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12,13,25,26-TETRAAZA-2,15-DITHIA[3.3]PHENANTHROLINOPHANE. SYNTHESIS, CONFORMATIONAL STUDY AND COMPLEXATION REACTIONS

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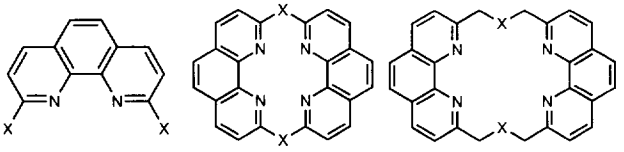
Abstract: 12,13,25,26-Tetraaza-2,15-dithia[3.3]phenanthrolinophane **7** was prepared from a cyclization reaction of 2,9-bis(bromomethyl)phenanthroline **3**. The *syn* isomer of **7** was kinetically favoured while the *anti* isomer was the thermodynamically more stable product isolated. The macrocycle **7** formed 1:1 complexes, namely **10** and **11**, respectively, with zinc(II) and cadmium(II) ions. A tetragonal-pyrimidal configuration is proposed for these complexes. A comparison of the ^{1}H NMR spectral data of **7**, **10** and **11** suggests that the complexation results in a symmetrical structure through the four nitrogen donor atoms. The sulfur atoms in the bridges do not seem to coordinate strongly to the metal ions.

1,10-Phenanthroline **1** forms complexes of great stability with transition metal ions,[1] and has been used for many years as a chelating agent. Reported results in the literature shows that 1,10-phenanthroline is able to stabilise unusual metal ion oxidation states[2] and appears to act as a 'non-innocent' ligand, with considerable electron delocalisation between the metal ion and the nitrogen base system.[3] Many derivatives of **1** have been shown to interact with a long list of cations.[4] The synthesis of several bridged systems (cyclophanes) with two phenanthroline units such as **4**,[9] **5**,[10,11] and **6**[12] have been reported. The length of the bridging chain in these macrocycles is the main factor which affects the hole size and conformation of the molecules thereby leading to different complexation properties. Due to a small hole size and a rigid conformation, the sulphur and nitrogen atoms in the bridges of **4** and **5**, respectively, show no coordinating properties. The conformationally mobile marcocycle **6** was shown to complex to a series of cations. There was, however, also no indication that the two nitrogen atoms in the bridges in **6** could participate in the complexation.

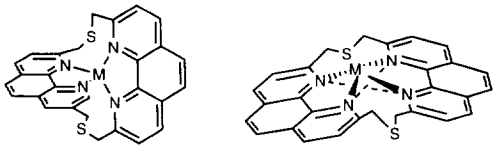
The macrocyclic ligand **7** containing two divalent sulfur in the bridges is expected to experience less steric interactions compared to **6** and thus may exhibit a different conformational behavior. The "isolated" methylene protons in **7** would still be useful in the ^{1}H NMR spectral analysis of the conformation of **7** and its metal complexes. It would also be interesting to study whether the sulphur atoms in **7**, due to a relatively larger hole size and higher conformational mobility, will serve as donor atoms in complexation.

Synthesis and Conformational Study of (7).—Many examples of dithia[3.3]cyclophanes have been prepared from coupling reactions between a bis(bromomethyl)- and a bis(mercaptomethyl)-compound.[13-15] An alternative is a cyclization/dimerization reaction of a bis(bromomethyl)-compound with sodium sulfide.

Preparation of 2,9-bis(bromomethyl)-1,10-phenanthroline **3** from the commercially available 2,9-dimethyl-1,10-phenanthroline **2** has been reported.[16] Our attempt in a cyclization reaction of dibromide **3** with sodium sulphide under high dilution condition[13-15] led to the isolation of **7**.



X		X		X	
1	H	**4**	S	**6**	NHTs
2	CH_3	**5**	NH	**7**	S
3	CH_2Br				



M		M	
twist **7**	Absent	**10**	Cd
8	Cd	**11**	Zn
9	Zn		

The mass spectrum of the product mixture indicates a molecular ion at *m/z* 476 thus supporting the general structure of **7**. The ^{1}H NMR spectrum, however, clearly suggests the presence of two isomers of **7** (Table 1). The product mixture was unstable in air, and slowly decomposed when exposed to light on prolonged standing. Decomposition of **7** was also observed on silica gel and thus all attempts in chromatographic separation were carried out on neutral alumina. Neither of the isomers could, however, be isolated free from the other by chromatography. The macrocycle **7** in fact is expected to exist as the *anti* and *syn* conformers, a conformational behaviour common to many dithia[3.3]cyclophanes.[17] Assignment of the two conformers on the basis of a ^{1}H NMR spectrum of the mixture (Table 1) is, however, not trivial. An attempt to separate the conformers in another sample of the initial product mixture by recrystallization from benzene-methanol unexpectedly resulted in the irreversible conversion of one conformer to another. The thermal conversion could in fact be observed by a separate ^{1}H NMR experiment at a temperature of 50°C although a gradual decomposition of the compound(s) was evident on prolonged heating. Only the conformer with signals at δ 7.74, 7.58, 7.29 and 4.42, m.p. 185-187 °C, was recovered after chromatography.

In isolation, the most stable conformers (also optimizing the most stable conformation for the C-S-C bridges) of *anti* **7** and *syn* **7**, respectively, suggested by our semiempirical molecular orbital PM3[18-20] calculations are illustrated in Figure 1. The *anti* conformer is found to be *ca.* 23.8 kJ mol^{-1} more stable than the *syn* conformer. Another conformer, the *twist* **7** similar to one suggested for **6**,[12] is unlikely to be a stable conformer based on our calculations. Only one conformer was reported for **6** and it was shown to be the *syn* conformer in the solid state.[12] Although their ^{1}H NMR spectra were taken in different solvents, the chemical

shifts reported for *syn* **6** ($(CD_3)_2SO$) and those of the thermodynamically less stable conformer of **7** (CD_3OD) are very similar (Table 1). Our attempts in obtaining crystals of **7** suitable for crystallographic studies were unsuccessful. Nevertheless the above results suggest that the thermodynamically more stable conformer isolated in the synthesis is *anti* **7**. Integration of the respective pairs of signals (Table 1) in the ^1H NMR spectrum of the original product mixture, however, shows a 2:3 ratio of *anti* **7** to *syn* **7**. This suggests that kinetically the *syn* conformer was formed preferentially in the cyclization reaction. The *syn* conformer of many dithia[3.3]cyclophanes[17] was found to be a preferred conformer possibly due to unfavorable torsional strains in the bridges of the corresponding *anti* conformer.[21-23] This factor could account for the initial formation of *syn* **7** kinetically. The stacking of the two phenanthroline in *syn* **7** as illustrated in Figure 1 would, however, experience unfavorable π-π interactions. Thus thermally *syn* **7** is expected to undergo a conformational flipping of one of the phenanthroline ring to afford the thermodynamically more stable *anti* **7**. Protons in *anti* **7** and *syn* **7** are readily assigned (Table 1) on the basis of their splitting patterns and chemical shifts which are similar to those reported for *syn* **6**.[12]

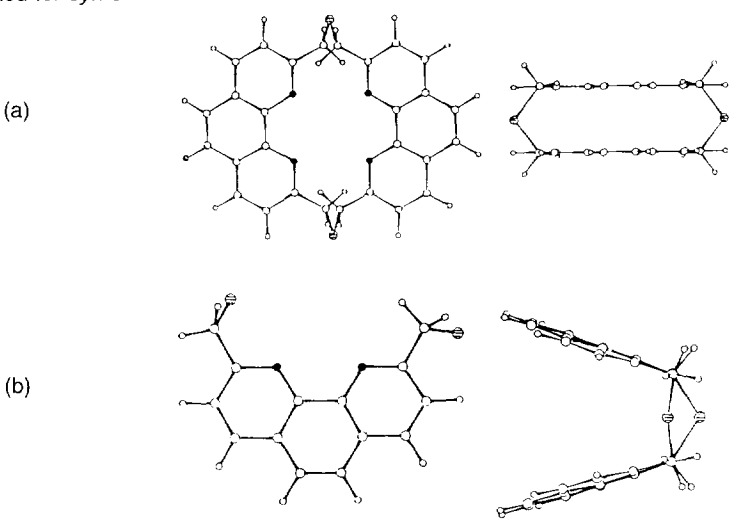


Figure 1. Optimized conformation of (a) *anti* **7** and (b) *syn* **7** derived from semiempirical molecular orbital calculations.

Metal Complexes ***(8)*** *and* ***(9)***. A study of suitable molecular models suggests that conformationally coordination of all four nitrogen atoms to a metal ion in a stacked configuration (Figure 1) of *syn* **7** is considered unlikely. The bridges in **7** are also too short to allow the phenanthroline rings to be orthogonal (*twist* **7**) and form a tetrahedral configuration in a metal complex, such as that shown in **8** and **9**. The two phenanthroline units in *anti* **7** are aligned in a stepped configuration (Figure 1). Its macrocyclic cavity should, however, be sufficiently large to allow the formation of a square plane when the metal ion coordinates symmetrically to all four nitrogen atoms. We have established by ^1H NMR studies that *anti* **7** does not convert to *syn* **7** in solution at room temperature. Thus a study of the complexation reactions of the thermodynamically

more stable isomer of **7** would indirectly help confirm its *anti* stereochemistry.

Reacting *anti* **7** with nicke(II) ion failed to give any isolable product. A reaction[24] carried out by mixing separate solutions of $CdCl_2 \cdot H_2O$ and *anti* **7** in methanol, however, resulted in the formation of a cadmium(II) complex **10** isolated as red solids, m.p. 280-282 °C. The elemental analysis of this complex confirms a metal to ligand ratio of 1:1. A similar reaction between *anti* **7** and $ZnCl_2$ in methanol afforded a zinc(II) complex **11**. Attempts in purifying the complex by recrystallization indicated thermal decomposition of the complex. Results from several elemental analyses suggest a metal to ligand ratio of 1:1 but no single satisfactory analysis (≤0.3%) could be obtained. Selected crystals of the complex, however, showed a consistent melting point of 260-262 °C. The structure of complex **11** is also supported by the similar ^{1}H NMR spectra observed for **10** and **11** (Table 1). Both the complexes **10** and **11** are amorphous powders at room temperature. However, no single crystals of either complex suitable for structural determination could be obtained after many attempts. The complexes were found to be insoluble in water and most common organic solvents, but were slightly soluble in methanol, nitromethane or acetonitrile. Dissolution of the complexes in DMSO was possible but decomposition of the complexes was observed on prolonged standing.

Table 1. ^{1}H NMR chemical shifts for *syn* **6**,[12] *syn* **7**, *anti* **7** and the cadmium and zinc complexes **10** and **11**, respectively.

Compound	H-5,10,18,23[a]	H-6,9,19,22[a]	H-7,8,20,21[b]	CH_2
syn **6**	7.39	7.89	7.36	4.85[b]
syn **7**	7.41	7.82	7.39	4.37[b]
anti **7**	7.58	7.74	7.29	4.42[b]
8	8.17	8.83	8.22	4.0-4.3[c]
9	8.21	8.92	8.31	4.02,[a] 4.15[a]

[a]Part of an AB quartet. [b]A singlet. [c]Unresolved broad signals.

In the FT-IR spectra of **7** and its complexes **10** and **11**, absorption bands in three regions are of particular interests: the out-of-plane bending of the ring C-H bonds at 900-700 cm^{-1}; the skeletal vibrations involving C=C or C=N stretching within the ring at 1600-1400 cm^{-1}, and the aromatic C-H stretching bands at 3100-3000 cm^{-1}. A general trend observed is that the respective absorption bands of the ligand are clearly shifted towards higher frequencies on complex formation. These results are consistent with those reported for a series of coordination compounds.[25-29]

Using Dreiding molecular models of **7**, the distance between two diagonal nitrogen donor atoms is estimated to be about 5.5 Å when the four nitrogen atoms are held planar with minimum deviation. Given the ionic radius of Zn(II) ion (0.74 Å)[30] and a Zn(II)-N bond distance[31] of about 2.1 Å, the central cavity of **7** would be too large for a Zn(II) ion. The phenanthroline units in the zinc(II) complex **11** could, however, be expected to tilt slightly, thus decreasing the cavity size of the ligand **7**, so that the four nitrogen donor atoms form the basic plane of a tetragonal-pyramidal coordination around the zinc(II) ion. Zinc(II) complexes adopting such a configuration have been reported.[32] The ionic radius[30] of M(II) ion and M(II)-N bond distance[31] for Zn(II) and Ni(II) are similar. The failure of **7** in forming a complex with Ni(II) is, however, not understood. With a larger

ionic radius of 0.95 Å,[30] the Cd(II) complex **10** could be expected to adopt a relatively more planar configuration than **11**.

The respective ^{1}H NMR spectral data (Table 1) of the two complexes **10** and **11** are consistent with a symmetrical structure for each complex. The sharp melting point observed for each complex also supports the presence of one single complex with a specific conformation. Going from the free ligand **7** to metal complexes **10** and **11**, the splitting patterns of the aromatic protons (Table 1) are retained but their respective chemical shifts are shifted significantly downfield. This is consistent with the fact that coordination of phenanthroline to an electropositive (electron-withdrawing) metal ion will result in a decrease in electron density in the aromatic system leading to a decreased shielding of the ring protons. The ^{1}H NMR spectra of the aromatic protons of **10** and **11** thus confirms a symmetrical coordination of the four nitrogen atoms to the central metal ion. The methylene protons of **10**, however, appear as a multiplet in the range of δ 4.0-4.3 suggesting some restricted movement of the bridges compared to that in *anti* **7** (a singlet for CH_2). This is further supported by an observed AB quartet for the methylene protons in **11** indicating that the bridges in **11** are likely to be conformationally rigid. Attempts in dynamic ^{1}H NMR studies of these complexes were, however, unsuccessful due to their low solubility in organic solvents and thermal decomposition, particularly the zinc complex **11**, at high temperatures. Going from *anti* **7** to complexes **10** and **11**, a significant deshielding[32] of the methylene protons is expected should the sulfur atoms in the bridges coordinate strongly to the respective metal ions. From the observed ^{1}H NMR data (Table 1) there is no evidence to support the participation of the sulfur atoms as donor atoms in **10** and **11**. Thus the complexes **8** and **9** are believed to involve only coordination of the four nitrogen atoms. At room temperature, the bridges in *anti* **7** are conformationally mobile, those in **10** may experience various degree of restricted pseudorotation while those in **11** are expected to be rigid.

Experimental Section

All melting points are uncorrected. ^{1}H NMR (CD_3OD; 500 MHz), FT-IR and mass (EI; 70 eV) spectra were determined on a Bruker AMX-500, a Perkin Elmer 1725X and a VG Micromass 7035 spectrometer, respectively. Microanalyses were performed by the Microanalytical Laboratory of the Department of Chemistry, National University of Singapore.

*12,13,25,26-Tetraaza-2,15-dithia[3,3]phenanthrolinophane **(7)**.* A solution of the dibromide **3** (0.50 g, 1.37 mmol) in benzene (200 cm^3) and a solution of $Na_2S.9H_2O$ (0.35 g, 1.37 mmol) in water (50 cm^3) and 95% ethanol (150 cm^3) were prepared. These solutions in separate rotaflow dropping funnels were added at the same rate into vigorously stirred 95% ethanol (1 dm^3) under nitrogen over a period of 5 h. The mixture was further stirred for another 15 h and the solvent removed under reduced pressure. The residue was extracted with dichloromethane and the organic layer was dried and evaporated. The residue was preadsorbed onto neutral alumina and chromatographed using dichloromethane as eluent to give a mixture of *anti* and *syn* isomers of **7** (0.33 g, 49%). Recrystallization from benzene and methanol afforded pale red crystals of *anti* **7**, m.p. 185-187 °C; ^{1}H NMR δ 7.74 (d, 4 H, *J* 8.3 Hz, H-5,10,18,23), 7.58 (d, 4 H, *J* 8.3 Hz, H-6,9,19,22), 7.29 (s, 4 H, H-7,8,20,21), 4.42 (s, 8 H, CH_2); MS *m/z* 476 (4), 444 (20), 443 (45), 411 (14), 238 (22), 208 (92), 207 (35); FT-IR (KBr) 2920, 2850, 1670, 1620, 1590, 1550, 1500, 1420, 1390, 1360, 1280, 1200, 1140, 1090, 920, 890, 860, 820, 750 cm^{-1}. Anal. Calcd for $C_{28}H_{20}N_2S_2.2H_2O$: C, 65.60; H, 4.72; N, 10.95. Found: C, 65.10; H, 4.59; N, 10.79. ^{1}H NMR spectrum of *syn* **7** was derived from a comparison of the spectrum of the mixture and that of *anti* **7**: δ 7.81 (d, 4 H, *J* 8.2 Hz, H-5,10,18,23), 7.41 (d, 4 H, *J* 8.2 Hz, H-6,9,19,22), 7.39 (s, 4 H, H-7,8,20,21), 4.37 (s, 8 H, CH_2).

*Cadmium(II) complex **(10)**.* A solution of $CdCl_2.H_2O$ (0.017 g, 0.084 mmol) in methanol (10 cm^3) was added to a solution of *anti* **7** (0.040 g, 0.084 mmol) in methanol. The solution was stirred for 24 h at room temperature. The red solids formed were filtered and recrystallized from methanol to give the complex **10** as pale red crystals

(0.050 g, 58 %), m.p. 280-282 °C; ^{1}H NMR δ 8.83 (d, 4 H, *J* 7.7 Hz, H-5,10,18,23), 8.22 (s, 4 H, H-6,9,19,22), 8.17 (d, 4 H, *J* 7.7 Hz, H-6,9,19,22), 4.0-4.3 (m, 8 H, CH_2); FT-IR (KBr) 3400, 3045, 2965, 2925, 2848, 1619, 1590, 1499, 1430, 1408, 1590, 1559, 1499, 1430, 1366, 1144, 864, 781, 725, 686, 655 cm^{-1}. Anal. Calcd for $C_{28}H_{20}N_4S_2CdCl_2$: C, 50.96; H, 3.05; N, 8.49. Found: C, 50.46; H, 3.54; N, 8.47.

Zinc(II) complex ***(11)***. A solution of $ZnCl_2$ (0.20 g, 0.42 mmol) in methanol (10 cm^3) was added dropwise to a solution of *anti* **7** (0.06 g, 0.42 mmol) in methanol. This mixture was stirred at room temperature for 24 h. The pink solids formed were filtered and recrystallized from methanol to yield the complex **11** as colorless crystals (0.20 g, 77 %), m.p. 260-262 °C; ^{1}H NMR δ 8.92 (d, 4 H, *J* 8.4 Hz, H-5,10,18,23), 8.31 (s, 4 H, H-7,8,20,21), 8.21 (d, 4 H, *J* 8.4 Hz, H-6,9,20,22), 4.15, 4.02 (ABq, 8 H, *J* 14.2 Hz, CH_2; FT-IR (KBr) 3060, 2920, 2850, 1620, 1590, 1570, 1500, 1420, 1370, 1315, 1220, 1150, 1105, 965, 865, 790, 720 cm^{-1}.

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