Conformational Properties and Intramolecular Weak Interactions in Substituted Dithia[3.3.1]metacyclophanes

Tetsuji Moriguchi,* Megumi Inoue, Kazunori Sakata, and Akihiko Tsuge*
Department of Applied Chemistry, Faculty of Engineering, Kyushu Institute of Technology, Sensui-cho, Tobata-ku, Kitakyushu 804-8550

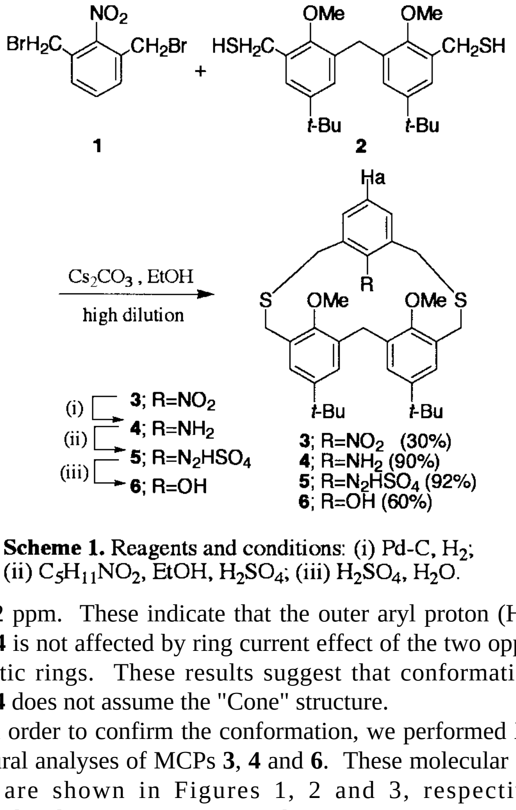
(Received March 26, 2001; CL-010270)

Relationship between conformational properties and intramolecular weak interactions of dithia[3.3.1]metacyclophanes carrying a nitro or an amino group on their inner position was studied by ^{1}H NMR, IR spectra and X-ray structural analyses. It was found out that intramolecular hydrogen-bonding between hydroxy group and one of the methoxy groups or NH–π interaction between amino protons and two opposite aromatic rings exerts a major influence on the conformations of these cyclophanes.

Conformations of medium-sized cyclophane compounds have been attracting many interests to organic and organophysical chemists.[1] [3.3.n]Metacyclophanes (MCPs) are known to assume the "Folded-Inward" or "Cone" conformation depending on their molecular structures.[2] We have reported preparative methods of various kinds of dithia[3.3.n]MCPs and related compounds.[3] We also studied the conformational behaviors by ^{1}H NMR, however, detailed relationship between the conformation and the structure of dithia[3.3.n]MCP is still obscure. In this paper, we report the preparation of dithia[3.3.1]MCPs having an electron-withdrawing or an electron-releasing substituent on their internal positions on one aromatic ring and discuss their conformational properties in terms of intramolecular weak interactions.

2,6-Bis(bromomethyl)nitrobenzene **1** and bis(5-*t*-butyl-3-mercaptomethyl-2-methoxyphenyl)methane **2** were prepared according to the previously outlined procedure.[4] Nitro[3.3.1]MCPs **3**[5] was prepared from **1** and **2** by using high-dilution technique. Nitro[3.3.1]MCP **3** was readily reduced with hydrogen gas in the presence of 10% Pd/C as a catalyst to give amino[3.3.1]MCP **4**[6] in excellent yield (90%). MCPdiazonium salt **5** was prepared and dediazoniated in aqueous media to afford MCP **6**[7] in moderate yield (60%) (Scheme 1). These MCPs prepared above were confirmed by MS and elemental analyses and also characterized by the ^{1}H NMR and IR spectra.

In the ^{1}H NMR spectra, MCPs **3**, **4** and **6** show quite broad peak patterns at room temperature. At 213 K in $CDCl_3$, two couples of two doublets for their bridge protons were appeared. In detail, one of the coupling constant (J = 14.0 Hz) in **3** is the same as the constant in **6**. The other coupling constant (J = 13.7 Hz) has also a similar tendency. On the contrary, MCP **4** exhibits different coupling pattern and coupling constants from those of **3** and **6**. Such differences of the peak patterns and the coupling constants of their bridge protons of MCPs could be affected by the difference in their conformational properties. Outer aryl proton (Ha) of aminoMCP **4** appeared in downfield region (δ = 6.47 ppm) compared with that of nitroMCP **3** (δ = 6.12 ppm). Furthermore, internal NH_2 protons were observed at 3.52 ppm. These indicate that the outer aryl proton (Ha) of MCP **4** is not affected by ring current effect of the two opposite aromatic rings. These results suggest that conformation of MCP **4** does not assume the "Cone" structure.



Scheme 1. Reagents and conditions: (i) Pd-C, H_2; (ii) $C_5H_{11}NO_2$, EtOH, H_2SO_4; (iii) H_2SO_4, H_2O.

In order to confirm the conformation, we performed X-ray structural analyses of MCPs **3**, **4** and **6**. These molecular structures are shown in Figures 1, 2 and 3, respectively. Intramolecular NH–π interaction between two amino protons and opposite two aromatic rings are indicated from the X-ray analyses, which are shown by dotted lines. Conformation of aminoMCP **4** is not "Cone" form but "Folded-Inward" form. Lengths between amino protons and the two opposite aromatic

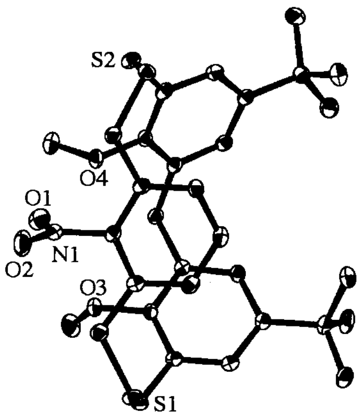


Figure 1. Molecular structure of nitrodithia[3.3.1]MCP **3**. Hydrogen atoms are omitted for clarity.

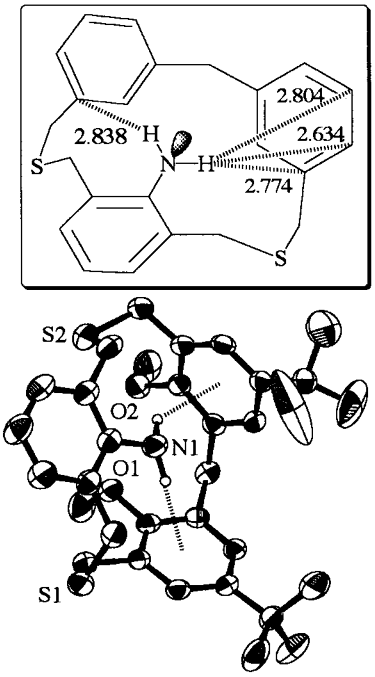


Figure 2. Molecular structure of aminodithia[3.3.1]MCP **4**. Hydrogen atoms are omitted for clarity except for amino protons. NH–π interaction is shown by dotted lines. Distance (Å) between the amino protons and the opposite aromatic carbons in aminodithia[3.3.1]MCP **4** is shown in the column.

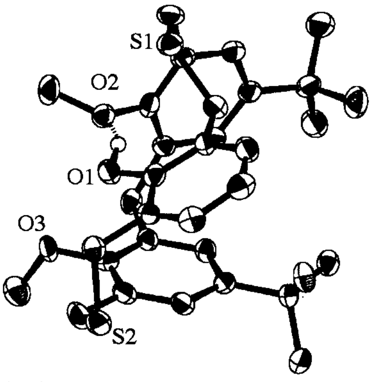


Figure 3. Molecular structure of hydroxydithia[3.3.1]MCP **6**. Hydrogen atoms are omitted for clarity except for hydroxy proton and the hydrogen-bonding is shown by dotted line.

carbon atoms in aminoMCP **4** are also shown in Figure 2. Some of these values are smaller than the sum of van der Waals radii of proton and carbon (2.90 Å). This result strongly suggests existence of two NH–π interaction between the two amino protons and the two opposite aromatic rings in this system.

Interestingly, conformation of hydroxyMCP **6** is "Cone" form. This can be explained by the intramolecular hydrogen-bonding (ca. 1.92 Å) between the hydroxy proton and the oxygen atom of the methoxy group in the opposite aromatic ring restricting the ring inversion of the opposite aromatic ring.

In the IR spectra, wavenumbers of symmetric and asymmetric stretching vibrations of the amino group in aminoMCP **4** appeared at 3432 and 3363 cm^{-1}, respectively. The corresponding vibrations of 2,6-dimethylaniline **7** were observed at 3484 and 3400 cm^{-1}, respectively. Values of MCP **4** are 52 and 37 cm^{-1} smaller than these of **7**. In MCP **6**, vibrational absorption of hydroxy group appeared in 3399 cm^{-1}. This value is also 10 cm^{-1} smaller than that of 2,6-dimethylphenol **8** (3409 cm^{-1}). These results strongly support that weak interactions exist in these structures.

It can therefore be presumed that the conformations of dithia[3.3.1]MCPs are affected by not only the steric hindrance and the electronic properties of the internal substituent but also the intramolecular weak interaction such as NH–π interaction or hydrogen-bonding.

Financial support from Izumi Science and Technology Foundation is gratefully acknowledged.

References and Notes

1 "Cyclophanes," ed. by P. M. Keehn and S. M. Rosenfeld, Academic Press, New York (1983) Vol. I and II; V. Boekelheide, "Topics in Current Chemistry," ed. by F. L. Boschke, Springger-Verlag, Berlin (1987); F. Diederich, "Cyclophanes," The Royal Society of Chemistry, Cambridge (1989); "Monographs in Supramolecular Chemistry," ed. by J. F. Stoddart; The Royal Society of Chemistry, Cambridge (1989), Vol 1; J..M. Lehn, "Supramolecular Chemistry," VCH, Weinheim (1995); "Suplamolecular Control of Structure and Reactivity," ed. by A. D. Hamilton, Weiley, Chichester (1996).

2 T. Otsubo, M. Kitagawa, and S. Misumi, *Bull. Chem. Soc. Jpn.*, **52**, 1515 (1979); M. F. Semmelhack, Y. Thebtaranonth, and L. Keller, *J. Am. Chem. Soc.*, **99**, 959 (1977).

3 K. Böckmann and F. Vögtle, *Chem. Ber.*, **114,** 1965 (1981); A. Tsuge, H. Takeo, H. Kabashima, T. Moriguchi, S. Mataka, and M. Tashiro, *Chem.Lett.*, **1996**, 425.

4 R. H. Mitchell and V. Boekelheide, *J. Am. Chem. Soc.*, **96**, 1547 (1973).

5 Crystal data for **3**: Recrystallized from hexane. $C_{33}H_{41}NO_4S_2$, M_r = 579.81, monoclinic, a = 15.169(4) Å, b = 12.719(7) Å, c = 17.684(3) Å, β = 114.97(1)°, V = 3092.6599 $Å^3$, $P2_1/c$ (#14), Z = 4, D_{calc} = 1.245 g/cm^3, T = 103.2 K, R = 0.058, R_w = 0.069; 6686 unique reflections with $2\theta \leq 55.6°$. Of these, 6076 $I > 2.00\ \sigma(I)$.

6 Crystal data for **4**: Recrystallized from hexane. $C_{33}H_{43}NO_2S_2$, M_r = 549.83, monoclinic, a = 13.415(2) Å, b = 14.115(4) Å, c = 16.489(6) Å, β = 95.63(2)°, V = 5933.9(6) $Å^3$, $P2_1/n$ (#14), Z = 4, D_{calc} = 1.175 g/cm^3, T = 293.2 K, R = 0.063, R_w = 0.114; 4620 unique reflections with $2\theta \leq 60.1°$. Of these, 3433 $I > 3.00\ \sigma(I)$.

7 Crystal data for **6**: Recrystallized from hexane. $C_{33}H_{42}O_3S_2$, M_r = 550.81, monoclinic, a = 11.497(2) Å, b = 16.640(3) Å, c = 15.500(2) Å, β = 94.727(4)°, V = 2955.2(7) $Å^3$, $P2_1/n$ (#14), Z = 4, D_{calc} = 1.238 g/cm^3, T = 93.2 K, R = 0.074, R_w = 0.236; 6093 unique reflections with $2\theta \leq 55.6°$. Of these, 1914 $I > 2.00\ \sigma(I)$. Intensity data for MCP **3** and **6** were collected on a Rigaku RAXIS-4 imaging plate with graphite-monochromatized Mo Kα radiation. Intensity data for MCP **4** were collected on a Rigaku AFC-7R diffractmeter with graphite-mono-chromatized Mo Kα radiation. All structures were solved with teXsan crystallographic software package of Molecular Structure Corporation.