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Metal-Induced Steric Control of Bis-Paracyclophane Conformation

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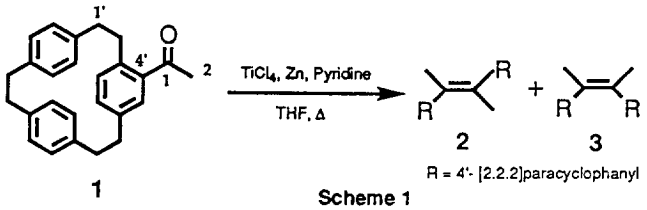
Abstract: Ligand **2** and its bis-silver(I) complexes **4** were investigated by ^{1}H and ^{13}C NMR spectroscopy, X ray crystallography and molecular mechanics calculations. We conclude that **2** adopts a conformation in solution and in the solid state in which the two [2.2.2]paracyclophanyl groups are *syn*, whereas **4** displays an *anti*-conformation.

Supramolecular systems that undergo conformational changes on binding metal ions have attracted attention as enzyme models[1]. In particular, various bis-crown ether derivatives[2], the molecular clips of Nolte[3], the calixarenes of Shinkai[1b] and the bis-pyrazylmethane derivatives of Rodriguez-Ubis[4] share central pivoting elements that allosterically control their complexation properties.

During our investigations of polyenes substituted with π-metal-complexing cyclophane groups on either end, we prepared (*E*)-2,3-bis-4'-[2.2.2]paracyclophanyl-but-2-ene **2**. [2.2.2]Paracyclophane and its derivatives are known to form stable endo-π-complexes with Ag(I)[5] and other metals[6]. We now report that the central *trans*-2-butene linkage of molecule **2** can also function as a pivot when activated by binding of Ag(I) to the [2.2.2]paracyclophanyl groups.



Scheme 1

Compound **2**[7] was prepared in 15% yield together with its (*Z*)-diastereomer **3** (in 22% yield) through McMurry coupling[8] of ketone **1**, itself obtained through Friedel-Crafts acetylation of [2.2.2]paracyclophane[9]. The broad absorption of the methyl groups in its ^{1}H NMR spectrum at 28° C indicated that, in contrast to its diastereomer **3**, compound **2** equilibrates between several distinct conformations which could not be associated with the flexibility of [2.2.2]paracyclophane[10]. Upon cooling to -50° C, this signal was resolved into 2 major and 4 minor signals (Fig. 1). However, signal broadness prevented analysis of the thermodynamic parameters[11]. ^{13}C NMR spectra at 28° C and -10° C gave similar results (Table 1).

Table 1. ^{13}C NMR Shifts of Methyl Protons in Ligand **2** and Complex **4a**[a]

compound	temperature, C	solvent	δ, ppm
2	100	$(CDCl_2)_2$	22.22
2	25	$CDCl_3$ or CD_2Cl_2	no signals visible
2	-10	CD_2Cl_2	22.70, 23.09 (21.24, 21.45, 21.67, 23.46)[b]
4a	25	CD_2Cl_2	23.05
4a	-10	CD_2Cl_2	22.92

[a]: ^{13}C NMR spectra measured at 100 MHz. [b]: Signals of lesser intensity.

The crystal structure of **2**[12] showed a *syn-R,S (S,R)*-conformation of the [2.2.2]paracyclophanyl residues to one another, whereby the primary ring of each [2.2.2]paracyclophanyl residue forms a torsional angle of ca. 107° with the central but-2-ene moiety (Figure 2). The conjunction of these residues forms a hydrocarbon macrocavity, rendering the methyl groups anisotropic. A closer analysis of the molecular geometry is prevented by disorder around the central double bond[13].

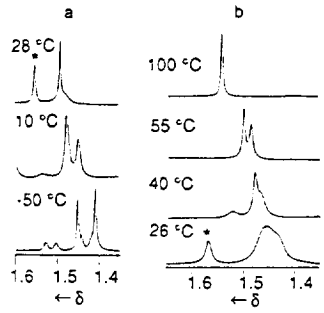


Figure 1. Temperature Dependence of Methyl Signals in ^1H NMR Spectrum of **2**. a: in CD_2Cl_2, b: in $(CDCl_2)_2$, *: Water.

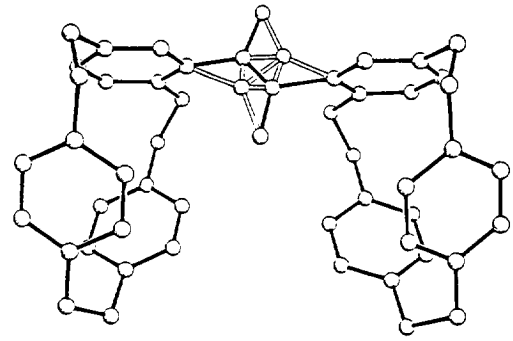
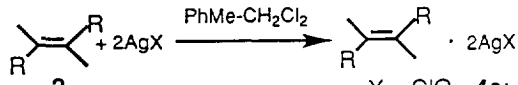


Figure 2. Structure of Bis-[2.2.2]paracyclophane **2**, Showing the two Disorder Components.

These findings were further supported by molecular mechanics calculations[14], which determined an array of most stable conformations having approximate *syn-R,S (S,R)-* or *-R,R (S,S)*-geometry over a 3.7 kJ/mole range. An ideally symmetrical *anti-R,S (S,R)-meso*-conformation was also indicated to be the next most stable and to lie 6.5 kJ/mol above the most stable of the *syn-R,S (S,R)*-conformations. We interpret the appearance of a second singlet in the ^1H NMR spectrum of **2** at 40 to 60° C as evidence of a third conformation present in this temperature range and having this geometry[15]. A single sharp signal did not occur in the ^1H and ^{13}C NMR spectra until ca. 100° C (Fig. 1 and Table 1).

The preparation of the bis-$AgClO_4$-complex of ligand **2**, compound **4a** was accomplished through addition of two equivalents of $AgClO_4$ in toluene to **2** in dichloromethane (Scheme 2). The ^{13}C NMR spectrum of the material obtained after removal of the solvent showed a single resonance from the methyl groups (Table 1) in the -10° to 25° C range, as would be demanded of an *anti-R,S (S,R)-meso*-conformation.



Scheme 2

The bis-$AgSbF_6$-complex **4b** was prepared similarly[16]. After 4 weeks, single crystals formed[12]. The complex **4b** crystallizes in an *anti-R,S (S,R)*-conformation with crystallographic inversion symmetry (Fig. 3). The geometry and site of bonding of silver in **4b** resembles that found in the silver complexes of [2.2.2]paracyclophane[5b]. Ag···C distances vary between 251 and 262 pm, while the metal atom is located 18 pm outside of the cavity edge. Two equivalents of water occur in the crystal and they connect the nearest silver atoms and the two nearest SbF_6 counterions through hydrogen bonding (Ag···O: 251 pm; O···F: 284, 289 pm).

We consider two mechanisms to account for the conformations of ligand **2** and bis-complex **4**. Binding of Ag(I) stiffens the [2.2.2]paracyclophanyl ring system[17]. Thus, the formation of **4** could be accompanied by steric repulsion between the inner rim of the [2.2.2]paracyclophanyl and the geminal methyl group, thereby forcing an *anti*-conformation. Electrostatic repulsion between the two Ag cations could also be responsible: An Ag···Ag - distance of 1056 pm is observed in **4b**. For a *syn-R,S (S,R)*-conformation, this distance would be ca. 960 pm (calculated from the structure of **2**). This corresponds to a potential difference of 14 kJ/mol[18].

The differentiation between these effects and their application to further "switchable" macrocavities will be the subject of future investigations.

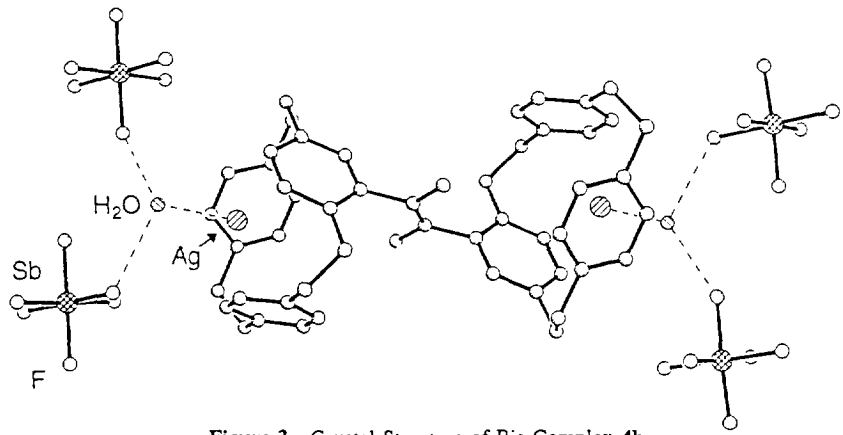


Figure 3. Crystal Structure of Bis-Complex **4b**.

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7. The separation of isomers **2** and **3** was accomplished through column chromatography (silica gel, 1:2-dichloromethane:hexane) followed by repeated plate chromatography (Kieselgel 60/Merck, eluent: 10:90-chloroform:cabontetrachloride). Compound **2**: m.p. 204.5-205.4°; EI-MS (70 eV): m/z (%) = 676 ($M^{+\cdot}$, 100%), compound **3**: m. p. 202.4-204.0; the properties of **3** will be reported later. Both isomers were characterized by ^{1}H and ^{13}C NMR, IR, UV and EI MS spectroscopy and elemental analysis.

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11. ^{1}H-^{1}H-spin-spin-coupling-experiments at -20° C showed only exchange between the major and the minor signals.

12. Crystal data: **2**: $C_{52}H_{52}$, $P2_1/c$, a = 1699.0(5), b = 989.5(4), c = 2383.6(6) pm, β = 101.68(3)°, Z = 4, λ(Mo $K\alpha$) = 71.073 pm, T = -120° C, 6869 reflections, program SHELXL-93 (G.M. Sheldrick, University of Göttingen) $wR(F^2)$ 0.356, $R(F)$ 0.109, 471 parameters. **4b**: $C_{52}H_{56}Ag_2F_{12}O_2Sb_2$, $P2_1/n$, a = 1319.4(3), b = 1373.0(4), c = 1414.6(4) pm, β = 94.44(3)°, Z = 2, T = -100° C, 4499 reflections, $wR(F^2)$ 0.145, $R(F)$ 0.047, 317 parameters. Details of the structure determinations have been deposited at the Fachinformationszentrum Karlsruhe, Gesellschaft für Wissenschaftlich-technische Information mbH, D-76344 Eggenstein-Leopoldshafen, Germany, with deposition numbers CSD 380074 (**2**), 380075 (**4b**).

13. Similar situations arise for other derivatives of (*E*)-α,α'-dimethylstilbene: Ogawa, K.; Sano, T.; Yoshimura, S.; Takeuchi,Y.; Toriumi, K. *J .Am. Chem. Soc.*, **1992,** *114,* 1041-1051, Finder, C. J.; Newton, M. G.; Allinger, N. L. *Acta Cryst.*, **1974,** *B30*, 411-414.

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15. The absorption of traces of water in this region of the ^{1}H NMR spectrum of **2** prevented an analysis of the Arrhenius-parameters of this process.

16. Compound **4b**: m.p. 240-260 °C (dec); satisfactory ^{1}H and ^{13}C NMR, IR, FAB MS spectra and elemental analysis (C, H) for the dihydrate were also obtained.

17. The aromatic rings and ethylenic bridges of **2** and related compounds appear in their ^{1}H NMR spectra as broad and formless bands at 25° C and as distinct AB- and AA'-spin systems in the corresponding $AgClO_4$-complexes. Contrast to *allosterically* impeded molecular brakes: Kelly, T. R.; Bowyer, M. C.; Bhaskar, K. V.; Bebbington, D.; Garcia, A.; Lang, F.; Kim, M. H.; Jette, M. P. *J. Am. Chem. Soc.*, **1994**, *116*, 3657-3658.

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