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9,21,22-Triaza-2,11-dithia[3.3](2,6)pyridino(2,9)phenanthrolinophane: a five-donor macrocycle functioning as a bidentate ligand

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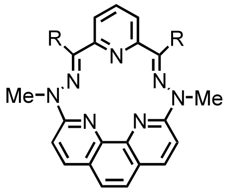
Abstract—9,21,22-Triaza-2,11-dithia[3.3](2,6)pyridino(2,9)phenanthrolinophane **4** was prepared from a cyclization reaction of 2,6-bis(mercaptomethyl)pyridine **5** and 2,9-bis(bromomethyl)phenanthroline **6**. Results from ^{1}H NMR analysis are inconclusive but those derived from semi-empirical molecular orbital PM3 calculations support a preference for a *syn* conformation for **4**. The conformation barrier for interconversion between two *syn* isomers of **4** was estimated to be 36.5 kJ mol^{-1} on the basis of a dynamic ^{1}H NMR study. The manganese(II) and zinc(II) complexes of **4** were prepared and the metal to ligand ratios were found to be 1:1 and 2:1, respectively, by elemental analyses. Results from an ^{1}H NMR analysis of the zinc(II) complex of **4** suggest that only the two nitrogen atoms of the phenanthroline moiety participate in the co-ordination. © 2003 Elsevier Science Ltd. All rights reserved.

One of the most common families of macrocyclic ligands described in coordination chemistry[1] are tetradentate and commonly possessing an N_4 donor set. Several families of novel, pentadentate macrocyclic N_5 donor ligands, namely **1**–**3**,[2] have been reported. These macrocycles form complexes with a series of metal ions exhibiting some structural features similar to porphyrins. Synthetically, the macrocyclic ligands **1**–**3** have been prepared by template condensation reactions and thus the complexes were isolated directly from the respective reactions. The metal complexes of **1**–**3** are always nearly planar perhaps due to conjugation effects derived from the presence of nitrogen atoms and C=N bonds in the bridges. There is, however, no information available on the physical properties particularly concerning the conformational behavior of the macrocyclic ligands **1**–**3**. In view of the fact that dithiacyclophanes can be prepared readily by cyclization reactions under high dilution conditions,[3] a N_3S_2 macrocycle such as **4** should be readily assessable. N_3S_2 ligands are rare and whether the 15-membered ring in **4** would adopt a near-planar conformation and allow the sulphur atoms to participate effectively leading to a pentadendate system, or whether coordination would involve only the three more effective nitrogen donor atoms, is of special interest.



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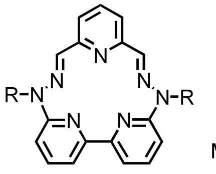

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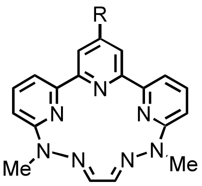

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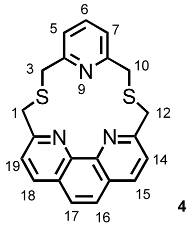

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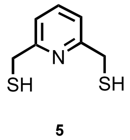

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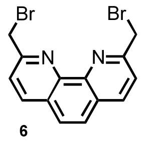

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A cyclization reaction between compounds **5**[4] and **6**[5] was carried out under high dilution conditions[3] in the presence of KOH at a reaction temperature of ca. 60°C. The dithiacyclophane **4** was isolated in 58% yield. The ^{1}H NMR spectrum of **4** at room temperature clearly suggests that it is conformationally mobile. The two sets of bridging methylene protons appear as averaged singlets at δ 4.12 and 3.44, respectively. H-16,17 appear as a singlet at δ 7.73; H-14,19 and H-15,18 are observed as two separate doublets at δ 7.70 and 8.19, respectively. H-5,7 appear as a doublet at δ 7.63 while the expected triplet of H-6 overlaps with signals of H-

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Keywords: pyridinophenanthrolinophane; five-donor macrocycle; conformational behavior; tetrahedral zinc; bidentate ligand.

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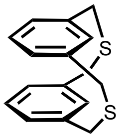
Table 1. Dynamic ^{1}H NMR (500 MHz) spectral data (CD_2Cl_2) for dithiacyclophane **4**

T (K)	H-15,18	H-16,17	H-6	H-14,19	H-5,7	CH_2[a]	CH_2[b]
297	8.28	7.82	7.87	7.74	7.70	4.06	3.33
206	8.32	7.85	7.98	7.77[c]	7.77[c]	4.07	T_c[d]
193	8.33	7.86	8.0[e]	7.8[c]	7.8[c]	T_c[d]	3.62, 2.96[f]
183	8.34	7.87	8.0[e]	7.8[c]	7.8[c]	4.11, 4.04[g]	3.64, 2.95[h]

[a] Methylene protons adjacent to the phenanthroline ring.
[b] Methylene protons adjacent to the pyridine ring.
[c] The respective doublets of H-14,19 and H-5,7 overlap.
[d] The coalescence temperature.
[e] The triplet was no longer resolved.
[f] Slightly resolved into two broad singlets.
[g] Resolved into an AB quartet; the outer lines nearly overlap with the respective inner lines.
[h] Resolved into two doublets.

14,16,17,19. In an NOE experiment, irradiation of the signal at δ 3.44, subsequently assigned to the methylene protons adjacent to the pyridine ring, resulted in an enhancement of the doublet at δ 7.63. A similar experiment involving irradiation of the signal at δ 4.12 (methylene protons adjacent to the phenanthroline ring) led to a significant enhancement of the doublet at δ 7.70.[†] When a ^{1}H NMR spectrum of **4** was taken at 183 K (Table 1), the observed spectral data support the presence of only one frozen conformation. The *syn* conformation of a dithia[3.3]-metacyclophane system, e.g. *syn* **7**,[6] usually results in an upfield shift of the aromatic protons in both rings due to mutual shielding effects of the two near-parallel aromatic rings.[7] Going from 297 to 183 K, the signals of the aromatic protons of **4** show only very small changes in their chemical shifts. The preference for the *syn* or *anti* (similar to that of *anti* **8**)[6] conformation in **4** is thus inconclusive on the basis of this study.



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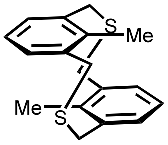

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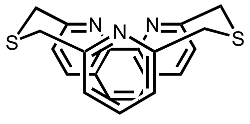

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The relative stability of the *anti* and *syn* conformers of **4** was then estimated by semi-empirical molecular orbital PM3[8] calculations (also optimizing the most stable conformation for the C–S–C bridges). Only one minimum was observed for the *anti*-*trans* (referring to the stereochemistry of the two aromatic rings and the two sulphur atoms, respectively) conformation [Fig. 1(a)]. Two minima were, however, observed for the *syn* conformation: the *syn*-*cis* [Fig. 1(b)] and the *syn*-*trans* [Fig. 1(c)], respectively. The *syn*-*cis* conformer **9** [Fig. 1(b)] is the most stable, being ca. 11 and 76 kJ mol^{-1} more stable than the *anti*-*trans* and *syn*-*trans* conformers, respectively. Thus the averaged ^{1}H NMR spectrum of **4** observed at room temperature could represent a fast interconversion between *syn*-*cis* conformers of **4** with the *anti*-*trans* conformer as an intermediate of relatively high energy (Fig. 2).

In the dynamic ^{1}H NMR studies of **4**, either set of the bridging methylene protons could in principle be used as a probe. Although the respective coalescence temperatures for the methylene protons adjacent to the phenanthroline and those to the pyridine rings were found to be at 193 K and 206 K (Table 1), respectively, the AB quartet of those adjacent to the phenanthroline ring were not sufficiently resolved to allow the measurement of their coupling constant. In the high temperature (297 K) spectrum, the respective singlets of the methylene protons appeared at the average positions (±<0.1 ppm) of the corresponding AB quartets in the low temperature (183 K) spectrum. When a sample cooled to 183 K was warmed to room temperature again, the original spectrum at room temperature was

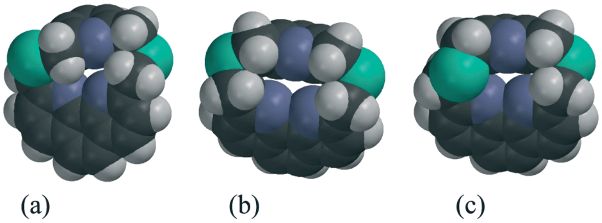

Figure 1. Optimized structures of (a) *anti*-*trans*, (b) *syn*-*cis* and (c) *syn*-*trans* conformers of **4** derived from semi-empirical molecular orbital calculations.

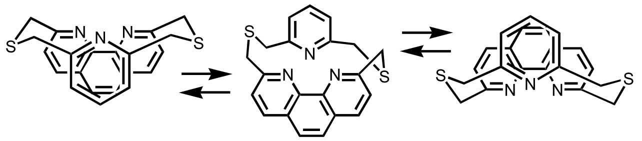

Figure 2. A schematic representation of the interconversion between two *syn*-*cis* conformers of **4** via the intermediate *anti*-*trans* conformer.

[†] Macrocycle **4** was isolated as a yellow solid (0.15 g, 58 %), mp 182–184°C. FT-IR (KBr) 3053–2973 (broad), 2930, 2883, 1588, 1490, 1447, 1393, 1361, 1100, 850, 790, 620 cm^{-1}; *m*/*z* 375 (70%), 374 (18), 342 (100), 341 (180, 308 (40), 238 (55), 208 (30); δ (CD_2Cl_2) 8.19 (d, 2H, *J* 8.2 Hz), 7.73 (s, 2H), 7.70 (t, 1H, *J* 7.5 Hz), 7.69 (d, 2H, *J* 8.2 Hz), 7.63 (d, 2H, *J* 7.5 Hz), 4.06 (s, 4H), 3.40 (s, 4H). Anal. calcd for $C_{21}H_{17}N_3S_2$: C, 67.43; H, 4.66; N, 10.97; S, 16.98. Found: C, 67.17; H, 4.56; N, 11.19; S, 17.08.

Table 2. A comparison of the ^{1}H NMR (500 MHz) spectral data (CD_3OD) of dithiacyclophane **4** and its zinc(II) complex

Cpd	H-14,19	H-15,18	H-16,17	H-5,7	H-6	CH_2[a]	CH_2[b]
4	7.70	8.19	7.73	7.63	7.7[c]	4.12	3.44
Zn complex	8.14	8.85	8.23	7.42	7.87	(3.34, 3.31),[d] (3.31, 3.30)[e]	

[a] Methylene protons adjacent to the phenanthroline ring.

[b] Methylene protons adjacent to the pyridine ring.

[c] Overlaps with signals of H-14,16,17,19.

[d] The inner lines of an AB system; the outer lines are not observable.

[e] An AB system with $J = 1.6$ Hz.

observed, indicating a true fluxional process between the proposed *syn-cis* conformers of **4** (Fig. 2) rather than a conversion from *syn-cis* to *anti-trans* or vice versa. An estimate of the conformational energy barrier for the *syn-cis–syn-cis* interconversion process in **4** was thus calculated on the basis of the data observed for the methylene protons adjacent to the pyridine ring. With the coalescence temperature (T_c) of the signals at 206 K and their measured frequency separation ($\Delta\nu$) and coupling constant of 345 and 15.8 Hz, respectively, the free energy of activation ($\Delta G_c^{\ddagger}$)[9] was estimated to be 36.5 kJ mol^{-1}.

The manganese(II) complex of **4** was obtained as a yellow solid (powder), mp 252–254°C, in 47% yield from the treatment of **4** with $MnCl_2{\cdot}4H_2O$ in methanol. The elemental analysis[‡] of this complex indicates a molecular formula of $MnCl_2{\cdot}$**4**$\cdot 2H_2O$. Although the manganese(II) complex of **4** has an appreciable solubility in methanol, its ^{1}H NMR spectrum shows only weak and broad signals which could not be readily identified and assigned. The manganese(II) ion has an (Ar)$4s^03d^5$ configuration, and d^5 complexes would be expected to be paramagnetic for either high or low spin configuration. High spin Mn(II) complexes normally have tetrahedral co-ordination geometries and are often pale yellow in color. Our observation on the color of the isolated complex and its ^{1}H NMR behavior is thus consistent with a high spin Mn(II) complex. The broad and unresolved ^{1}H NMR spectrum of the complex clearly suggests that **4** must be associated with the metal (on the NMR time scale) thereby resulting in such line broadening.

The zinc(II) complex of **4** was prepared by the reaction of **4** and $ZnCl_2{\cdot}2H_2O$. The product, mp 236–239°C, was isolated as a white solid. Results from the elemental analysis[§] unexpectedly suggest a metal to ligand ratio of 2:1 consistent with **4**$\cdot Zn_2Cl_4$. The ^{1}H NMR spectrum (Table 2) of the zinc(II) complex of **4** is reproducible using samples obtained from separate reactions. The aromatic protons in the zinc complex of **4** could be assigned readily by decoupling experiments and a comparison with the corresponding protons in **4**. The two sets of methylene protons in the zinc complex appear within a range of 0.4 ppm but are only partially resolved. One AB quartet with a small coupling constant of 1.6 Hz is clearly observable. Only the inner lines of the other AB quartet could be identified with the outer lines too weak to be located. The assignment of these AB quartets to the respective sets of methylene protons is, however, not possible. A comparison of the respective aromatic proton chemical shifts (Table 2) indicates more significant shifts of the protons on the phenanthroline ring than those on the pyridine ring in going from **4** to its zinc(II) complex. Only one pair of the methylene protons in the zinc complex has shifted some 0.8 ppm from the chemical shift (δ 4.12) of the methylene protons adjacent to the phenanthroline ring in **4**.

The above observation suggests that the ligand **4** coordinates strongly to the zinc(II) ion only via the two nitrogen atoms in the phenanthroline moiety. The significant downfield shifts of the protons in the phenanthroline ring going from **4** to its zinc(II) complex are consistent with those observed for the zinc(II) complex of **1** having a pentagonal-pyramidal 5-coordination geometry.[2b] Should the nitrogen in the pyridine ring and the two sulphur atoms in the bridges of **4** also participate in coordination in its zinc(II) complex, significant changes in the chemical shifts of the ring protons in pyridine and all methylene protons would be expected. With a preference for the *syn-cis* conformation, the ligand **4** will be unable to employ all five donor atoms to coordinate to a metal ion. This would compel **4** to behave as a bidentate ligand via the phenanthroline moiety.

[‡] The Mn(II) complex was isolated as a yellow solid (47%), mp 252–254°C. FT-IR (KBr) 3055–2960, 3124, 2916, 1626, 1589, 1569, 1497, 1454, 1418, 1405, 1393, 1372, 1219, 1202, 1179, 1147, 1097, 1008, 961, 907, 882, 860, 813, 786, 766, 729, 648, 606 cm^{-1}. Anal. calcd for $C_{21}H_{17}N_3S_2{\cdot}MnCl_2{\cdot}2H_2O$: C, 46.94; H, 3.94; N, 7.82; S, 11.93; Mn, 10.22. Found: C, 46.76; H, 4.05; N, 7.95; S, 11.53; Mn, 9.82.

[§] The Zn(II) complex was isolated as a white solid (93%), mp 236–239°C. FT-IR (KBr) 3319, 3066–2963, 2911, 2831, 2718, 1604, 1593, 1572, 1503, 1458, 1423, 1405, 1373, 1227, 1183, 1174, 1104, 1012, 911, 877, 852, 801, 783, 729, 698 cm^{-1}. Anal. calcd for $C_{21}H_{17}N_3S_2{\cdot}Zn_2Cl_4$: C, 38.92; H, 2.64; N, 6.48. Found: C, 39.27; H, 3.13; N, 6.58.

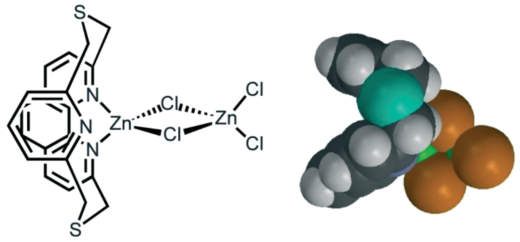

Figure 3. Optimised structure of the preferred minimum of the zinc(II) complex derived from semi-empirical molecular orbital PM3 calculations.

Neither of the Mn(II) and Zn(II) complexes forms satisfactory crystals for X-ray structural analysis. Several examples of dimeric zinc(II) complexes with central bridging oxygen forming a Zn–O–Zn–O four-membered ring have been reported.[10] On the other hand dimeric metal complexes with two central bridging chloride atoms forming a M–Cl–M–Cl four-membered ring are also relatively well known.[11] A recent report on the molecular dynamics simulation of $\mathrm{ZnCl_2}$ solutions suggest formation of clusters which contain more than one zinc with bridging chloride ions.[12] Estimation derived from semi-empirical molecular orbital PM3[8] calculations indicated a strongly preferred minimum for the Zn(II) complex (Fig. 3) isolated in our work. It involves two tetrahedral zinc ions and two bridging chloride atoms. Such a structure would account for the experimental results observed in earlier elemental and ^{1}H NMR analyses although the possibility of a solvated complex such as $\mathbf{4}\cdot(\mathrm{CH_3OH})_n\mathrm{Zn}^{2+}\mathrm{ZnCl_4}^{2-}$ could not be ruled out in the NMR study. Work is in progress to investigate the complexation behavior of **4** with other metal ions with varied ionic radii. The zinc(II) complex of **4** may also exhibit properties similar to reported tetrahedral zinc complexes of biologically important ligands.[13]

Acknowledgements

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