# Two Kinds of Intermolecular $\pi$ - $\pi$ Interactions Controlling the Crystalline State Structure of 12,13,25,26-Tetraaza-2,15-dithia[3.3]phenanthrolinophane

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The structural characterization of a dithiaphenanthrolinophane was performed. The stable structure in the crystalline state was found to be different from that in solution. The intermolecular face-to-face and edge-to-face $\pi$ - $\pi$ interactions of the aromatic rings play important roles in stabilization of the crystalline state conformation.

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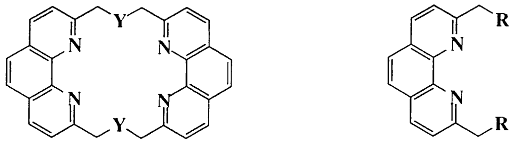
Over the past two decades, macrocyclic compounds have drawn the attention of organic chemists not only for their unique structures but also for their chemical properties.[1] We have also studied the stereochemistry of several kinds of cyclophanes.[2] Recently we prepared dithiaphenanthrolinophane **1** and worked on its conformational analysis in solution and solid states. Very recently, Lai and co-workers synthesized the same compound and reported on its two conformers in solution and complexes with $Cd^{2+}$ and $Zn^{2+}$.[3] Our conformational analysis, however, did not give the same conclusion as theirs, which urged us to report our present data. In this paper we describe the stable structure of **1** in the solid state, which clearly shows two kinds of $\pi-\pi$ interactions. We also showed the most stable solution conformation by comparison of the $^1H$ NMR spectral data for **1** and reference compound **2**.



**1** Y = S
**4** Y = NTs

**2** R = $SCH_3$
**3** R = Cl

**Chart 1**

Dithiaphenanthrolinophane (**1**) was synthesized by coupling 2,9-bis(chloromethyl)-1,10-phenanthroline (**3**)[4] with sodium sulfide in a mixed solvent of methanol and acetone under high dilution conditions in moderate yield.[5] Compound **1** was purified by column chromatography (neutral alumina) and then recrystallized from 1,2-dichloroethane and cyclohexane to give pale brown prisms which were suitable for single crystal X-ray crystallographic analysis.

The precise molecular geometry in the solid state of **1** was obtained by single crystal X-ray crystallography (MAC Science MXC18HF).[6] The ORTEP drawing[7] of **1** with two water molecules is shown in Figure 1 (For clarity one 1,2-dichloroethane molecule was omitted). Clearly, the two phenanthroline rings of compound **1**, $C_i$ symmetric, were antiperiplanar in orientation. It is quite different from the X-ray structure of **4** in which two phenanthroline units are in the *syn* orientation.[8] Hydrogen bonds between the four nitrogen atoms and water hydrogens clearly existed. The distances between water oxygens and phenanthroline nitrogens were 3.113 and 3.364 Å, respectively. The oxygen-oxygen distance of the two water molecules was 4.041 Å.

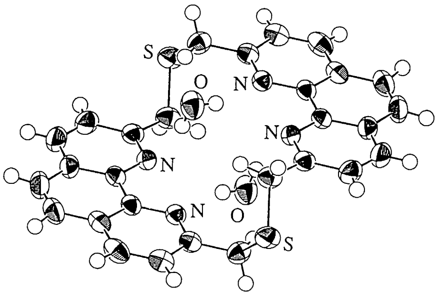


**Figure 1**. ORTEP drawing of $1 \cdot 2H_2O$.

In order to predict the predominant conformation of **1** in solution, AM1 calculations were carried out using the CAChe MOPAC 94 program.[9] Several conformers obtained are shown on the basis of their relative formation energies within 20 kJ/mol in Figure 2. The formation energy of the **S1** structure is 5.52 kJ/mol lower than the second most stable structure **A1**, which has been found in the crystalline state.

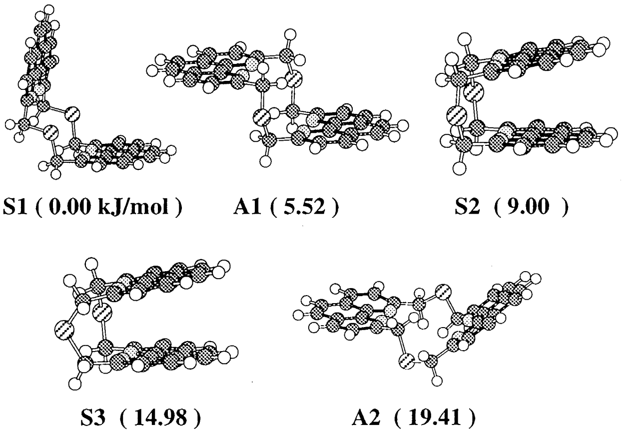

**S1** ( **0.00 kJ/mol** ) **A1** ( **5.52** ) **S2** ( **9.00** )
**S3** ( **14.98** ) **A2** ( **19.41** )

**Figure 2.** Relative energies of the conformers of **1**.

The induced chemical shifts of aromatic hydrogens were formerly used for conformational analysis of a series of cyclophanes.[10] Particularly in the case of short-bridged [3.3]orthocyclophanes, the $^1H$ NMR chemical shift of the bridging methylene hydrogens proved to be a useful probe for assignment of structure.[2] Lai *et al.* used $^1H$ NMR spectroscopy to deduce the presence of *anti* and *syn* conformations in solution. Our conclusions from the $^1H$ NMR spectral data of **1** differed from those of Lai *et al.* and are detailed in the following discussion. The predominant conformation in solution can be determined by examining the relative arrangements of the two aromatic rings, estimated by chemical shift differences between the cyclophane and its reference compound.[2] Table 1 shows the chemical shift values for **1** and **2**. The $^1$H NMR spectral data of **1** showed downfield shifts for the bridging methylene hydrogens and upfield shifts for the aromatic protons comparing to **2**. This result suggests **S1** is the predominant conformer in solution. Only in the **S1** structure, are all four hydrogens of the two bridging methylenes located in the deshielding region of the other phenanthroline ring. Additionally, all the aromatic protons of one phenanthroline are in the shielding region of the other.

**Table 1.** $^1$H NMR Chemical Shifts (ppm in $CDCl_3$)$^a$

| Compound | $CH_2$ | Aromatic | | |
|---|---|---|---|---|
| | | $H_{5,10,18,23}$$^b$ | $H_{6,9,19,22}$$^b$ | $H_{7,8,20,21}$$^c$ |
| **1** | 4.445 | 7.576 | 7.737 | 7.283 |
| **2** | 4.218 | 7.829 | 8.236 | 7.768 |
| $\Delta\delta_{1\text{-}2}$ | 0.227 | - 0.253 | - 0.499 | - 0.485 |

$^a$A minus sign denotes upfield shift. $^b$AB quartet. $^c$Singlet.

To confirm that the **S1** structure is the only stable solution conformer and to analyze the conformational dynamic process, variable temperature $^1$H NMR spectra of **1** were measured at 300 MHz over the temperature range between 163 and 293 K. On lowering the temperature, the sharp singlet of the bridging methylene became broad at 218 K ($T_c$) and then split into an AB quartet pattern below 198 K. Because no chemical shift change or additional signals were observed in the region, the **S1** conformer must be highly populated, and the contribution of other minor conformers is negligible. The rate constant ($k_c$) of the observed conformational interconversion at $T_c$ was calculated as 400 $s^{-1}$. The free energy of activation ( $\Delta G_c^{\neq}$ ) of the conformational dynamic process at coalescence was estimated as 41.8 kJ/mol ($T_c$ = 218 K).[11] From the dynamic behavior, it was confirmed that the **S1** conformation predominates in solution and the conformational dynamic process is due to the rapid interconversion between **S1** and its mirror image by inverting the phenanthroline rings.

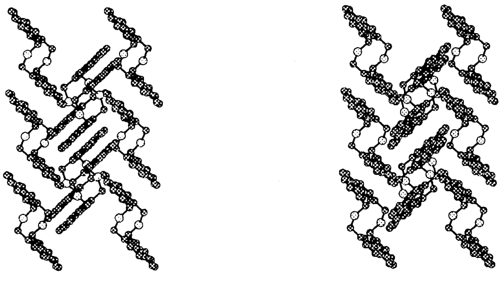


**Figure 3**. Molecular packing diagram of **1** (stereoview).

In order to clarify the reasons for the solid state structure being different from that found in solution, the crystal packing for **1** was studied (Figure 3).[12] The distance between the closest two aromatic rings is 3.48 Å, and the distance between a phenanthroline ring and the hydrogen attached to the perpendicular aromatic ring of another phenanthroline is 3.26 Å. These distances suggest that two simultaneous non-covalent bonding interactions exist, (i) an intermolecular face-to-face $\pi - \pi$ stacking interaction and (ii) an edge-to-face $\pi - \pi$ stacking interaction between intermolecular phenanthroline rings in the crystalline state. Many experimental facts supporting these hypotheses have been found.[13] Since the antiperiplanar oriented **A1** conformation has higher symmetry than **S1**, two kinds of $\pi$ - $\pi$ interactions can exist more effectively. Therefore **A1** becomes more stable in the crystalline state than **S1**.

The structural characterization of dithiaphenanthrolinophane **1** was performed using single crystal X-ray crystallography and nuclear magnetic resonance spectra. The stable solid state structure of **1** was found to be different from the predominant conformer in solution. The difference of their structures was due to the intermolecular $\pi$ - $\pi$ interactions available in the non-solvated crystalline state which make the **A1** conformation more stable than **S1**. Further studies on chelation features of **1** are in progress in our group.

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†† Domestic Research Fellow of Science and Technology Agency.

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5 The compounds **1** and **2** were identified by $^1$H and $^{13}$C NMR spectra, IR and Mass spectra, and elemental analysis.

6 Crystal data for **1**·$2H_2O{\cdot}C_2H_4Cl_2$: $C_{28}H_{20}N_4S_2{\cdot}2H_2O{\cdot}C_2H_4Cl_2$. FW=611.62, monoclinic, $P2_1/n$, $a$=16.286 (5), $b$=8.578 (3), $c$=10.650 (3) Å, β=104.94 (2)°, Z=2, V=1437.5 (8) Å$^3$, R=0.057.

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