5%; 4 × 50 cm^3) and water (100 cm^3), dried over Na_2SO_4 and the solvent evaporated under reduced pressure. Chromatography of the crude residue with LP–$CHCl_3$ (7:3) as eluent, gave the pure title compound **4c** (2.14 g); mp 159–160 °C (from $CHCl_3$) (Found: C, 43.4; H, 2.5; N, 2.8; S, 25.7; M^+, 497. $C_{18}H_{12}INS_4$ requires C, 43.46; H, 2.43; N, 2.82; S, 25.78%; *M*, 497); δ_H 5.95 (1 H, d, *J* 2.50, 4-H), 6.10 (2 H, s, 2 × SCHS), 6.80–7.05 (8 H, m, ArH) and 9.15 (1 H, br m, NH); δ_C[$(CD_3)_2CO$] 47.51 and 48.98 (d, *J* 156, SCHS), 94.19 (s, 3-C), 113.82 (d, *J* 182, 4-C), 121.83, 122.21 and 125.76 (d, *J* 161, ArCH), 129.26 and 135.02 (s, 2-C and 5-C) and 136.54 and 136.65 (s, ArCS); *m/z* 497 (M^+). The by-product 2,5-bis(1,3-benzodithiol-2-yl)-3,4-diiodopyrrole **5b** was also isolated in 3% yield (0.19 g); physical and spectroscopic properties were identical to those reported below.

2,5-Bis(1,3-benzodithiol-2-yl)-3-(4-tolylsulfinyl)pyrrole 4d

A solution of toluene-*p*-sulfinyl chloride (3.48 g, 20 mmol) in anhydrous 1,2-dichloroethane (20 cm^3) was added, dropwise over 30 min, to a stirred solution of compound **3** (3.71 g, 10 mmol) in the same solvent (40 cm^3) at −15 °C. Stirring and cooling were continued for 6 h until completion of the reaction (TLC: LP–$CHCl_3$, 7:3). The resulting white precipitate was collected by filtration and washed several times with water (200 cm^3) and then with small amounts of EtOH (5 cm^3). After drying under reduced pressure, essentially pure (TLC, NMR) title compound **4d** was obtained (4.84 g); mp 187–188 °C (from $CHCl_3$–LP) (Found: C, 59.0; H, 3.8; N, 2.71; S, 31.45%; M^+, 509. $C_{25}H_{19}NOS_5$ requires C, 58.91; H, 3.76; N, 2.75; S, 31.45%; *M*, 509); δ_H(270 MHz) 2.94 (3 H, s, Me), 6.08 (1 H, d, *J* 2.66, 4-H), 5.97 and 6.65 (2 H, 2 s, 1:1, 2 × SCHS), 6.99–7.07 and 7.07–7.16 (8 H, 2 m, 1:1, ArH), 7.27 and 7.50 (4 H, 2 d, 1:1, *J* 8.33, Ph-H) and 9.30 (1 H, br m, NH); δ_C 24.71 (q, *J* 130, Me), 49.68 and 51.27 (d, *J* 160, SCHS) and 109.69 (d, *J* 180, 4-C), 125.86, 126.11, 127.88, 128.06, 129.71 and 129.88 (d, *J* 160, ArCH and PhCH), 133.51 (s, 3-C), 136.36 and 137.95 (s, ArCS), 140.20 and 140.46 (s, 2-C and 5-C), 143.98 (s, MeCPh) and 146.63 (s, SOCPh); *m/z* 509 (M^+).

No traces of 2,5-bis(1,3-benzodithiol-2-yl)-3,4-bis(4-tolylsulfinyl)pyrrole were obtained, even when using a larger amount of toluene-*p*-sulfinyl chloride.

2,5-Bis(1,3-benzodithiol-2-yl)-3-cyanopyrrole 4e

A solution of hydroxylammonium chloride (1.58 g, 20 mmol) in anhydrous DMF (12 cm^3) was added to a solution of aldehyde **4a** (3.99 g, 10 mmol) in anhydrous 1,2-dichloroethane (28 cm^3). The solution was stirred and heated at 40 °C for 30 min, until a TLC test ($CHCl_3$–LP, 7:3) showed the disappearance of the starting compound **4a** and the presence of the corresponding oxime. After dilution with Ac_2O (12 cm^3), the solution was heated at 80 °C until completion of the reaction (2.5 h; TLC: $CHCl_3$–LP, 7:3). Then the reaction mixture was cooled, poured into aq. $NaHCO_3$ (5%; 100 cm^3) and extracted with $CHCl_3$ (2 × 100 cm^3). The combined organic phases were washed successively with aq. NaOH (5%; 2 × 100 cm^3) and water (2 × 100 cm^3) and dried over Na_2SO_4. The solvent was removed under reduced pressure and the crude residue was purified by column chromatography, eluting with $CHCl_3$–LP (7:3), to afford pure title compound **4e** (2.85 g); mp 211–212 °C (from MeCN–EtOH) (Found: C, 57.6; H, 3.1; N, 7.1; S, 32.4; M^+, 396. $C_{19}H_{12}N_2S_4$ requires C, 57.55; H, 3.05; N, 7.06; S, 32.34%; *M*, 396); δ_H([$^2H_6$]DMSO) 6.39 (1 H, d, *J* 2.00, 4-H), 6.30 and 6.52 (2 H, 2 s, 1:1, 2 × SCHS), 6.95–7.52 (8 H, m, ArH), and 12.07 (1 H, br m, NH); δ_C 46.05 and 47.04 (d, *J* 160, SCHS), 111.40 (d, *J* 170, 4-C), 115.70 (s, CN), 122.08, 122.30, 125.93 (d, *J* 160, ArCH), 128.44 (s, 3-C), 133.15 (s, 2-C and 5-C) and 136.08, 136.25 and 138.92 (s, ArCS); *m/z* 396 (M^+).

2,5-Bis(1,3-benzodithiol-2-yl)-3-methylpyrrole 4f

To a solution of aldehyde **4a** (3.99 g, 10 mmol) in anhydrous THF (40 cm^3), $LiAlH_4$ (0.76 g, 20 mmol) was added in four portions (each of 0.19 g) every 20 min, with vigorous stirring. An exothermic reaction occurred. After the addition was complete, the heterogeneous mixture was heated at 40 °C for 1 h to complete the reduction (TLC: $CHCl_3$). Then the reaction mixture was quenched by careful addition of ice-cold aq. NH_4Cl (10%)–$CHCl_3$ (200 cm^3, 1:1). The aqueous layer was separated and extracted again with $CHCl_3$ (2 × 50 cm^3). The combined organic extracts were washed with HCl (1%; 2 × 100 cm^3) and water (2 × 100 cm^3) and dried over Na_2SO_4. The solvent was removed under reduced pressure and the crude residue was purified by column chromatography, eluting with $CHCl_3$, to afford pure title compound **4f** (2.96 g); mp 185 °C (from EtOH) (Found: C, 59.1; H, 3.85; N, 3.6; S, 33.3; M^+, 385. $C_{19}H_{15}NS_4$ requires C, 59.19; H, 3.92; N, 3.63; S, 33.26%; *M*, 385); δ_H 2.00 (3 H, s, Me), 5.92 (1 H, d, *J* 3.00, 4-H), 6.13 and 6.40 (2 H, 2 s, 1:1, 2 × SCHS), 6.87–7.18 (8 H, m, ArH) and 8.65 (1 H, br s, NH); δ_C 10.71 (q, *J* 120, Me), 48.64 and 49.91 (d, *J* 15, SCHS), 110.33 (d, *J* 168, 4-C), 117.88 (s, CMe), 124.06 (s, 3-C), 122.00 and 125.80 (d, *J* 160, ArCH) and 137.03 and 137.28 (s, ArCS); *m/z* 385 (M^+).

2,5-Bis(1,3-benzodithiol-2-yl)-3,4-dibromopyrrole 5a

Method A. A solution of compound **3** (3.71 g, 10 mmol) and anhydrous pyridine (0.79 g, 10 mmol) in CH_2Cl_2–AcOH (65 cm^3; 1.5:1) was cooled at −15 °C, under stirring. A solution of bromine (3.60 g, 22.5 mmol) in AcOH (40 cm^3) was added dropwise during 15 min. After the addition was complete, a TLC test (LP–$CHCl_3$, 7:3) showed the disappearance of the starting compound **3** and the presence of two products, *i.e.* **4b** and **5a**. Stirring and cooling were continued until disappearance of the intermediate **4b** (30 min). Then the reaction mixture was poured into ice-cold aq. $NaHCO_3$ (5%; 100 cm^3) and extracted with CH_2Cl_2 (2 × 100 cm^3). The collected organic phases were washed successively with aq. $Na_2S_2O_3$ (5%; 2 × 100 cm^3) and water (100 cm^3), dried and evaporated under reduced pressure. Column chromatography of the crude residue with LP–$CHCl_3$ (7:3) as eluent, afforded pure title compound **5a** (2.64 g); mp 181–182 °C (from $CHCl_3$–LP) (Found: C, 40.9; H, 2.05; N, 2.7; S, 24.3; M^+, 527. $C_{18}H_{11}{}^{79}Br_2NS_4$ requires; C, 40.84; H, 2.09; N, 2.65; S, 24.23%; *M*, 527); δ_H 6.12 (2 H, s, 2 × SCHS), 6.92–7.21 (8 H, m, ArH) and 8.98 (1 H, br s, NH); δ_C 46.43 (d, *J* 160, SCHS), 99.04 (s, 3-C and 4-C), 121.63 and 125.75 (d, *J* 164, ArCH), 127.39 (s, 2-C and 5-C) and 136.61 (s, ArCS); *m/z* 527 (M^+).

Method B. The reaction mixture, prepared as described in Method A starting from compound **4b** (4.50 g, 10 mmol) and pyridine (0.79 g, 10 mmol) in CH_2Cl_2–AcOH (65 cm^3; 1.5:1) and bromine (3.60 g, 22.5 mmol) in AcOH (40 cm^3), was stirred at −15 °C for 30 min. The above work up afforded pure title compound **5a** (3.17 g).

2,5-Bis(1,3-benzodithiol-2-yl)-3,4-diiodopyrrole 5b

Method A. A suspension of finely divided iodine (5.58 g, 22 mmol) in anhydrous CH_2Cl_2 (30 cm^3) was cooled to 0–5 °C with an ice-bath, under an N_2 atmosphere with stirring. A solution of compound **3** (3.71 g, 10 mmol) and anhydrous pyridine (1.74 g, 22 mmol) in the same solvent (60 cm^3) was added dropwise over 20 min, cooling and stirring being maintained for a further 30 min. Five other portions of pyridine in CH_2Cl_2 and iodine were then added every 30 min [each of pyridine (0.44 g, 5.5 mmol) in CH_2Cl_2 (5 cm^3) and iodine (1.40

g, 5.5 mmol)], cooling being maintained. The reaction mixture was then poured into ice-cold aq. $NaHCO_3$ (5%; 100 cm^3) and extracted with CH_2Cl_2 (2 × 100 cm^3). The collected organic phases were washed successively with aq. $Na_2S_2O_3$ (5%; 2 × 100 cm^3) and water (100 cm^3), dried and the solvent evaporated under reduced pressure. Column chromatography of the crude residue with LP–$CHCl_3$ (7:3) as eluent afforded pure title compound **5b** (2.93 g); mp 174–175 °C (from CCl_4–LP) (Found: C, 34.6; H, 1.85; N, 2.3; S, 20.5; M^+, 623. $C_{18}H_{11}I_2NS_4$ requires C, 34.68; H, 1.78; N, 2.25; S, 20.57%; *M*, 623); δ_H 6.09 (2 H, s, 2 × SCHS), 6.87–7.17 (8 H, m, ArH) and 9.20 (1 H, br m, NH); δ_C 48.50 (d, *J* 160, SCHS), 78.33 (s, 3-C and 4-C), 121.65 and 126.76 (d, *J* 162, ArCH), 131.29 (s, 2-C and 5-C) and 136.66 (s, ArCS); *m/z* 623 (M^+).

Method B. A solution of compound **4c** (4.97 g, 10 mmol) and pyridine (0.87 g, 11 mmol) in CH_2Cl_2 (100 cm^3) was added in one portion to a suspension of iodine (2.79 g, 11 mmol) in the same solvent (50 cm^3), at 0–5 °C with vigorous stirring. Cooling and stirring were maintained for 2 h, until monitoring (TLC: LP–$CHCl_3$, 7:3) indicated that the starting compound **4c** had disappeared. The above work up afforded pure title compound **5b** (3.43 g).

Hydrolysis of 2,5-bis(1,3-benzodithiol-2-yl)pyrroles 4 and 5 to pyrrole-2,5-dicarbaldehydes 6 and 7

General procedure. According to the procedure previously reported[1] for the hydrolysis of 2,5-bis(1,3-benzodithiol-2-yl)-3-formylpyrrole **4a** to pyrrole-2,3,5-tricarbaldehyde **5a**, a mixture of compound **4** or **5** (10 mmol), HgO (13 g, 60 mmol), 35% aq. HBF_4 (30 cm^3) and DMSO (120 cm^3) was heated at 60 °C and stirred until completion of the reaction (TLC: $CHCl_3$). The reaction mixture was worked up as described previously.[1] Pure title compounds **6** and **7** were obtained by column chromatography.

Reaction times at 60 °C and chromatographic solvents are reported below together with the physical, analytical and spectral data of all the compounds. Yields are reported in Table 1.

3-Bromopyrrole-2,5-dicarbaldehyde 6b. 7.5 h; CH_2Cl_2 and then CH_2Cl_2–AcOEt (9.8:0.2); mp 152–153 °C (from acetone); ν_{max}/cm^{-1} (CCl_4) 1660 and 1680 (2 CHO) (Found: C, 35.6; H, 2.05; N, 7.0; M^+, 201. $C_6H_4{}^{79}BrNO_2$ requires C, 35.67; H, 2.00; N, 6.93%; *M*, 201); δ_H[$(CD_3)_2CO$] 7.15 (1 H, d, *J* 2.41, 4-H), 9.80 and 9.83 (2 H, 2 s, 1:1, 2 CHO); δ_C[$(CD_3)_2CO$] 107.17 (s, 3-C), 120.31 (d, *J* 187, 4-C), 132.43 and 136.24 (2 s, 2-C and 5-C) and 180.59 and 181.69 (2 d, *J* 182, 2 CHO); *m/z* 201 (M^+).

3-Iodopyrrole-2,5-dicarbaldehyde 6c. Hydrolysis was carried out on the crude reaction mixture from the synthesis of **4c**. 6 h; $CHCl_3$; mp 170–171 °C (from acetone–LP); ν_{max}/cm^{-1} 1665 and 1690 (2 CHO) (Found: C, 29.0; H, 1.65; N, 5.7; M^+, 249. $C_6H_4INO_2$ requires C, 28.94; H, 1.62; N, 5.63%; *M*, 249); δ_H 7.15 (1 H, d, *J* 2.57, 4-H), 9.68 and 9.73 (2 H, 2 s, 1:1, 2 CHO); δ_C[$(CD_3)_2CO$] 74.10 (s, 3-C), 126.99 (d, *J* 180, 4-C), 132.26 and 132.93 (2 s, 2-C and 5-C) and 182.48 and 183.03 (2 d, *J* 182, 2 CHO); *m/z* 249 (M^+).

3-(4-Tolylsulfinyl)pyrrole-2,5-dicarbaldehyde 6d. 6.5 h; CH_2Cl_2–AcOEt (4:1); mp 146–147 °C (from acetone–LP); ν_{max}/cm^{-1} 1675 and 1695 (2 CHO) (Found: C, 59.8; H, 4.3; N, 5.3; S, 12.3; M^+, 261. $C_{13}H_{11}NO_3S$ requires C, 59.76; H, 4.24; N, 5.36; S, 12.27%; *M*, 261); δ_H 2.40 (3 H, s, Me), 7.07 (1 H, d, *J* 1.80, 4-H), 7.32–7.64 (4 H, 2 d, *J* 9.00, Ph-H), 9.69 and 10.19 (2 H, 2 s, 1:1, 2 CHO) and 11.18 (1 H, br s, NH); δ_C($CDCl_3$) 20.59 (q, *J* 130, Me), 115.23 (d, *J* 180, 4-C), 124.29 and 129.22 (d, *J* 168, CHPh), 132.37 (s, 3-C), 134.49 and 134.66 (s, 2-C and 5-C), 140.79 and 141.11 (2 s, PhCSO and PhCMe) and 180.41 and 180.52 (2 d, *J* 191, 2 CHO); *m/z* 261 (M^+).

3-Cyanopyrrole-2,5-dicarbaldehyde 6e. 4 h; CH_2Cl_2–AcOEt (9.8:0.2); mp 208–209 °C (from acetone–LP); ν_{max}/cm^{-1} 1675 and 1685 (2 CHO) (Found: C, 56.7; H, 2.75; N, 19.0; M^+, 148. $C_7H_4N_2O_2$ requires C, 56.76; H, 2.72; N, 18.91%; *M*, 148); δ_H([$^2H_6$]DMSO) 7.60 (1 H, s, 4-H), 9.73 and 9.82 (2 H, 2 s, 1:1, 2 CHO); δ_C 112.58 (s, CN), 121.12 (d, *J* 180, 4-C), 134.23 (s, 3-C), 136.54 and 136.98 (2 s, 2-C and 5-C) and 179.27 and 180.69 (2 d, *J* 182, 2 CHO); *m/z* 148 (M^+).

3,4-Dibromopyrrole-2,5-dicarbaldehyde 7a. 3 h; $CHCl_3$; mp 178–179 °C (from CCl_4–pentane); ν_{max}/cm^{-1} 1667, 1687 and 1711 (2 CHO) (Found: C, 25.6; H, 1.05; N, 5.05; M^+, 279. $C_6H_3{}^{79}Br_2NO_2$ requires C, 25.66; H, 1.08; N, 4.99%; *M*, 279); δ_H[$(CD_3)_2CO$] 9.79 (2 H, s, 2 CHO) and 12.30 (1 H, br m, NH); δ_C 110.54 (s, 3-C and 4-C), 131.16 (s, 2-C and 5-C) and 179.59 (d, *J* 184, CHO); *m/z* 279 (M^+).

Hydrolysis was also carried out directly on the crude reaction mixture from the synthesis of **5a**. A greater amount of title compound **7a** was obtained (see Table 1).

3-Methylpyrrole-2,5-dicarbaldehyde 6f. The procedure previously reported[1] for the hydrolysis of 2,5-bis(1,3-benzodithiol-2-yl)pyrrole to pyrrole-2,5-dicarbaldehyde was slightly modified as follows: a solution of compound **4f** (3.85 g, 10 mmol) in DMSO (30 cm^3) was cooled to 0–5 °C in an ice-bath, the hydrolysis reagent, HgO (4.34 g, 20 mmol) and 35% aq. HBF_4 (10 cm^3) in DMSO (10 cm^3), was added dropwise over a period of 1 h, and stirring and cooling were maintained for 15–30 min until a TLC test ($CHCl_3$) showed the complete disappearance of the starting compound and the presence of two intermediates of partial hydrolysis. The ice-bath was then removed and a second portion of the hydrolysis reagent, HgO (8.68 g, 40 mmol) and 35% aq. HBF_4 (20 cm^3) in DMSO (20 cm^3), was added and the reaction mixture was warmed in an oil-bath to 60 °C. This temperature was maintained for 2 h, until the disappearance of the intermediates was observed. The reaction mixture was then worked up as previously described[1] and the crude residue was purified by chromatography, eluting with $CHCl_3$. Pure title compound **6f** was obtained (1.18 g); mp 91 °C (from acetone–LP) (lit.,[7a] mp 83 °C; lit.,[7b] mp 82–83 °C); IR and ^1H NMR data are identical to those reported;[7a,b] δ_C 10.53 (q, *J* 130, Me), 120.11 (d, *J* 170, 4-C), 130.63 (s, 3-C), 132.61 and 134.79 (s, 2-C and 5-C) and 180.47 and 181.35 (d, *J* 180, 2 CHO); *m/z* 137 (M^+).

3,4-Diiodopyrrole-2,5-dicarbaldehyde 7b. According to the above procedure, the crude reaction mixture obtained from synthesis of **5b** (Method A) was dissolved in DMSO (50 cm^3) and added dropwise, over a period of 30 min, to a solution of HgO (9.75 g, 45 mmol) and 35% aq. HBF_4 (22.5 cm^3) in DMSO (50 cm^3), maintaining the temperature at 0–5 °C. The reaction mixture was then warmed in an oil-bath to 60 °C, and the temperature maintained until completion of the hydrolysis (4 h; TLC: $CHCl_3$). The crude residue obtained after the usual work up was chromatographed with LP–$CHCl_3$ (7:3) as eluent, to afford pure title compound **7b** (1.65 g); mp 210–211 °C (from acetone–LP); ν_{max}/cm^{-1} 1670 and 1690 (2 CHO) (Found: C, 19.2; H, 0.85; N, 3.7; M^+, 375. $C_6H_3I_2NO_2$ requires C, 19.22; H, 0.81; N, 3.74%; *M*, 375); δ_H([$^2H_6$]DMSO) 9.60 (2 H, s, 2 CHO) and 13.80 (1 H, br s, NH); δ_H([$^2H_6$]DMSO) 88.50 (s, 3-C and 4-C), 135.16 (s, 2-C and 5-C) and 181.98 (d, *J* 181, CHO); *m/z* 375 (M^+).

Attempts to chlorinate 2,5-bis(1,3-benzodithiol-2-yl)pyrrole 3

Numerous attempts were made to chlorinate compound **3** using a range of chlorinating agents in various conditions as follows: (i) NCS in THF at −18 °C and in DMF at −45 °C; (ii) SO_2Cl_2 in $CHCl_3$ at −18 and 0 °C, in Et_2O at 0 °C and in CH_2Cl_2 at −78 and −18 °C ⟶ room temperature; (iii) Cl_2 in AcOH, pyridine and CH_2Cl_2 at −45 and −18 °C. From all the reaction mixtures yellow solid substances separated immediately. MS analysis indicated that the products were mixtures of sulfur compounds derived from detachment of the 1,3-benzodithiol-2-yl group and from its following reactions. GC–MS analysis of the organic solutions showed the presence of 5-(1,3-benzodithiol-2-yl)pyrrole-2-carbaldehyde in variable amounts. Only in the first case did GC–MS analysis reveal

traces of 3-chloro-2,5-bis(1,3-benzodithiol-2-yl)pyrrole: m/z 405 (M^+).

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