NMR Study of Pressure Effect on the Hindered Rotation in *cis*-1,12-Disubstituted[12]paracyclophanes

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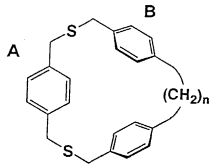
Effect of hydrostatic pressure on the rate of internal rotation of title compounds has been examined by DNMR method. A quartz high-pressure NMR cell was used to realize the high-pressure experiment up to 300 MPa. The rate of internal rotation, ln *k* was found to increase linearly up to 300 MPa.

Dynamic conformational behavior represents one of the most intriguing aspects of cyclophane chemistry and has been studied intensively by a DNMR method with the solvent and the temperature as the variables.[1] To our knowledge, however, only a few NMR studies at high pressure have so far been reported of this type of compounds, where interest has been restricted mainly to the pressure effects on *static* behaviors.[2] Because of a conformational flexibility arises from the macrocyclic structure, an application of hydrostatic pressure may possibly give rise to a pressure induced change in the molecular characteristics in various ways. We report here the first example of a high-pressure, high-resolution *DNMR* (HPHR-DNMR) study of cyclophane molecules,[3] in which our interest was focused to the effect of increased hydrostatic pressure on the internal rotation of the title compounds.

Our previous HPHR-NMR study on 2,11-dithia[3.3.n]-paracyclophanes (n = 1,2) (**1**) has shown that proton chemical shift for the benzene ring **A** exhibits a notable high-field shift upon pressurization (+8 ~ +9 Hz at ν_0 = 100 MHz/ΔP = 150 MPa), while the ring protons of the ring **B** give a low-field shift (−4 ~ −5 Hz).[2a]



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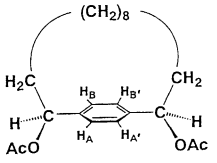

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Reduction of a partial volume under high pressure, being effected by changes in the dihedral angles accompanying some contraction of the macrocyclic structure, was considered to be responsible for the abnormal pressure chemical shifts. For the *cis*-1,12-disubstituted [12]paracyclophanes, our preliminary experiments at 1 atm have shown that a change in ring size of the methylene bridge by one CH_2 group alters the rotation rate by a factor larger than 10^2 ~ 10^3. Thus the pressurization was supposed to induce a slowdown of the rotation because it expectedly causes contraction of the ring structure as it was inferred in the case for the thiacyclophane system.[2a]

HPHR-NMR measurements were conducted on a Jeol FX-90Q spectrometer at 83 °C and at 105 °C. The temperatures were calibrated by the chemical shift of ethylene glycol[5] in a glass cell similar in shape and size to the one employed in the high-pressure experiment. A solution consisting of 6 mol% of the *cis*-1,12-diacetoxy compound,[6](**2**) 5 mol% of 1,1,2,2-tetrachloroethane, and 89 mol% of 1,1,2,2-tetrachloroethane-d_2 was introduced into a CSX type[7] *quartz* high-pressure cell with o.d./i.d. = 2.7 mm/0.8 mm and with a length 23 mm (shoulder to shoulder), having a long capillary tail.

The 1,1,2,2-tetrachloroethane was used as a reference to monitor the resolution of proton spectra. At each measurement, time averaging of 100 scans was made with the external NMR lock field control. For the *cis*-1,12-dihydroxy compound, a 0.6 mol% solution in the same solvent was measured with time averaging of 500 scans.

Since coupling constants, J_{AB} and $J_{AB'}$ are negligibly small as compared with the chemical shift $\Delta\delta_{AB}$ (= $\Delta\delta_{AB'}$), a very simple resonance pattern of the ring protons (only two singlet peaks, an AB pattern with J_{AB} = 0) was observed.[4] Upon warming, the benzene ring is beginning to rotate rapidly through the loop of the polymethylene bridge so that the sets of protons ($H_AH_{A'}$ and $H_BH_{B'}$) are rendered to be indistinguishable on NMR time scale.

Figure 1 (b) shows pressure dependence of the ring proton signal of the diacetoxy compound (**2**) at 105 °C. Their simulated spectra are shown in Figure 1 (a), where the simulations[10] were made assuming the AB pattern with J_{AB} = 0.[4]

Clearly, increasing pressure accelerates the rotation of the benzene ring. For the *cis*-1,12-dihydroxy compound,[6] the obtained result was qualitative one, because of a low S/N ratio

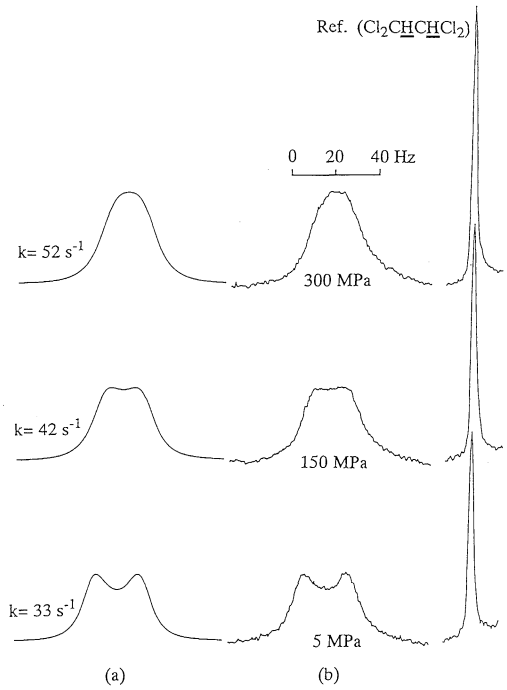

Figure 1. Pressure dependence of the ring proton signal at 105 °C. Simulated (a) and observed (b) spectra. The chemical shift differences, $\Delta\delta_{AB}$, are 25.0 Hz, 24.0 Hz, and 23.5 Hz at 5 MPa, 150 MPa, and 300 MPa, respectively.[8]

of the ring proton signal. It can be said, however, that the pressure also accelerates the rotation. All these results are contrary to our expectation. For the moment, the following pictures are considered to provide tentative interpretations for the present observations.

A contribution of a negative activation volume plays an important role in increasing the rotational rate at high pressure, a contribution from the pressure-induced distortion (a contraction of the ring size) being negligible. If we assume that the pressure effect is attributed only to the activation volume, $\Delta V^{\ddagger}$ = difference in partial molar volume between ground and transition states,[11] the data can be fitted to the well known equation.

$$d\ln k/dP = -\Delta V^{\ddagger}/RT$$

The approximately linear relation between ln k and pressure as shown in Figure 2 gives $\Delta V^{\ddagger} = -6 \sim -7$ cm^3 mol^{-1} at 105 °C, which means that the partial molar volume of the transition state is smaller than that of the ground state. The high-pressure experiment at 83 °C was found to give a similar result ($\Delta V^{\ddagger} = -5 \sim -10$ cm^3 mol^{-1}).

These negative $\Delta V^{\ddagger}$'s are attributed to the considerable difference in geometry of this molecule between ground and transition states of the rotating process:

(i) In the ground state, the molecule should have a non-planar geometry, where the methylene bridge is perpendicular to the benzene ring. This non-planar shape is considered to be unfavourable to a tight packing with the solvent molecules.[2b,13] This leads to a larger partial molar volume, contributing to produce a negative activation volume.

(ii) In the transition state, a void space inside the methylene bridge is occupied by about a half of the benzene ring, so that the intrinsic molecular volume is reduced. The resulting almost planar molecular shape is considered to facilitate a tight packing with the solvent molecules, which again gives rise to a smaller molar volume. A pressure-induced increase in polarity of the solvent molecule may lead to a strengthened solvation of the transition state molecule. These contribute to produce the negative activation volume.

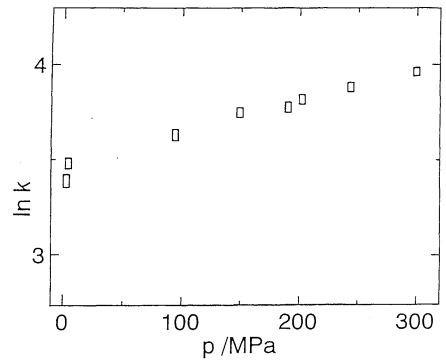

Figure 2. Pressure effect on rate of internal rotoation of *cis*-1,12-Diacetoxy[12]paracyclophane at 105 °C.

These explanations are, however, not conclusive at the present stage. Further experiments at various conditions (pressure, solvent, temperature) are needed before we can provide clearer understanding of the pressure effects.

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References and Notes

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3 The first DNMR study of *cis*-1,12-disubstituted[12]paracyclophanes at 1 atm has been reported by Nakazaki et al.[4]

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8 A similar pressure dependence of $\Delta\delta_{AB}$ is noted in the experiments at lower temperatures. For example, at 27°C: 23.4 Hz, 22.0 Hz, and 20.8 Hz at 5 MPa, 150 MPa, and 300 MPa, respectively.

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