Synthetic, Spectroscopic, and X-ray Crystallographic Studies of [1,2,7,8]Tetrathiacyclododecino[4,3-*b*:5,6-*b*′:10,9-*b*′′:11,12-*b*′′′]tetraindoles

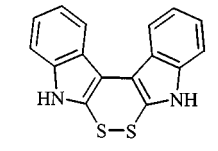
Tomasz Janosik,[a,b] Jan Bergman,*[a,b] Ivan Romero,[a,b] Birgitta Stensland,[c] Claes Stålhandske,[d] M. Manuel B. Marques,[e] Maria M. M. Santos,[e] Ana M. Lobo,[e] Sundaresan Prabhakar,[e] M. Filomena Duarte,[f] and M. Helena Florêncio[f]

Keywords: Sulfur heterocycles / X-ray diffraction / NMR spectroscopy / Nitrogen heterocycles

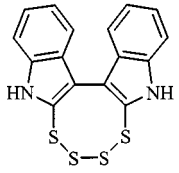
Two conformationally different [1,2,7,8]tetrathiacyclododecino[4,3-*b*:5,6-*b*′:10,9-*b*′′:11,12-*b*′′′]tetraindoles **9a** and **9b** have been isolated in good yields, and the existence of a third conformer **9c** in solution was demonstrated by mass spectrometry and ^{1}H NMR spectroscopy. The interconversions of the tetraindoles **9a**–**c** have also been studied. The conformation of **9b** was confirmed by X-ray crystallography, while the conformations of **9a** and **9b** were assigned on the basis of spectroscopic data, and were also supported by molecular modelling studies. In addition, the elusive dithiin **3** was isolated and the structure was proven by X-ray crystallography.

Introduction

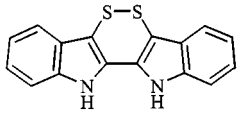
While indolocarbazoles[1] have attracted considerable interest over the years due to the fact that they display a wide range of biological activities, only a limited number of sulfur-containing analogues of these systems have been discussed and studied in the literature. For example, the dithiin **1** was claimed as a product from the treatment of the tetrasulfide **2** with sodium borohydride, followed by addition of acetic acid.[2] The isomeric dithiin **3** might theoretically, as has been discussed previously,[3] be formed by electrocyclization of its valence tautomer, dithioindigo (**4**). Although thionated derivatives of indigo (**5**) and indigoids have repeatedly been discussed in the literature over the years, neither **4** nor **6** have previously been isolated or characterized.[4] Thus, for example, attempts to prepare an *N,N*′-dimethylated derivative of **1**, or the corresponding thioindigoid compound **6** (R = CH_3), gave only the cyclic molecule **7**,[4c,4e] the structure of which has also been proven by X-ray crystallography.[4c]



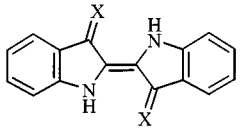
1



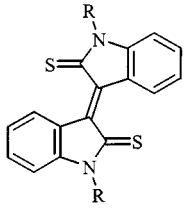
2



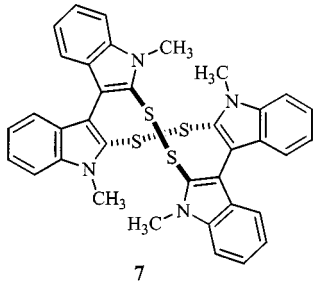
3



4 X = S
5 X = O



6 R = H or CH_3

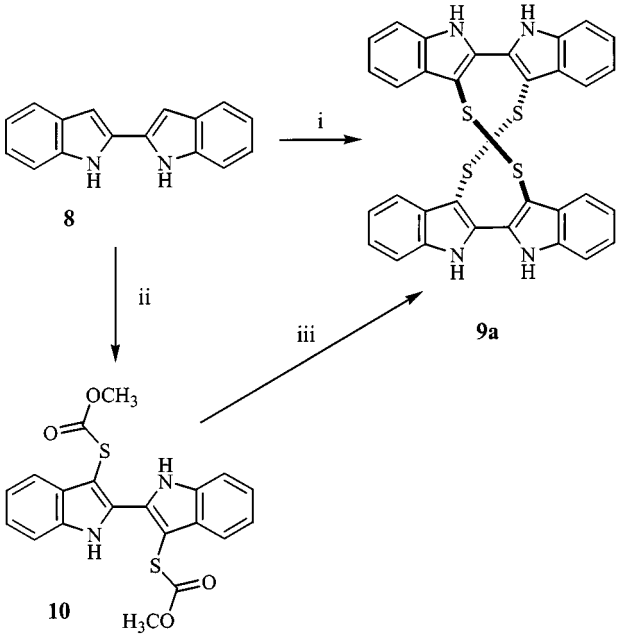


7

[a] Unit for Organic Chemistry, CNT, Department of Biosciences at Novum, Karolinska Institute,
Novum Research Park, 141 57 Huddinge, Sweden
[b] Södertörn University College,
141 04 Huddinge, Sweden
[c] Preformulation and Biopharmaceutics, Solid State Analysis AstraZeneca PAR & D/SBBG B341:3,
151 85 Södertälje, Sweden
[d] Department of Inorganic Chemistry 2, Chemical Center,
Box 124, 221 00 Lund, Sweden
[e] Secção de Química Orgânica Aplicada, Departamento de Química, Centro de Química Fina e Biotecnologia and SINTOR-UNINOVA, campus Faculdade de Ciências e Tecnologia, Universidade Nova de Lisboa,
Quinta da Torre, 2829 Monte de Caparica, Portugal
[f] Departamento de Química e Bioquímica, Faculdade de Ciências, Universidade de Lisboa,
Bloco C8, Campo Grande, 1747 Lisboa, Portugal
Supporting information for this article is available on the WWW under http://www.eurjoc.com or from the author.

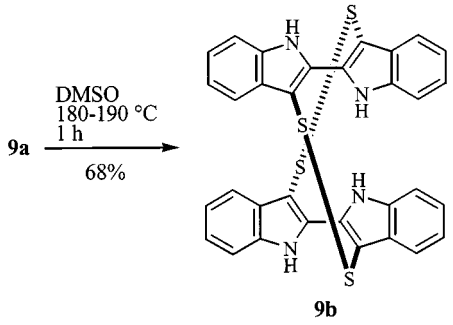
Results and Discussion

In our attempts to prepare the dithiin **3** or its corresponding dimer in a simple and straightforward way by treatment of 2,2′-biindolyl[5] (**8**) with elemental sulfur in refluxing xylene (mixture of isomers), one major product could be isolated in good yield, namely the previously described yellow compound with the proposed structure **9a**[4e] (Scheme 1). The tetraindole **9a** was found to be insoluble in all common organic solvents, except chloroform, in which it has limited solubility. In an alternative approach adapted from the literature,[4c−4e,6] **9a** was also prepared from the readily available 2,2′-biindolyl (**8**) in two steps via compound **10**, which was subsequently treated with KOH in ethanol, leading to **9a** after introduction of air into the reaction mixture, to give the desired product as a fine yellow precipitate. In none of these experiments were the still unknown molecules dithioindigo (**4**) or the dithiin **3** observed, in line with previous observations during attempts to synthesise these compounds.[4d,4e]



Scheme 1. Reagents and conditions: (i) S_8, xylene, reflux 34−36 h, 70−76%; (ii) $H_3COCOSCl$, CH_2Cl_2, room temp. 90 min, 94%; (iii) KOH, EtOH, reflux 1 h; then O_2 (air), 77%

We were intrigued by the unusual behaviour of compound **9a**, as it soon became evident that it undergoes transformation to two other, closely related, but differently coloured, species when dissolved in highly polar solvents such as DMSO or DMF. For instance, attempted NMR analysis of **9a** in [D_6]DMSO failed, as the yellow initially insoluble **9a** fairly quickly produced a deep-red solution, which gave two independent sets of signals in the ^1H NMR spectrum. Based on these findings, compound **9a** was heated in DMSO for 1 h, and a transformation into the red conformer **9b** was observed (Scheme 2). Recrystallization of **9b** from acetonitrile/*N,N*-dimethylacetamide (DMA) gave analytically pure material, which was further recrystallized from a mixture of acetic anhydride/DMA to provide crystals of high quality. These crystals were subsequently used in the determination of the structure of **9b** by X-ray crystallography (Figure 1).



Scheme 2.

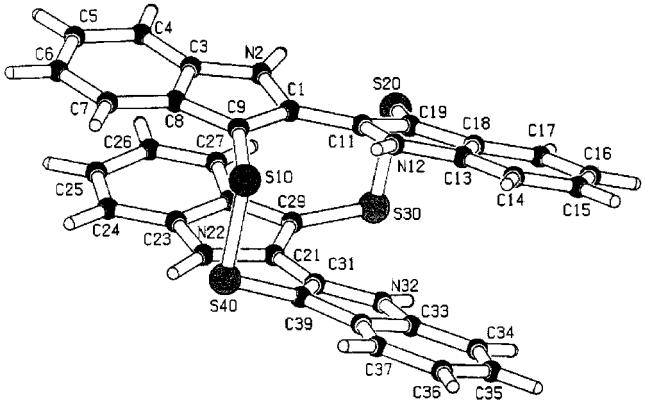
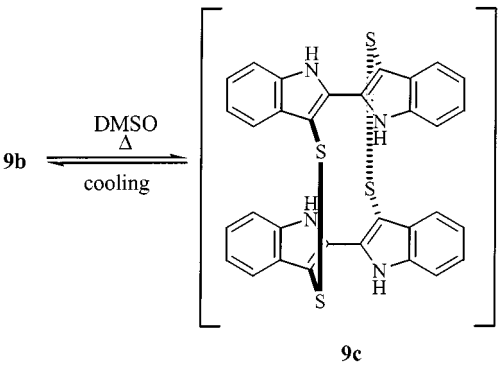


Figure 1. X-ray molecular conformation of **9b** showing the adopted atom labelling scheme used in the crystal structure refinement

Further experiments demonstrated that the red compound **9b** produces a third deep-red conformer, with the suggested structure **9c**, almost exclusively upon heating in DMSO (145 °C) (Scheme 3). This conformer was identified as the prevailing component of the warm product mixture resulting from heating **9a** in DMSO. The conformer **9c** could, however, never be isolated, as it undergoes transformation back to **9b** on cooling, and the only crystalline material obtained from such solutions was compound **9b**.



Scheme 3.

Interestingly, heating **9b** in DMA only, followed by filtration when hot and subsequent slow evaporation of the filtrate at room temperature, provided red crystals of a material which was identified by X-ray crystallography as the dithiin **3**, containing a disordered molecule of DMA (Figure 2). Apparently, the presence of co-solvents such as acetonitrile or acetic anhydride during the recrystallization experiments on **9b** prevent the extensive cleavage of the *S,S*-bridges, perhaps due to the lower boiling points of these solvent mixtures, although the intermediacy of **3** in the interconversions between the tetraindoles **9a/9b/9c** cannot be ruled out. All attempts to obtain NMR spectroscopic data of **3** failed, as dissolution of the crystals in $CDCl_3$ rapidly produced a mixture of **9a** and **9b**, while the presence of [D_6]DMSO gave predominantly the tetraindole **9c**, and trace amounts of **9b**.

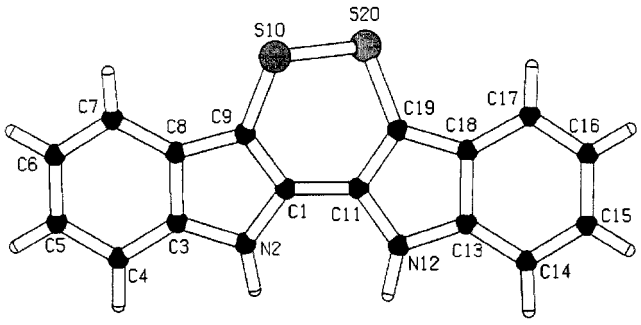


Figure 2. Molecular structure of **3** showing the atom numbering used in the crystal structure refinement; the disordered DMA molecule co-crystallized with **3** is omitted for clarity

The transformation of **9a** to **9b/9c** also occurs in hot DMF, and EI-MS analysis of such a solution revealed the existence of these two compounds, both with m/z = 588. The existence of **9c** could also be demonstrated by high temperature ^{1}H NMR experiments in [D_6]DMSO, as heating a solution of pure **9b** gave two sets of signals, one originating from the starting compound, and a second set from the deep-red newly formed conformer **9c** (Figure 3).[7] Analogous results were obtained when the same series of variable temperature ^{1}H NMR experiments on **9b** were performed in [D_7]DMF. Similar observations have previously been reported for other related oxygen-containing systems.[8]

The conformation of **9a** was elucidated on the basis of ^{1}H NMR spectroscopic data recorded in $CDCl_3$, as a resonance at δ = 5.59 suggested considerable shielding from a neighbouring aromatic ring, which can only be the case in structure **9a**, since the other two conformers **9b** and **9c** have their indole moieties placed more or less directly above each other. The chromophore of the yellow **9a** is also consistent with a strong twist of the 2,2′ bonds of the bisindole moieties. Again, we turned our attention to NMR experiments on **9a**. As discussed above, heating a [D_6]DMSO solution of **9a** also readily produces a mixture of **9b** and **9c**, thus suggesting that **9c** is an intermediate in the transformation of **9a** into **9b**. In fact, the transformation of **9a** into **9b/9c**,

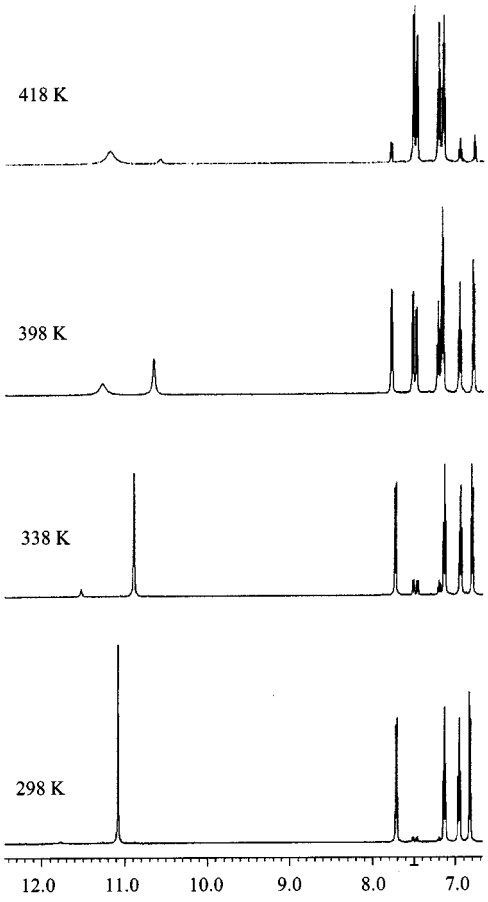


Figure 3. Variable temperature ^{1}H NMR (500 MHz) experiments in [D_6]DMSO on conformer **9b**, producing a mixture of **9b** and **9c**; the conformer **9c** becomes prevalent at >400 K

or possibly into **9b** via **9c**, takes place even at room temperature in [D_6]DMSO and the solution turns increasingly red (vide supra). A mixture containing **9b** and **9c** in [D_6]DMSO has recently probably been encountered by Schroth et al., who incorrectly assigned the NMR spectroscopic data thus obtained to the conformer **9a** and "oligomeric cyclic disulfides".[4e] Taken together, our ^{1}H and ^{13}C NMR spectroscopic data for **9b** and **9c** are in nice agreement with those previously assigned by Schroth[4e] to the mixture of **9a** and the purported oligomeric material. The structure of **9a** easily leads to that of **9b** by opening the dihedral angle of the 2,2′-biindolyl moieties to values close to 180°, thus providing a rationalisation of the bathochromic shift observed in the UV spectra. An examination of the X-ray structure of **9b** clearly reveals that the 2,2′-biindolyl moieties display an almost planar *trans* arrangement. Similarly to the observations made during the heating experiments on **9b**, all three conformers were found to coexist when a preheated solution of **9a** in DMF was analysed by electron impact mass spectrometry (direct inlet method). The mass spectrum showed three compounds (**9a/9b/9c**), with different retention times according to the total ion chromatogram (TIC), producing fairly strong molecular ions with m/z = 588 (cf. Exp. Sect. for details concerning the EI-MS measurements).

Also, a small fraction of a compound with $m/z = 294$ could be detected, which possibly suggests the formation of minute amounts of the monomeric species **3** at elevated temperatures. This fact might help to rationalise the reaction mechanism when **9a** was reacted with maleimide at an elevated temperature for a prolonged period of time to produce the alkaloid arcyriaflavin A.[9] The existence of isolable larger oligomeric species could not be detected in any of the experiments, but cannot be ruled out, as the formation of small amounts of different unidentified species can be observed by ^{1}H NMR spectroscopy when the preheated [D$_6$]DMSO solutions of, for example, **9a** are stored for a period of 3−4 weeks. It should be emphasized that the transformations of the different conformers are also dependent on the concentration, although this issue has not been studied in detail. The conformations of **9a**−**c** have also been simulated by molecular modelling,[10] giving results in line with the spectroscopic and X-ray crystallographic data. For more details see the electronic supporting information.

Experimental Section

General: NMR spectra were recorded on a Bruker DPX 300 (300 MHz), a Varian Unity Plus (400 MHz), or a JEOL Eclipse 500 (500 MHz) spectrometer. IR spectra were recorded on a Perkin−Elmer 1600 FT-IR instrument. MS (ESI) spectra were obtained using a Perkin−Elmer API 150 EX spectrometer. UV spectra were measured using a Pharmacia Biotech Ultrospec 3000 spectrophotometer. EI-MS was performed on a Fisons GC 8000 series chromatograph coupled to a MS TRIO 1000 quadrupole mass spectrometer at 70 eV, with introduction of the samples via the solids probe and the following temperature program: 2 min at 40 °C, 20 °C/min to 180 °C, 10 min at 180 °C, and finally 50 °C/min to 650 °C. The elemental analysis was performed by H. Kolbe Mikroanalytisches Laboratorium, Mülheim an der Ruhr, Germany. High resolution mass spectra were performed by E. Nilsson, University of Lund, Sweden. Melting points were measured on a Reichert Kofler hot stage apparatus and are uncorrected. Solvents were of analytical grade and were used as received.

3,3′-Bis(methoxycarbonylsulfenyl)-2,2′-biindolyl (10): Methoxycarbonylsulfenyl chloride (0.98 mL, 10.3 mmol) was added slowly to a suspension of 2,2′-biindolyl[5] (**8**) (1.16 g, 5.0 mmol) in dichloromethane (30 mL). The mixture was stirred for 2 h at room temp. The beige precipitate was collected by filtration, washed with dichloromethane and dried. Yield 1.94 g (94%). This product decomposes slowly and was used directly in the next step; m.p. 248−250 °C. IR (KBr): $\tilde{\nu}$ = 3351, 3062, 2954, 1711, 1579, 1427, 1387, 1340, 1235, 1190, 1140, 1010, 930, 816, 768, 754, 739 cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 3.69 (s, 6 H), 7.20 (ddd, J = 8.0, 7.6, 1.2 Hz, 2 H), 7.29 (ddd, J = 8.0, 7.6, 1.2 Hz, 2 H), 7.52−7.56 (m, 4 H), 12.27 (s, 2 H). ^{13}C NMR (100.6 MHz, [D$_6$]DMSO): δ = 54.5 (q), 97.6 (s), 112.2 (d), 119.0 (d), 120.8 (d), 123.3 (d), 129.5 (s), 133.2 (s), 136.5 (s), 169.0 (s). MS (ESI): m/z = 411 [M − H]$^-$.

5,6,17,18-Tetrahydro[1,2,7,8]tetrathiacyclododecino[4,3-*b*:5,6-*b*′:10,9-*b*′′:11,12-*b*′′′]tetraindole 9a from Compound 10: Compound **10** (206 mg, 0.5 mmol) was heated at reflux with KOH (0.2 g, 3.5 mmol) in ethanol (5 mL) for 60 min. Air was thereafter bubbled through the mixture during 30 min producing a yellow precipitate. Water (10 mL) was added, the yellow solid was collected by filtration, washed with ethanol and dried, to give **9a** (110 mg, 75%). This material was identical in all respects to that prepared from 2,2′-biindolyl (**8**) and sulfur in refluxing xylene (vide infra).

5,6,17,18-Tetrahydro[1,2,7,8]tetrathiacyclododecino[4,3-*b*:5,6-*b*′:10,9-*b*′′:11,12-*b*′′′]tetraindole 9a from 2,2′-Biindolyl (8): Finely powdered 2,2′-biindolyl[5] (**8**) (2.32 g, 10.0 mmol) was heated at reflux with finely powdered sulfur (1.0 g, 31.2 mmol) in xylene (mixture of isomers, 20 mL) for 34 h. The mixture was allowed to cool somewhat, and the yellow solid was then collected by filtration. This material was washed first with xylene, then with hexane, followed by acetonitrile, methanol, and warm chloroform, and was finally dried to yield **9a** (2.25 g, 76%); m.p. > 260 °C. IR (KBr): $\tilde{\nu}$ = 3370, 3056, 1486, 1424, 1374, 1338, 1235, 1173, 1148, 1114, 1009, 742 cm^{-1}. UV ($CHCl_3$): λ_{max} = 308, 385 nm. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.60 (d, J = 8.0 Hz, 4 H), 7.22 (partially obscured dd, 4 H), 7.43 (app. t, J = 7.6 Hz, 4 H), 8.00 (d, J = 8.0 Hz, 4 H), 8.80 (s, 4 H). MS (EI): m/z (%) = 588 (2), 326 (4), 294 (100), 262 (48), 261 (39), 232 (14). HRMS (EI): m/z = 588.0582 ($C_{32}H_{20}N_4S_4$ requires 588.0571).

5,6,17,18-Tetrahydro[1,2,7,8]tetrathiacyclododecino[4,3-*b*:5,6-*b*′:10,9-*b*′′:11,12-*b*′′′]tetraindole 9b: 5,6,17,18-Tetrahydro-[1,2,7,8]tetrathiacyclododecino[4,3-*b*:5,6-*b*′:10,9-*b*′′:11,12-*b*′′′]-tetraindole (**9a**; 588 mg, 1.0 mmol) was heated in DMSO (10 mL) at 180−190 °C for 1 h. The hot mixture was filtered and allowed to cool. The mixture was left standing at room temp. for 48 h, whereupon a red crystalline product was collected, washed with methanol and dried, to give **9b** (190 mg) as red crystals. A second crop of **9b** (210 mg) was obtained from the mother liquor after slow evaporation over several days. The total yield of **9b** was 400 mg (68%). An analytical sample was obtained by recrystallization from DMA/acetonitrile. Red crystals, m.p. > 260 °C. IR (KBr): $\tilde{\nu}$ = 3376, 1425, 1373, 1338, 1233, 1146, 1114, 1008, 734 cm^{-1}. UV (DMF): λ_{max} = 310, 338, 430 nm. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 6.83 (d, J = 8.1 Hz, 4 H), 6.96 (ddd, J = 8.1, 7.5, 1.0 Hz, 4 H), 7.14 (ddd, J = 7.8, 7.5, 0.7 Hz, 4 H), 7.72 (d, J = 7.8 Hz, 4 H), 11.10 (s, 4 H). ^{13}C NMR (75.4 MHz, [D$_6$]DMSO): δ = 106.6 (s), 111.9 (d), 118.3 (d), 120.1 (d), 123.1 (d), 129.3 (s), 132.9 (s), 135.9 (s). MS (ESI): m/z = 587 [M − H]$^-$. MS (EI): m/z (%) = 588 (7), 294 (100), 262 (22), 261 (30). HRMS (EI): m/z = 588.0568 ($C_{32}H_{20}N_4S_4$ requires 588.0571). $C_{32}H_{20}N_4S_4$ (588.8): calcd. C 65.28, H 3.42, N 9.52; found C 65.36, H 3.40, N 9.49.

[1,2]Dithiino[4,3-*b*:5,6-*b*′]diindole·*N*,*N*-dimethylacetamide (3): A small sample of **9b** was heated in DMA for about 10 minutes to ensure complete dissolution of the starting compound. The resulting deep-red solution was filtered hot, and the filtrate was allowed to concentrate by slow evaporation at room temperature producing red crystals of **3**, which were found to have co-crystallized with DMA. M.p. > 260 °C. IR (KBr): $\tilde{\nu}$ = 3545, 3476, 3412, 3388, 3253, 3056 (w), 2926 (w), 1617, 1606, 1425, 1370, 1335, 1235, 1010, 739 cm^{-1}.

X-ray crystallography: X-ray data for the two compounds **3** and **9b** were collected at room temperature on an Enraf−Nonius kappa-CCD diffractometer equipped with a graphite-monochromator and Mo-K_α radiation. The KappaCCD Server,[12] Collect[12] and Denzo-SMN[13] programs were used to control the unit-cell determinations, diffraction data collections and reduction of the intensity data sets. Both structures were solved by direct methods (SIR92[14]) and refined with full-matrix least-squares based on F with the maXus software program package.[15] The non-H atoms

were refined with anisotropic displacement factors, whereas H-atoms were refined isotropically in their calculated geometrical positions located at a distance of 0.96 Å from the parent atom. The displacement factors of all H-atoms were set to $U(iso) = 0.05$ Å^2. No absorption corrections were applied.[16]

Crystal Data for 9b: $C_{32}H_{20}N_4S_4$, $M_r = 588.80$, space group: $P2_1/c$ (no. 14). Unit cell parameters: $a = 12.303(1)$, $b = 14.107(1)$, $c = 16.091$ (1) Å, $\beta = 102.21(1)°$, $V = 2729.6(4)$ Å^3, $Z = 4$, $D_x = 1.433(1)$ g/cm^3, $F(000) = 1216$. μ(Mo-K_α) = 3.79 cm^{-1}. Crystal dimensions: 0.09 × 0.14 × 0.14 mm. Colour: red. 3475 independent reflections with $F^2 > 3\sigma(F^2)$ were refined to give $R = 0.0368$ and $R_w = 0.0373$ for 362 parameters. [$w = 1/\sigma^2F_0^2 + (0.30300)F_0^2$]. $(\Delta/\sigma)_{max} = 0.0011$, $\Delta\rho_{max} = 0.25$ eÅ^{-3}, $\Delta\rho_{min} = -0.23$ eÅ^{-3}, $\Delta\rho_{mean} = 0.04$ eÅ^{-3}. GOF = 1.424. The crystal structure of **9b** is highly symmetric. The two covalently bonded bisindole moieties are bridged by two sulfur atoms at each side to a tetrathiacyclotetraindole cluster (Figure 1). It is notable that all four indolic nitrogen atoms are oriented in different directions and that the planes of the covalently bonded bisindole moieties are almost parallel to its counterpart. The interplane distances are approximately 3.7 Å, facilitating π-stacking interactions between the π-orbitals in the aromatic indole ring planes. All four nitrogen atoms are exploited in intramolecular H-bond interactions to the closest neighbouring sulfur atom. These contacts, which are the only H bonds found in the structure, most probably help to stabilise the planarity of the dimeric molecular conformation

Crystal data for 3: $C_{16}H_{10}N_2S_2{\cdot}C_4H_9ON_2$, $M_r = 294.40 + 87.12 = 381.52$, space group: *Pbca* (No. 61). Unit cell parameters: $a = 8.527(1)$, $b = 18.418(1)$, $c = 24.378$ (1) Å, $V = 3828.6(5)$ Å^3. $Z = 8$, $D_x = 1.324(1)$ g/cm^3, $F(000) = 1600$. μ(Mo-K_α) = 2.92 cm^{-1}. Crystal dimensions: 0.06 × 0.06 × 0.23 mm. Colour: red. 1623 independent reflections with $F^2 > 3\sigma(F^2)$ were refined to give $R = 0.0486$ and $R_w = 0.0466$ for 233 parameters. ($w = 1/\sigma^2F_0^2 + (0.30300)F_0^2$). $(\Delta/\sigma)_{max} = 0.0002$, $\Delta\rho_{max} = 0.20$ eÅ^{-3}, $\Delta\rho_{min} = -0.24$ eÅ^{-3}, $\Delta\rho_{mean} = 0.05$ eÅ^{-3}. GOF = 1.774. In the crystal structure of **3** (Figure 2), two sulfur atoms participate in bridging the two covalently bonded indole rings, orienting the indolic nitrogen atoms in the same direction. The angle between the slightly twisted indole planes is 15.5(6)°. The DMA solvate molecule is disordered. The atoms of the DMA molecule are equally distributed over two atom-site positions with the oxygen atom in common. The oxygen atom, which is positioned at approximately the same distance from the two indolic nitrogen atoms, participates as an acceptor in the only classical H-bonds found in the crystal packing network. The two N···O distances are 2.826(9) and 2.837(9) Å.

Acknowledgments

We thank the Fundação para a Ciência e Tecnologia (Lisbon, Portugal) for partial financial support and for research grants to M. M. B. M and M. M. M. S.

[1] For reviews, see: [1a] G. W. Gribble, S. J. Berthel, in *Studies in Natural Products Chemistry* (Ed.: Atta-ur-Rahman), Elsevier, Amsterdam, **1993**, vol. 12, p. 365. [1b] M. Prudhomme, *Curr. Pharm. Des.* **1997**, *3*, 265−290. [1c] U. Pindur, Y.-S. Kim, F. Mehrabani, *Curr. Med. Chem.* **1999**, *6*, 29−69. [1d] J. Bergman, T. Janosik, N. Wahlström, *Adv. Heterocycl. Chem.* **2001**, *80*, 1−71.

[2] W. Carpenter, M. S. Grant, H. R. Snyder, *J. Am. Chem. Soc.* **1960**, *82*, 2739−2742.

[3] H. Sieghold, PhD thesis, Göttingen, **1973**.

[4] [4a] R. Gompper, K. Hartmann, K. Polborn, *Tetrahedron Lett.* **1994**, *35*, 9195−9196. [4b] W. Schroth, E. Hintzsche, H. Viola, R. Winkler, H. Klose, R. Boese, R. Kempe, J. Sieler, *Chem. Ber.* **1994**, *127*, 401−408. [4c] W. Schroth, M. Felicetti, E. Hintzsche, R. Spitzner, M. Pink, *Tetrahedron Lett.* **1994**, *35*, 1977−1980. [4d] W. Schroth, E. Hintzsche, M. Felicetti, R. Spitzner, J. Sieler, R. Kempe, *Angew. Chem.* **1994**, *106*, 808−810; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 739−741. [4e] W. Schroth, R. Spitzner, M. Felicetti, C. Wagner, C. Bruhn, *Eur. J. Org. Chem.* **2000**, 3093−3102 and references cited therein.

[5] J. Bergman, E. Koch, B. Pelcman, *Tetrahedron* **1995**, *51*, 5631−5642 and references cited therein.

[6] W. Schroth, E. Hintzsche, H. Jordan, T. Jende, R. Spitzner, I. Thondorf, *Tetrahedron* **1997**, *53*, 7509−7528.

[7] Spectroscopic data for compound **9c**: ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ = 7.14 (app. t, J = 7.4 Hz, 4 H), 7.20 (app. t, J = 7.8 Hz, 4 H), 7.47 (d J = 7.8 Hz, 4 H), 7.51 (d J = 8.3 Hz, 4 H), 11.4 (br. s, 4 H). ^{13}C NMR (125.7 MHz, [D$_6$]DMSO): δ = 101.1 (s), 112.3 (d), 118.7 (d), 120.7 (d), 122.8 (d), 125.4 (s), 130.6 (s), 136.0 (s). MS (EI): *m*/*z* (%) = 588 (20) [M$^+$], 294 (100), 262 (41), 261 (52). The UV data for **9c** were measured directly from a preheated DMF solution; λ_{max} = 252, 340, 468 nm.

[8] W. Schroth, D. Ströhl, I. Thondorf, W. Brandt, M. Felicetti, T. Gelbrich, *Tetrahedron* **1995**, *51*, 8853−8862.

[9] M. M. B. Marques, A. M. Lobo, S. Prabhakar, P. S. Branco, *Tetrahedron Lett.* **1999**, *40*, 3795−3796.

[10] Molecular modelling studies of the dimers' conformations were performed using the Sybyl force field implemented in the Spartan program.[11]

[11] Sybyl force field, MacSpartan Plus, Wavefunction Inc., 18401 Von Karman Ave., Irvine, CA 92612, USA.

[12] B. V. Nonius, *KappaCCD Server* and *Collect.* Software for cell-determination and data collection, B. V. Nonius, Delft, The Netherlands, 2000.

[13] Z. Otwinowski, W. Minor (1997). *Denzo-SMN program package. Processing of X-ray Diffraction Data Collected in Oscillation Mode. Methods in Enzymology* **1998**, *276*, 302−326; *Macromolecular Crystallography* (Eds.: C. W. Carter, Jr., R. M. Sweet), Academic Press, Inc. **1997**.

[14] A. Altomare, M. C. Burla, M. Camalli, G. Cascarano, C. Giacovazzo, A. Guagliardi, G. Polidori. *SIR92* (1992). Program for automatic solution of crystal structures from X-ray diffraction data.

[15] S. Mackay, C. Edwards, A. Henderson, C. Gilmore, N. Stewart, K. Shankland, A. Donald (1999). *MaXus program package.* A state-of-the art computer program for solving, refining and publishing crystal structures from X-ray diffraction data. Chemistry Department, The University, Glasgow, Scotland. Developed for Mac Science Co., Japan and Nonius, The Netherlands.

[16] CCDC-171547 (**3**) and CCDC-171548 (**9b**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; Fax: (internat.) +44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

Received December 6, 2001
[O01574]