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Synthesis and Conformational Analysis of Dibenzodithiocin Derivatives*

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***N*-(3,4-Dialkoxyphenylthiomethyl)aroylamides (1a, b) reacted with phosphoryl chloride to give not only the expected 4*H*- and 2*H*-1,3-benzothiazine derivatives (4a, b and 5a, b), but also dibenzodithiocins of new (dibenzo[*d,g*][1,3]dithiocins 2a, b) and known (dibenzo[*b,f*][1,5]dithiocins 3a, b) types. The analogous reaction of the 4-methylaroylamide 8a furnished the 4*H*-1,3-benzothiazine 9a, the dibenzo[*b,f*][1,5]dithiocin derivative 10a and benzonitrile. In contrast, 8b (the chloro analogue of 8a) furnished only benzonitrile and bis(4-chlorophenylmercapto)methane (11). The structures of the new compounds were confirmed by IR, ^{1}H and ^{13}C NMR, and (in part) by mass spectrometry. Temperature-dependent ^{1}H NMR studies were used for the conformational analysis of 2a and its disulphone 6a; the nature and free enthalpies of activation of the two different conformational motions occurring at higher temperatures were determined.**

KEY WORDS Dibenzodithiocins Synthesis ^{1}H and ^{13}C NMR Conformation Structural isomerism

INTRODUCTION

In the course of our studies on 1,3-benzothiazines we have previously reported the ring closure of *N*-(3,4-dialkoxyphenylthiomethyl)aroylamides to 1,3-benzothiazines, effected by phosphoryl chloride.[2] In these reactions the expected 1,3-benzothiazine derivatives are formed in highly variable yields, depending on the nature of the aryl substituents, owing to side reactions. In order to clarify these processes we set out to determine the structures of the by-products by IR, ^{1}H and ^{13}C NMR and (in part) mass spectrometry.

SYNTHESIS

After the isolation of **4a** and **5a** (Scheme 1), the usual work-up[2] of the mixture obtained from the $POCl_3$ cyclization of *N*-(3,4-dimethoxyphenylthiomethyl)benzamide (**1a**) gave 3,4-dimethoxythiophenol and a large amount of benzonitrile. The former compound results from acid cleavage of the thioether **1a**, while benzonitrile is formed via the elimination of water from the other cleavage product, i.e. the benzamide derivative.

2,3,9,10-Tetramethoxy-6*H*,12*H*-dibenzo [*d,g*] [1,3] dithiocin (**2a**), representing a new ring system, was isolated as the main component of the remainder of the reaction mixture; it was accompanied by a small amount of the new 2,3,8,9-tetramethoxy derivative of the known 6*H*,12*H*-dibenzo[*b,f*][1,5]dithiocin (**3a**).[3,4]

Similarly, the analogous reaction of *N*-(3,4-diethoxyphenylthiomethyl)benzamide (**1b**) gave, after the isolation of the two isomeric 1,3-benzothiazines (**4b**, **5b**), both benzonitrile and the isomeric dibenzodithiocin derivatives **2b** and **3b** (Scheme 1).

The disulphones **6a**, **b** and **7a** were also prepared for conformational studies by the peracetic acid oxidation of compounds **2a**, **b** and **3a**.

When *p*-thiocresol was condensed with *N*-(hydroxymethyl)benzamide the resulting acid amide thioether **8a**, containing no alkoxy groups, underwent ring closure with $POCl_3$ to give, in addition to benzonitrile, only 2-phenyl-6-methyl-4*H*-1,3-benzothiazine (**9a**) and 2,8-dimethyl-6*H*,12*H*-dibenzo[*b,f*][1,5]dithiocin (**10a**) as the isolable products. Compound **10a** was also synthesized in an independent manner by reacting *p*-thiocresol with paraformaldehyde in a solution of $POCl_3$ (Scheme 2).

Cyclization of the chloro analogue **8b** of the thioether **8a**, prepared from *p*-chlorothiophenol and *N*-(hydroxymethyl)benzamide, was also attempted with $POCl_3$; however, probably because of the absence of electron-donating groups, the formation of the 2,8-dichlorodithiocin **10b**, earlier synthesized in another manner,[5] was not observed. The only products isolated from the reaction mixture were benzonitrile and **11**.

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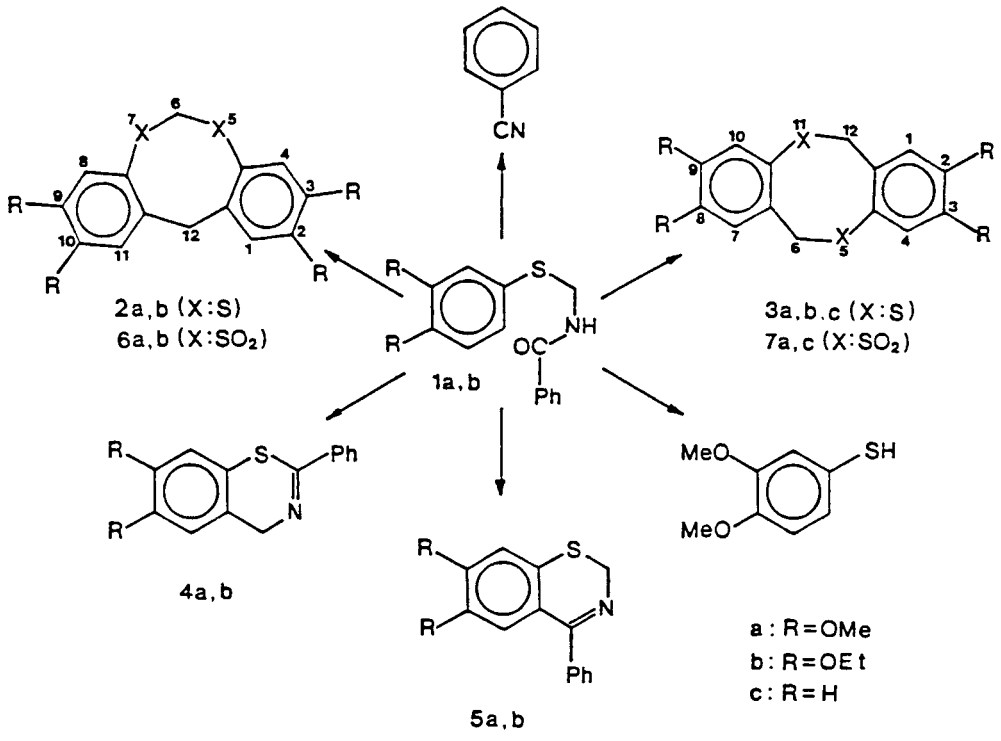


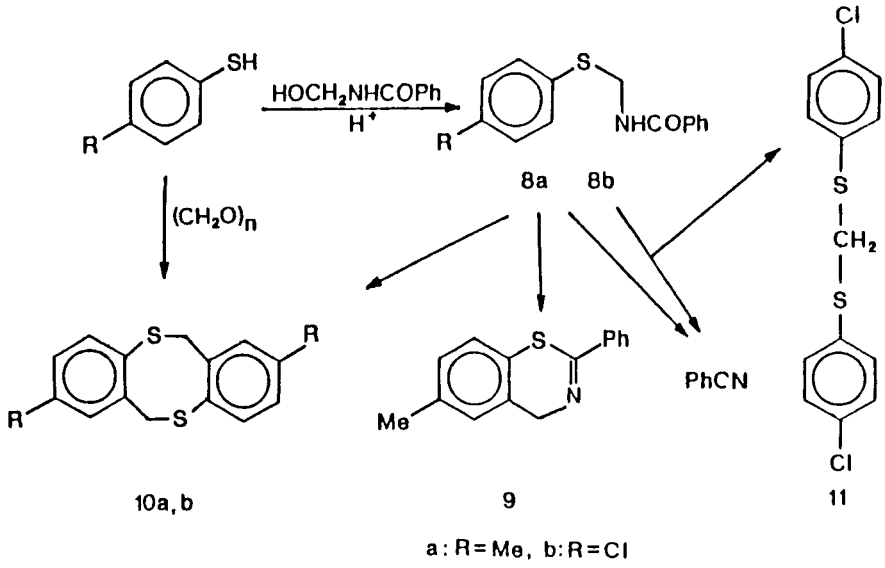
Scheme 1

STRUCTURE

The isomeric structures of **2a** and **3a** are supported by their electron impact-induced mass spectra (see Experimental). Both compounds gave abundant peaks of the molecular ion at *m/z* 364, and the isotopic pattern of the $M^{+\cdot}$ peaks shows the presence of two sulphur atoms in both molecules.

The fragmentations of **2a** and of **3a** resulted in a number of product ions with common *m/z* values, but with characteristically different abundances, indicating that the $M^{+\cdot}$ of **3a** is readily decomposed to give $M^{+\cdot}/2$ ions (via the cleavage of both S—CH_2 bonds), whereas the isomeric compound **2a** lost, very selectively, an S=CH_2 group (contraction of the eight-membered ring), followed by the loss of either a hydrogen from the bridging methylene group or a methoxy radical from the aromatic rings.

The ^1H NMR spectra (Table 1) also unequivocally confirm the isomeric structures **2** and **3**. In the spectra of **2a** and **3a**, **b**, the signals at room temperature are



Scheme 2

Table 1. ^{1}H NMR data (chemical shifts in δ, δ_{TMS} = 0 ppm; coupling constants in Hz) for compounds 2a, b, 3a, b, 6a, b, 7a and 10a at 250 MHz[a]

Compound	CH_3 (2, 3, 8/9, 9/10) $2\times s/t$ ($2\times 6H$)[b]		OCH_2 (2, 3, 8/9, 9/10) $2\times qa$ ($2\times 4H$)		CH_2(6, 12) $2\times 2d$ ($4\times 1H$)[c]				ArH (1, 4, 7/8, 10/11) $2\times s$ ($2\times 2H$)	
2a	380	392	—		4.45		4.15		7.00	7.04[d]
2b	139	145	401	412[d]	~37[d]	~495[d]	~39[d]	~445[d]	700	703[d]
3a	368	375	—		4.28				6.82	6.87
3b	123	129	392	402	4.28				677	6.82
6a	387[e]	399	—		385[e]	575	465	490	706[f]	7.46[g]
6b	142	149	405	418	388	572	465	485	702[f]	745[g]
7a	381	392	—		4.63		5.50		6.85	7.22[j]
10a	225	715[h]	—		4.34				6.90[i]	7.15[h]

[a] In $CDCl_3$ solution at room temperature for **2a, b, 6a, b** and **7a**. The data on **3a, b** and **10a** and the 6/12-methylene shifts of **2a** were obtained in DMSO-d_6 solution at about 155 °C (**2a** and **3a, b**) or 110 °C (**10a**). All signals of **3a, b** and **10a** and the methylene signals of **2a** are very broad at room temperature in $CDCl_3$ and also in DMSO-d_6, owing to the slow internal motion of the hetero ring. The characteristic, strong $\nu_{as}SO_2$ and ν_sSO_2 IR bands of **6a, b** appear (in KBr) at 1330 and 1150 (**6a**) and at 1320 and 1145 cm^{-1} (**6b**).
[b] For **2b, 3b** and **6b** *t*, $J(CH_3, CH_2) = 7$ Hz; *s* (6H) of 2,8-methyl groups (**10a**).
[c] For **2b** and **6a, b** an *AX*- and *AB*-type doublet pair for the 6- and 12-methylene protons, respectively, $J(A, X) \approx J(A, B) \approx 15$ Hz (**6a, b**). Owing to signal broadening it was not possible to determine the exact values of these coupling constants for **2b**. One *AB*-type doublet pair for **7a**, $J(A, B) \approx 15$ Hz. Coalesced at higher temperature to *s* (4H) for **3a, b** and **10a** or to $2\times s$ ($2\times 2H$) for **2a**.
[d] Broad signal.
[e] Overlapping signals.
[f] ArH-1,11.
[g] ArH-4,8.
[h] Overlapping singlet-like signals of ArH-1,7 and ArH-3,9.
[i] ArH-4,10, *d* ($J \approx 8$ Hz).
[j] ArH-4,10.

broadened owing to slow conformational motions; this is most marked in the case of the methylene signals which are hardly identifiable. However, the spectra obtained at higher temperatures and, in the case of **2b** the spectrum recorded even at room temperature, afford evidence for the structures.

In the ^{1}H NMR spectrum of **2b**, although the lines are also broadened at room temperature, it is readily possible to recognise each line of the two doublets of the *AB* and *AX* types due to the C-6 and C-12 methylene groups. The chemical non-equivalence of the two groups indicates that the methylene groups have different environments, proving structure **2**. In the spectrum of the analogue **2a** measured at 155 °C the *AX* and *AB* doublet pairs each coalesce to a singlet, while in **3a, b** the two methylene groups are chemically equivalent and absorb as a single line, in accordance with the molecular symmetry.

The ^{13}C NMR data are also definitive in proving the structures (Table 2). Owing to the very poor solubility, and to the signal broadening, useful spectra for **3a** could be obtained only in DMSO-d_6 at 140 °C. In the spectrum of the ethoxy analogue **3b**, recorded at room temperature in either DMSO-d_6 or $CDCl_3$, the two

Table 2. ^{13}C NMR chemical shifts (δ_{TMS} = 0 ppm) for compounds 2a, b, 3a, b, 6a, b, 7a and 10a in $CDCl_3$ unless stated otherwise[a] at 63 MHz[b]

Compound	CH_2 (2, 3, 8/9, 9/10)	CH_2 ⌈6⌊	CH_2 ⌈12⌊	OCH_2 (2, 3, 8/9, 9/10)	$C_{Ar}S$ (4a, 10a/7a)	$C_{Ar}(CH_2)$ (6a/11a, 12a)	$C_{Ar}H$ ⌈1, 7/11⌊	$C_{Ar}H$ ⌈4, 10/8⌊	$C_{Ar}O$ ⌈2, 8/10⌊	$C_{Ar}O$ ⌈3, 9⌊
2a	56.1	46.3[e]	41.5[e]	—	125.2[e]	140.3[e]	118.3[e]	113.0[e]	147.4[e]	150.1[e]
2a[a]	58.1	47.6	42.0	—	126.5	142.2	121.2	116.9	149.2	152.2
2b	14.9 15.0	46.6	41.6	65.3 65.4	125.7	140.7	121.1	116.2	147.5	150.1
3a[c]	55.9	37.9		—	125.5	134.7	119.0	114.8	147.3	149.5
3b	14.8	~38.0[d]		65.0 65.1	~125.0[e]	~135.0[e]	120.6[e]	116.0	147.6	149.6
6a	56.5 56.6	76.5	34.7	—	129.0	134.5	114.1	112.7	154.4	148.2
6b	14.7	76.8	34.9	65.5	129.2	134.6	116.1	114.9	154.3	148.0
7a	57.8 57.9	64.2		—	122.7	130.2	116.6	113.9	155.5	151.7
10a	21.0	39.3[e]		—	131.5[e]	142.3[e]	134.4[e]	127.9	138.7[f]	130.7[g]

[a] Compounds **3a** and **7a** were measured in DMSO-d_6, **2a** in $CDCl_3$ and also in DMSO-d_6 solution.
[b] Measuring frequency for **3a** 75 (see Acknowledgements) and for **10a** 20 MHz.
[c] Measuring temperature 140 °C. Owing to very poor solubility it was not possible to obtain an acceptable ^{13}C NMR spectrum of **3a** at room temperature.
[d/e] Very broad/broad signal due to the slow internal motion of the hetero ring.
[f] C_{Ar}(C)-2,8.
[g] C_{Ar}(H)-3,9.

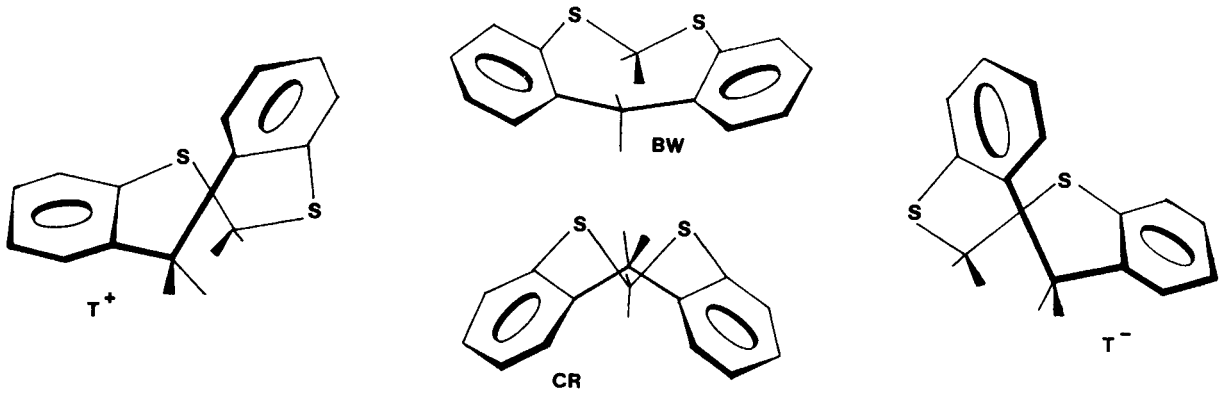


Figure 1. The relatively stable conformations of dibenzodithiocins **2a, b** and **6a, b**

methylene carbons give a common signal. Conversely, in the spectra of **2a, b** and **6a, b** two methylene carbon lines are found, and in the sulphones **6a, b** one of these lines shows a large downfield shift, corresponding to the substituent effect.[6a]

CONFORMATIONAL ANALYSIS

Detailed conformational analyses of 6*H*,12*H*-dibenzo-[*bf*][1,5]dithiocin (**3c**) and its disulphone **7c** have already been made by studying the temperature dependence of the ^{1}H NMR spectra.[7] It appeared to be interesting to compare the flexibilities of the isomeric pairs **2a–3a** and **6a–7a** for a study of the influence of the molecular symmetry and the presence of oxygen atoms on the internal motions. For this purpose the temperature dependence of the ^{1}H NMR spectra of **2a** and **6a** was examined.

Compound **3c** has a rigid and preferred chair conformation (C) which is separated from a flexible family of conformations by an energy barrier of approximately 14.4 kcal mol^{-1}.[7] Members with these latter conformations are the twisted boat inverses TB and TB*, which can be interconverted through the 'true' boat forms B and B*. It was established that the compound is flexible at room temperature; the interconversion C$\rightleftharpoons$B can be frozen at −14 °C; at lower temperatures only the pseudorotations TB$\rightleftharpoons$B$\rightleftharpoons$TB* or TB$\rightleftharpoons$B*$\rightleftharpoons$TB* take place, down to −40 °C, where this movement is also frozen.

The disulphone **7c** is conformationally homogeneous and at room temperature has form C. The ring inversion C$\rightleftharpoons$C* becomes free at approximately 70 °C ($\Delta G^{\neq} \approx 18.6$ kcal mol^{-1}).[7]

The new dithiocins **2a, b** and their disulphones **6a, b** exhibit similar conformational behaviour. In the former compounds the chair form C with C_i symmetry, occurring in the symmetric isomers **3** and **7**, is now substituted by the likewise rigid crown (CR) conformation with C_s symmetry (Fig. 1). Instead of the conformational family comprising the flexible boat, twisted boat, etc., forms (whose forms can be interconverted continuously without higher energy barriers through the cycle TB$\rightleftharpoons$B$\rightleftharpoons$TB*$\rightleftharpoons$B*), there are now two inverse conformational populations, in which two asymmetric entantiomeric twisted boat forms (T, T*) are interconverted through a butterfly-wing form (BW), representing the local energy maximum with C_s symmetry (Fig. 1).

In the sulphones **6a, b** the four bulky oxygen atoms increase the potential barrier of the conformational motion so much that these molecules behave as rigid systems in $CDCl_3$ solution at room temperature. Consequently, their ^{1}H NMR spectra have sharp signals. In the crown conformation (CR) the equatorial hydrogens of the 6-methylene group (of the $SO_2CH_2SO_2$ type) and the H-4,8 atoms are coplanar with one of the S—O bonds of each sulphone group; the resulting anisotropic effect[6b] gives rise to a considerable downfield shift of the corresponding signals. On the other band, the axial methylene hydrogens point towards the inside of the molecular skeleton; they are therefore strongly shielded (in the same way as, for example, the protons in analogous positions in dibenzocycloheptatrienes).[6c,8] As a consequence, the chemical shift difference $\Delta\delta AX$ in **6a, b** is unusually large (*ca.* 1.9 ppm), and this can be regarded as evidence of the suggested structure and the CR conformation.

In the spectrum of **6a** in DMSO-d_6 at room temperature, the 6-methylene hydrogens again appear as an *AB*-type pair of doublets, at 4.1 and 5.5 ppm (^2J = 14 Hz). The 12-methylene signal (aryl–CH_2–aryl) is a broad maximum that can be explained in terms of rapid interconversions of the enantiomeric conformational families T$^+\rightleftharpoons$BW$\rightleftharpoons$T$^-$ and T$^+$*$\rightleftharpoons$BW*$\rightleftharpoons$T$^-$*.

The activation free enthalpy of this movement ('flutter') is 60 kJ mol^{-1}. The two doublets of the 6-methylene group coalesce at 388 K, which means that the interconversion of all possible conformers (in relation to the NMR time scale) is rapid. The corresponding activation free enthalpy is 14 kJ mol^{-1} higher than that of the potential barrier mentioned above, i.e. 74 kJ mol^{-1}.

The conformational relationships in **2a, b** are analogous in every respect. For both methylene groups of **2a** the spectrum recorded in DMSO-d_6 at room temperature shows a diffuse maximum hardly emerging from the base line, but the integrals allow their unambiguous identification at approximately 3.5 and 4.65 ppm and at 4.0 and 4.75 ppm. On the basis of the coalescence temperature (T^1 338 K, T^2 348 K) the lower potential barrier is slightly higher (62 kJ mol^{-1}), whereas the higher barrier is much lower (67 kJ mol^{-1}) than the corresponding value for **6a**. It follows that the oxidation slightly facilitates the mobility of the 12-

methylene group, but significantly hinders that of the 6-methylene group, as expected.

Comparison of the asymmetric and symmetric isomers shows that structure **2** is slightly less mobile than the symmetric system of **3**, but in the corresponding sulphones the situation is reversed. Owing to the higher repulsion between the oxygen atoms the symmetric isomer **7** is much more rigid than the asymmetric analogues **6**, since the latter can avoid the most unfavourable steric hindrances by pseudorotation. This can also be seen from a study of molecular models, but our NMR measurements provided quantitative experimental proof.

In agreement with the greater mobility of structure **3**, of the ^{13}C NMR chemical shifts for **2a, b** and **3a, b** only those of the methylene and methylene-substituted aromatic carbons (6/11a,12a) differ significantly, i.e. these lines for isomers **3** are shifted upfield compared with the corresponding signals for **2a, b**. This can be explained by the field effect[9] due to steric hindrance between the methylene hydrogens and the unshared electron pairs of the sulphur atoms appearing during the conformational movements.

The more flexible structure of **3a, b** is also evidenced by the ^1H NMR spectra obtained at room temperature: the broadening of the signals is much less for **2a**, and particularly for **2b**, than for isomers **3a** and **3b**.

In accordance with the results of the conformational analysis, there is a considerable field effect (upfield shift of about 5.2 ppm) in the ^{13}C NMR signals of C-4a,10a in **7a** compared with the chemical shifts expected from substituent effects.[10] A slight shift (1.5 ppm) in the opposite direction is observed for **6a, b**, indicating the sterically less favoured structure of **7a**. The other five aromatic carbon signals display smaller steric compression shifts of about the same magnitude. A strong field effect (about 7 ppm) was found for the C-12 signal of the disulphones **6a, b** compared with the disulphides **2a, b** corresponding to the strong steric hindrance between the *endo* oxygens and the *endo* H-12 atom.

EXPERIMENTAL

The mass spectra were recorded on an AEI MS-902 double-focusing mass spectrometer with the following parameters: 70 eV, 8 kV, 100 μA and a source temperature of 200 °C. The samples were introduced via a direct probe.

IR spectra were recorded in KBr discs on a Bruker IFS-113v vacuum optic FT spectrometer controlled by an Aspect 2000 computer.

The NMR spectra were recorded in $CDCl_3$ or DMSO-d_6 solution in a 5 (^1H) or 10 mm (^{13}C) tube at different tempertures, on a Bruker WM-250 (^1H, ^{13}C) or WP 80 SY (^{13}C) FT spectrometer controlled by an Aspect 2000 computer at 250.13 (^1H) and 62.89 or 20.14 (^{13}C) MHz, with the deuterium signal of the solvent as the lock and TMS as internal standard. The most important measuring parameters were as follows: ^1H sweep width 5 kHz, pulse width 1 μs (*ca.* 20° flip angle), acquisition time 1.64 s, number of scans 16 or 32, computer memory 16K, Lorentzian exponential multiplication for signal-to-noise enchancement (line width 0.7 Hz) applied; ^{13}C, sweep width 15 or 5 kHz, pulse width 7.5 or 3.5 μs (*ca.* 30° flip angle), acquisition time 0.5 or 1.64 s, number of scans 284–36K, computer memory 32 or 16K; complete proton noise decoupling (*ca.* 3 or 1.5 W) and Lorentzian exponential multiplication were used for signal-to-noise enhancement (line width 1.0 or 2.0 Hz).

The DEPT[11] spectrum was recorded in a standard manner,[12] using only the $\theta = 135°$ pulse to separate the CH/CH_3 and CH_2 lines phased 'up and down,' respectively. Typical acquisition data were number of scans 128–12K, relaxation delay for protons 3 s and 90° pulse widths 10.8 and 22.8 μs for ^{13}C and ^1H, respectively. The estimated value for J(CH) resulted in a 3.7 ms delay for polarization.

The temperature-dependent spectra of **2a, 3a, 6a** and **7a** dissolved in DMSO-d_6 were measured by using the standard Bruker VT-1000 temperature stabilizer accessory. The coalescence temperatures, T_c, were determined with 2 °C accuracy. Free energies of activation were calculated according to Ref. 13.

Melting points are uncorrected.

Synthesis of 2a, 3a, 4a, 5a and 3,4-dimethoxythiophenol

1a (30.34 g, 0.1 mol) was heated with $POCl_3$ (30 ml) on a water-bath for 1 h. The reaction mixture was decomposed by pouring it on to ice, neutralized with Na_2CO_3 and extracted with benzene (200 ml). The extract was shaken with 10% HCl (200 ml) and allowed to stand for 1 h. The separated crystalline hydrochloride was filtered off and washed with 10% HCl and then with benzene. The base liberated from the salt was recrystallized from ethanol to give colourless needles (12.83 g, 45%), m.p. 100–101 °C. The product was identical in every respect with an authentic sample of **4a**.[14]

The hydrochloric acid phase was separated from the benzene layer and heated on a steam-bath for 1 h. Decolourizing carbon was added and the solution was filtered, neutralized with Na_2CO_3 and extracted with benzene (50 ml). After drying (Na_2SO_4), the solvent was evaporated and the residue was crystallized from ethanol (5 ml) to give pale-yellow needles (0.43 g, 1.5%), m.p. 142–143 °C. All properties of the product were identical with those of authentic **5a**.[14]

The benzene phase was dried (Na_2SO_4), the solvent was evaporated and the residue was distilled in the vacuum of a water pump on an air-bath at 195 °C. The distillate was dissolved in diethyl ether (40 ml) and extracted with 10% NaOH solution (5 ml). The alkaline phase was neutralized with HCl and the 3,4-dimethoxythiophenol was extracted with diethyl ether. The extract was dried (Na_2SO_4) and the solvent was evaporated to leave a colourless oil (0.65 g, 3.8%), identical in all respects with an authentic sample.[15]

The ethereal phase from the above procedure was dried (Na_2SO_4) and evaporated, and the residue was distilled, to give a colourless oil (3.1 g, 30%), b.p. 191–192 °C, n_D^{20} 1.52890, identical in all respects with authentic benzonitrile.

The residue of the distillation was dissolved in warm ethanol and left to crystallize for 1 week. The crystals

were then filtered off and treated with hot dioxane (10 ml). The insoluble, colourless, powdery crystals were filtered off and crystallized from DMSO, to give colourless crystals of **3a** (0.40 g, 2.2%), m.p. 250–252 °C. $C_{18}H_{20}O_4S_2$ (364.48): calculated, C 59.31, H 5.53, S 17.59; found, C 59.05, H 5.75, S 17.64%. Mass spectrum: *m/z* (*I*%): 366 (11); 365 (21); 364 (*100*), *M*; 331 (34), *M* − SH; 318 (25), *M* − SCH_2; 301 (16); 269 (13); 213 (20), *M* − $(MeO)_2C_6H_3CH_2$; 182 (48), *M*/2; 167 (52), 182/CH_3.

The dioxane solution was diluted with ethanol, resulting in the slow separation of **2a** in the form of plates with a pearly lustre (1.09 g, 6%). A sample was recrystallized from ethanol for analysis, m.p. 204–205 °C. $C_{18}H_{20}O_4S_2$ (364.48): calculated, C 59.31, H 5.53, S 17.59; found, C 59.45, H 5.63, S 17.70%. Mass spectrum: *m/z* (*I*%): 366 (4.5); 365 (8.7); 364 (42), *M*; 331 (10), *M* − SH; 318 (*100*), *M* − SCH_2; 317 (41), 318 − H; 303 (13); 301 (7.5); 287 (16); 195 (9.0); 182 (5.8), *M*/2; 167 (10), 182 − CH_3; 159 (15) $[M - SCH_2]^{2+}$.

Synthesis of compounds 2b, 3b, 4b and 5b

Proceeding in the same way as described in the previous experiment, **1b** (33.14 g, 0.1 mol) gave the following products.

Compound **4b** (12.76 g, 40.6%), m.p. 97–98 °C (from ethanol, identical in all respects with an authentic sample).[16] ^{1}H NMR ($CDCl_3$): CH_3 (6H), 1.41*, *t* (7.0 Hz); OCH_2 (2 × 2H), 4.02 and 4.04, 2 × *qa*; NCH_2 (2H), 4.71, *s*; H-5,8 (2 × 1H), 6.82 and 6.86, 2 × *s*; $H^{m,p}$ (Ph, 3H), 7.4 *m*; H^o (Ph, 2H), 7.98, *dd* (*ca.* 8 and *ca.* 2 Hz). ^{13}C NMR (63 MHz, $CDCl_3$): CH_3, 14.9*; NCH_2, 56.5; OCH_2, 65.4*; C-5,8, 113.1 and 113.6; C-4a,8a, 122.3 and 123.9; C^o (Ph), 127.7; C^m (Ph), 128.4; C^p (Ph), 130.9; C^i (Ph), 137.4; C-6,7, 149.2 and 149.3; C-2, 161.4.

Compound **5b** (1.12 g, 3.6%), pale yellow crystals from methanol, m.p. 122–123 °C. $C_{18}H_{19}NO_2S$ (313.40): calculated, C 68.99, H 6.11, N 4.47, S 10.23; found, C 68.73, H 6.35, N 4.25, S 10.53%. ^{1}H NMR ($CDCl_3$): CH_3 (2 × 3H), 1.34 and 1.47, 2 × *t* (7.0 Hz); OCH_2 (2 × 2H), 3.88 and 4.13, 2 × *qa*; SCH_2N (2H), 4.69, *s*; H-5,8 (2 × 1H), 6.80 and 6.88, 2 × *s*; $H^{m,p}$ (Ph, 3H), *ca.* 7.4, *m*; H^o (Ph, 2H), 7.53, *dd* (*ca.* 8 and *ca.* 2 Hz). ^{13}C NMR (63 MHz, $CDCl_3$): CH_3, 14.7*; NCH_2S, 49.2; OCH_2, 65.0 and 65.6; C-8, 112.6; C-5, 117.6; C-8a, 121.8; C^m (Ph), 128.0, C^o (Ph), 129.4; C^p (Ph), 129.6; C-4a, 131.3; C^i (Ph), 139.3; C-6, 146.5; C-7, 152.2; C-4, 167.8. Picrate: yellow crystals from methanol, m.p. 188–190 °C (decomp.). $C_{24}H_{22}N_4O_9S$ (542.51): calculated, C 53.13, H 4.09, N 10.33; found, C 53.02, H 4.26, N 10.05%.

Compound **3b** (0.12 g, 0.57%), colourless crystals from ethanol, m.p. 204–205 °C. $C_{22}H_{28}O_4S_2$ (420.57): calculated, C 62.82, H 6.71, S 15.25; found, C 62.60, H 6.49, S 15.27%.

Compound **2b** (1.2 g, 5.7%), colourless plates from ethanol, m.p. 138–139 °C. $C_{22}H_{28}O_4S_2$ (420.57): calculated, C 62.82, H 6.71, S 15.25; found, C 62.87, H 6.66, S 15.18%.

* Two overlapping signals.

2,3,9,10-Tetramethoxy-6*H*,12*H*-dibenzo-[*d*,*g*][1,3]dithiocin 5,7-tetroxide (6a)

Compound **2a** (0.72 g, 2 mmol) was allowed to stand in 5% peracetic acid (20 ml) for 1 day. The mixture was then poured on to ice and the separated crystals (0.65 g, 75.6%) were collected by filtration. Recrystallization from glacial acetic acid gave colourless needles, m.p. 238–239 °C. $C_{18}H_{20}O_8S_2$ (428.48): calculated, C 50.46, H 4.71, S 14.97; found, C 50.25, H 4.89, S 14.76%.

2,3,9,10-Tetraethoxy-6*H*,12*H*-dibenzo-[*d*,*g*][1,3]dithiocin 5,7-tetroxide (6b)

Compound **2b** (0.42 g, 1 mmol) was left to stand in 11.8% peracetic acid (5 ml) for 1 day. The product separated out when the reaction mixture was diluted with ice–water (0.36 g, 75%), colourless needles from ethanol, m.p. 188–190 °C. $C_{22}H_{28}O_8S_2$ (484.57): calculated, C 54.53, H 5.82, S 13.44; found, C 54.48, H 5.81, S 13.64%.

N-(4-Methylphenylthiomethyl)benzamide (8a)

4-Methylthiophenol (6.2 g, 50 mmol) and *N*-(hydroxymethyl)benzamide (7.6 g, 50 mmol) were dissolved in ethanol (25 ml). Ethanolic HCl (20 ml) was added to the solution, which was then allowed to stand.

The crystalline product (10.7 g, 83.2%) was collected by filtration, m.p. 111–112 °C (from ethanol). $C_{15}H_{15}NOS$ (257.34): calculated, C 70.00, H 5.89, N 5.44; found, C 70.00, H 6.08, N 5.22%.

Synthesis of 9 and 10

Following the procedure described above, refluxing of **8a** (5.14 g, 20 mmol) with $POCl_3$ (6 ml) for 1 h gave the following products.

2-Phenyl-6-methyl-4*H*-1,3-benzothiazine **9** (0.47 g, 9.8%), colourless crystals from ethanol, m.p. 104–105 °C. $C_{15}H_{13}NS$ (239.32): calculated, C 75.28, H 5.47, N 5.85, S 13.40; found, C 75.42, H 5.70, N 5.82, S 13.55%. ^{1}H NMR ($CDCl_3$): CH_3 (3H), 2.36, *s*; NCH_2 (2H), 4.75, *s*; H-7,8 (2H), 7.15*, *m*; H-5 (1H), *ca.* 7.25 *d* (*ca.* 2 Hz); $H^{m,p}$ (Ph, 3H), *ca.* 7.55, *m*; H^o (Ph, 2H), 8.00 *dd* (*ca.* 8 and *ca.* 2Hz). ^{13}C NMR (20 MHz, $CDCl_3$) (assignments were proved by DEPT measurements): CH_3, 21.0; NCH_2, 56.8; C-7,8, 126.4 and 127.5; $C^{o,m}$ (Ph), 127.7 and 128.4; C^p (Ph) and C-5, 128.3 and 130.9; C-4a, 131.3, C-6,8a and C^i (Ph), 137.3 and 137.4*; C-2, 161.6.

Compound **10a** (0.3 g, 11%), colourless plates from ethanol, m.p. 189–190 °C. $C_{16}H_{16}S_2$ (272.42): calculated, C 70.54, H 5.92, S 23.54; found, C 70.84, H 5.98, S 23.40%.

Benzonitrile (1 g, 49%), b.p. 191–192 °C, n_D^{20} 1.5279, identical with an authentic sample.

p-Thiocresol (0.4 g, 16%), m.p. 43–44 °C, identical in all respects with an authentic sample.

* Two overlapping signals.

2,8-Dimethyl-6*H*,12*H*-dibenzo[*b*,*f*][1,5]-dithiocin (10a)

p-Thiocresol (1.24 g, 10 mmol) and paraformaldehyde (0.30 g, 10 mmol) were heated in $POCl_3$ (5 ml) on a water-bath for 1 h. The mixture was poured on to ice, neutralized with NaOH and extracted with benzene. The organic phase was dried and the solvent was evaporated off. The residue was distilled under reduced pressure and the distillate crystallized from ethanol to give 0.4 g (29%) of the product, m.p. 189–190 °C. All of its properties were identical with those of **10a** prepared in the previous experiment.

N-(4-Chlorophenylthiomethyl)benzamide (8b)

4-Chlorothiophenol (7.23 g; 50 mmol) and *N*-(hydroxymethyl)benzamide (7.6 g; 50 mmol) were dissolved in ethanol (25 ml). Ethanolic HCl (20 ml) was added and the mixture was allowed to stand at room temperature. The crystalline product was collected by filtration (11.8 g; 85%); colourless crystals from ethanol, m.p. 136–137 °C. $C_{14}H_{13}ClNOS$ (277.77): calculated, C 60.53, H 4.36, N 5.04; found, C 60.70, H 4.52, N 5.24%.

Bis(4-chlorophenylmercapto)methane (11)

Compound **8b** (2.77 g, 10 mmol) was treated with $POCl_3$ (3 ml) on a hot water-bath for 1 h. The mixture was decomposed by mixing with ice. It was then neutralized with Na_2CO_3 and extracted with benzene. The extract was dried (Na_2SO_4) and the solvent was evaporated off. Distillation in the vacuum of a water pump gave an oil, from which **11** slowly crystallized. It was collected by filtration and washed with light petroleum to give 0.3 g (20%) of the product, m.p. 41–43 °C. $C_{13}H_{10}Cl_2S_2$ (301.25): calculated, C 51.83, H 3.35, Cl 23.54; found, C 51.45, H 3.25, Cl 23.22%. ^{1}H NMR ($CDCl_3$): CH_2 (2H), 4.27, *s*; ArH (2 × 2H), 7.27 and 7.33 *AA'BB'*-type *m*, *J*(*A*, *B*) = 8.8 Hz. ^{13}C NMR (20 MHz, $CDCl_3$): 1.5; CH_2, 41.5; C-2',6' (Ar), 129.3; C-3',5' (Ar), 132.5; C-1',4' (Ar), 133.3 and 133.8.

2,3,8,9-Tetramethoxy-6*H*,12*H*-dibenzo-[*b*,*f*][1,5]dithiocin 5,11-tetroxide (7a)

According to the procedure described for **6a**, compound **3a** (0.72 g, 2 mmol) gave **7a** (0.61 g, 71%) as colourless crystals, m.p. 292–294 °C (from acetic acid). $C_{18}H_{20}O_8S_2$ (428.27): calculated, C 50.45, H 4.71, S 14.97; found, C 50.20, H 4.99, S 14.99%.

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