Proton Driven Conformational Control of 12,13,25,26-Tetraaza-2,15-dithia[3.3]phenanthrolinophane

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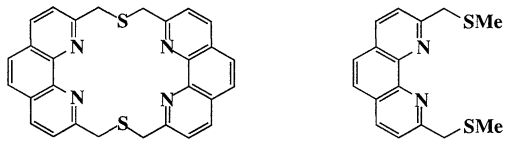
The conformational control of 12,13,25,26-tetraaza-2,15-dithia[3.3]phenanthrolinophane by protonation was accomplished both in solution phase and in the solid state as observed by nuclear magnetic resonance spectra and single crystal X-ray crystallographic analysis, respectively.

Amongst the stereochemical aspects of flexible molecules, which have been of particular theoretical interest for over the past two decades,[1] their conformational control is a most challenging problem.[2] Controlling the conformation of a flexible molecule to adapt a desired structure is a good starting point for the construction of functional molecules. We recently reported that the stable structure of dithiaphenanthrolinophane **1** (Chart 1) in



1 **2**

Chart 1.

the solid state was different from the predominant conformation in solution, originating in two kinds of intermolecular π - π interactions stabilizing the solid state structure,[3] contrasting to the claim by Lai, *et al.* for thermodynamically stable *anti* conformation of the non-protonated form.[4] Here we present that the *synclinal/anti* and *syn* conformational equilibrium of **1** both in solution phase and in the solid state were controlled easily using a proton as the driving force.

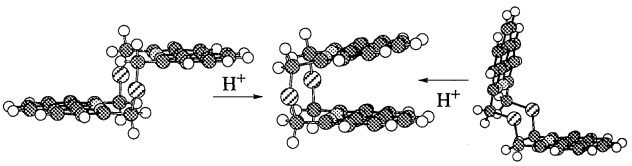
Since there are four aromatic nitrogen atoms in dithiaphenanthrolinophane **1**, it was expected to interact with acids. Then the proton based conformational control for **1** was examined. In order to study the structure of **1** in solution phase, the ^{1}H NMR spectra of both **1** and its reference compound: 2,9-bis(methylthiomethyl)phenanthroline (**2**) were taken in DMF-d_7, and the chemical shifts were represented in Table 1. As shown in Table 1, 0.22 ppm downfield shift from reference compound **2** was observed for bridging methylene hydrogens, while upfield shifts were observed at the aromatic region, suggesting the synclinal structure (**Sc**) was the predominant conformer as discussed previously.[3] To confirm the proton driven conformational change of **1** in solution, the ^{1}H NMR spectra of **1** and **2** after addition of one molar equivalent of hydrochloric acid were also measured (Table 1). Clearly, the aromatic hydrogens of **1** showed much larger upfield shift change from **2** when protonated than in the absence of HCl. This phenomenon suggests that the aromatic hydrogens at one phenanthroline ring received much more ring current effect from the other intramolecular phenanthroline ring (and *vice versa*) when **1** was protonated. This suggested the dihedral angle formed by the two intramolecular phenanthroline rings was reduced compared to that of the **Sc** form, that is the predominant conformer changed to **Syn** as discussed before,[3] in which the two phenanthroline rings became more parallel (Figure 1). This structure can satisfactorily explain the small downfield shift (0.07 ppm) of the bridging methylene hydrogens because of their location. In fact the **Syn** structure determined by ^{1}H NMR spectroscopy is almost identical to that observed by X-ray analysis (*vide infra*) for protonated **1**.

Table 1. ^{1}H NMR chemical shifts (ppm in DMF-d_7)[a]

Compound	CH_2	Aromatic		
		$H_{3,8}$	$H_{4,7}$	$H_{5,6}$
1	4.35	7.79	8.21	7.72
2	4.13	7.88	8.50	8.03
1·HCl	4.48	7.88	8.36	7.77
2·HCl	4.41	8.21	8.96	8.29
$\Delta\delta_{1\text{-}2}$	0.22	-0.09	-0.29	-0.31
$\Delta\delta_{1\text{·HCl-}2\text{·HCl}}$	0.07	-0.33	-0.60	-0.52

[a] A minus sign denotes upfield shift.

In order to confirm whether the **Syn** structure is the only conformation, variable temperature ^{1}H NMR spectra were taken using DMF-d_7 as solvent. When the temperature was lowered from 296 K to 218 K, a 0.04 ppm downfield chemical shift change for the bridging methylene hydrogens was observed. This indicates that the amount of the predominant conformer (**Syn**) increased over the reasonable minor conformer (**Sc**) when lowering the temperature (Table 1). Thus the conformational control of **1** in solution phase is more efficient at lower temperature.



Anti **Syn** **Sc**

Figure 1. Conformational control of **1** by protonation.

Definitive evidence for the proof of conformational control was obtained in the solid state by single crystal X-ray diffraction determination. Dithiaphenanthrolinophane **1** was recrystallized under two different conditions to confirm the conformational control in the solid state. One condition was recrystallization from 1,2-dichloroethane and cyclohexane in the absence of hydrochloric acid and the other condition was dimethyl sulfoxide in the presence of HCl. We present here a different crystal structure of **1**, obtained by recrystallization from dimethyl sulfoxide in the presence of one molar equivalent of HCl in detail.

The X-ray crystal structure analysis of **1**·HCl·3H_2O revealed[5] that the arrangement of two phenanthroline rings of **1** was almost parallel, the molecule was taking on the *syn* form as shown in Figure 2.[6,7] Clearly, the stable crystalline structure of **1** in the presence of HCl was different from that observed previously in the absence of HCl.[3] The orientation of the two phenanthroline rings of **1** changed from *antiperiplanar* to *syn* , showing that the addition of HCl can be a driving force to change the conformation of **1** from *anti* to *syn* form, owing to the high polarity of **1** in the

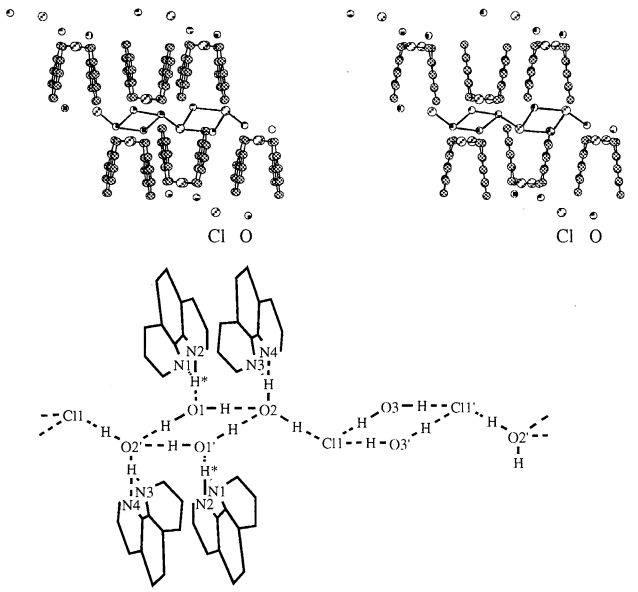


Figure 2. The stereoview of the molecular packing diagram for **1**·HCl·3H_2O (hydrogens were omitted for clarity) (top) and the schematic description of hydrogen bonds (bottom). The distances of selected atom pairs: [N1-O1(O1')]=2.807, [N2-O1(O1')]=3.070, [N3-O2(O2')]=3.176, [N4-O2(O2')]=2.943, [O1-O2']=[O1'-O2]=2.866, [O1-O2]=[O1'-O2']=2.847, [Cl1-O2(O2')]=[Cl1'-O2']=3.213, [Cl1-O3]=[Cl1'-O3']=3.287, [Cl1-O3']=[Cl1'-O3]=3.192 Å.

syn conformation. The closest distances between intra- and intermolecular phenanthroline ring pairs were 3.14 and 3.32 Å, respectively, indicating the presence of both intra- and intermolecular $\pi - \pi$ stacking interactions,[8] while the distance between the closest intermolecular phenanthroline ring pairs in the *anti* conformation was 3.48 Å.[3] Furthermore, Cl^- ion and incorporated water molecules also played important roles in stabilizing the *syn* conformation. Here the hydrogen H*, represented in the bottom of Figure 2, was derived from HCl. As shown in Figure 2, the closest [N-O] distances were 2.807, 3.070, 2.943, and 3.176 Å, respectively, indicating the presence of hydrogen bonds between four nitrogen atoms of one dithiaphenanthrolinophane and two water molecules. These hydrogen bonds connected two folds of **1** in the vertical direction. In the meantime, four water molecules, having hydrogen bonding interactions with each other, were located between two hydrophobic folds to fill out the crystal packing cavity. The [O-O] distances of waters were 2.847 and 2.866 Å, respectively. On the other hand, water molecules also formed hydrogen bonds with chloride ions,[9] filling a cavity formed by the hydrophobic parts of the other dithiaphenanthrolinophanes. The [Cl-O] distances were 3.192, 3.213 and 3.287 Å, respectively. These [O-H···Cl] hydrogen bonds connected phenanthrolinophanes in the horizontal direction (Figure 2).

Thus the conformational control of dithiaphenanthrolinophane **1** was successfully accomplished both in solution phase and in the solid state as observed by nuclear magnetic resonance and single crystal X-ray crystallography, respectively. Control of the conformational equilibrium of **1** by protonation allowed exclusive expression of the *syn* structure in solution and the solid state.

References and Notes

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5 Recrystallization of **1** from Me_2SO in the presence of hydrochloric acid afforded excellent crystals of **1**·HCl·3H_2O which were identified by IR, NMR and elemental analysis.

6 The single crystal X-ray crystallographic analysis was performed on MAC Science MXC18HF of National Institute of Materials and Chemical Research. Positional parameters of all hydrogen atoms were obtained from a difference Fourier map and refined with isotropic thermal parameters.
Crystal data for **1**·HCl·3H_2O: $C_{28}H_{20}N_4S_2$·HCl·3H_2O, FW=567.14, triclinic, $P\bar{1}$, a=11.153 (5), b=11.461 (4), c=11.980 (2) Å, α=72.37 (2), β=79.79 (2), γ=63.13 (4)°, Z=2, V=1300 (1) $Å^3$, D_{calc}=1.45 g cm^{-3}, R=0.070, R_w=0.077.

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