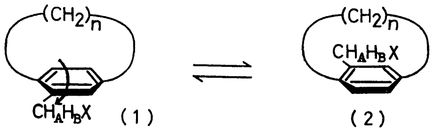
BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 45, 1562—1564(1972)

Hindered Rotation in [12]Paracyclophanes[1)]

Masao Nakazaki, Koji Yamamoto, and Susumu Okamoto
Department of Chemistry, Faculty of Engineering Science, Osaka University, Toyonaka, Osaka

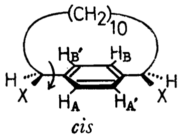
(Received October 19, 1971)

In our preceding communication,[2)] we examined the rates of internal rotation of the benzene rings in a series of [*n*]paracyclophane derivatives with CH_2X side chains on the benzene nucleus, by taking advantage of the phenomenon that the diastereotopic methylene protons (H_A, H_B) become indistinguishable on rapid interconversion between the conformational enantiomers (**1**), (**2**) on NMR time scale.



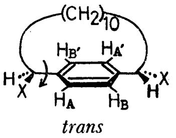
(1) (2)

In this communication, we report an NMR analysis of the hindered rotation in [12]paracyclophane deirvatives (**3**), (**4**) with substituents on benzylic positions of the bridges.



cis

(3) a,X=Br
b,X=OAc
c,X=OH



trans

(4) a,X=Br
b,X=OAc
c,X=OH

Bromination of [12]paracyclophane[3)] with *N*-bromosuccinimide in carbon tetrachloride afforded a mixture of dibromides which could be separated by recrystallization from *n*-hexane into *cis*-1,12-dibromo[12]paracyclophane (**3a**), mp 172—173°C and *trans*-1,12-dibromo[12]paracyclophane (**4a**), mp 155—156°C. Each of these dibromides was converted into the *cis*-diacetate (**3b**), mp 64—65°C and the *trans*-diacetate (**4b**), mp 82—83°C. Alkaline hydrolysis of the diacetates (**3b**) and (**4b**) gave the *cis*-diol (**3c**), mp 180—181°C and *trans*-diol (**4c**), mp 174—175°C respectively.

Their *cis*- and *trans*-configurational assignments are based on the following observations of their NMR spectra[4)] (Fig. 1, 2).

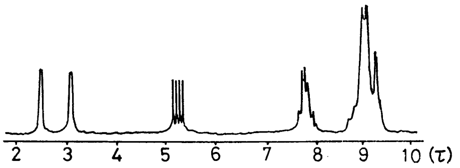


Fig. 1. 100-MHz NMR spectrum of *cis*-1,12-dibromo[12]-paracyclophane (**3a**) in CS_2 at +42°C.

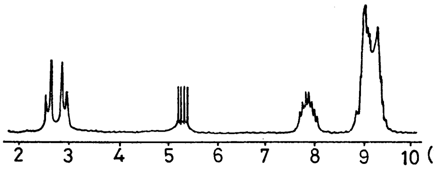


Fig. 2. 100-MHz NMR spectrum of *trans*-1,12-dibromo[12]-paracyclophane (**4a**) in CCl_4 at +25°C.

The *cis*-dibromide (**3a**) has C_s symmetry and its aromatic protons can be grouped into two enantiotopic pairs, $H_A/H_{A'}$ and $H_B/H_{B'}$, and the stereochemical

---

[1)] Presented in part before the 22nd Annual Meeting of the Chemical Society of Japan, Tokyo, March, 1969.

[2)] M. Nakazaki, K. Yamamoto, and S. Okamoto, *Tetrahedron Lett.*, **1969**, 4597.

[3)] D. J. Cram and H. Daeniker, *J. Amer. Chem. Soc.*, **76**, 2743 (1954); D. J. Cram, N. L. Allinger, and H. Steinberg, *ibid.*, **76**, 6132 (1954).

[4)] NMR spectra were taken on a Nucleomagnetic Resonance Spectrometer, JNM-4H-100, Japan Electron-Optics Laboratory Co., Ltd.

relationship between H_A and $H_{B'}$ (or between $H_{A'}$ and H_B) is diastereotopic.

C_2 symmetry of the *trans*-isomer (**4a**) generates two homotopic pairs $H_A/H_{A'}$ and $H_B/H_{B'}$: all the stereochemical relationships between these pairs in turn are diastereotopic.

Being proximate to the bromine atoms, the protons H_A and $H_{A'}$ are expected to be more heavily deshielded than H_B and $H_{B'}$ in both *cis*- and *trans*-dibromides. From their molecular geometries, the chemical shift difference between the diastereotopic set of protons H_A and H_B of the *cis*-isomer (**3a**) is expected much lager than that of the *trans*-isomer (**4a**). This consideration suggests that the dibromide (mp 172—173°C) with larger chemical shift difference (0.6 ppm) has the *cis*-configuration, and another dibromide (mp 155—156°C) exhibiting smaller chemical shift difference has the *trans*-configuration. This conclusion is further supported by their coupling patterns. In the *cis*-dibromide, it is safe to assume that the coupling constants $J_{AB}(para)$ and $J_{AB'}(meta)$ are negligibly small, and the same is also true for the coupling constants within the enantiotopic pairs, *i.e.* $J_{AA'}\approx 0$, $J_{BB'}\approx 0$. And these degeneracies explain a surprisingly simple resonance pattern of the *cis*-compound in aromatic region, which is otherwise expected to show a rather complicated AA′BB′ pattern. In the same token, AA′BB′ type[5] of spin coupling pattern in the *trans*-dibromide (**4a**) is reduced to become resemble a simple AB quartet due to the relatively large magnitudes of *ortho*-coupling constants (J_{AB}, $J_{A'B'}$) and negligibly small coupling constants between the protons in *para* and *meta* positions ($J_{AB'}\approx 0$, $J_{AA'}\approx 0$).

On warming, the benzene nucleus of the *cis*-dibromide (**3a**) becomes to rotate through the loop of the polymethylene bridge rendering the diastereotopic sets of protons ($H_AH_{A'}$ and $H_BH_{B'}$) indistinguishable on NMR time scale.

Figure 3 shows typical temperature dependence (71—148°C in diglyme) of the NMR spectrum in aromatic region of the *cis*-dibromide (**3a**), together with the calculated spectra generated for a range of values of the pre-exchange life time τ using the density matrix procedure,[6] in which approximation that all coupling constants are zero was made.

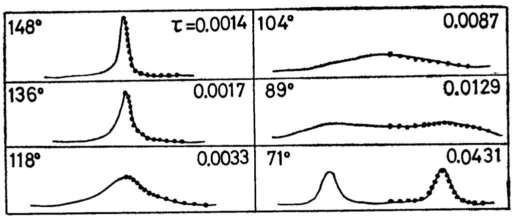


Fig. 3. Observed (——) and calculated (……) spectra for the aromatic protons of *cis*-1,12-dibromo[12]paracyclophane (**3a**) as a function of temperature. (Solvent: diglyme)

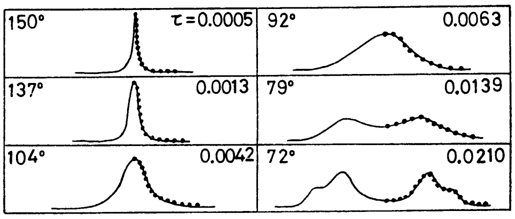


Fig. 4. Observed (——) and calculated (——) spectra for the aromatic protons of *trans*-1,12-dibromo[12]paracyclophane (**4a**) as a function of temperature. (Solvent: hexachloro-1,3-butadiene)

Also, in aromatic region of the *trans*-dibromide (**4a**) (in hexachlorobutadiene), the quartet changes to a broad doublet at 79°C, then coalesces into a broad singlet at 92°C which further transforms into a sharp singlet in higher temperature. In Fig. 4 are shown this temperature dependent NMR spectra with their calculated spectra which were computed on the approximation $J_{AB'}=0$ and $J_{AA'}=0$.

TABLE 1. COUPLING CONSTANTS AND CHEMICAL SHIFTS USED IN VARIABLE-TEMPERATURE ANALYSIS

Compd	Sol-vent	Temp. range (°C)	δ_{AB} (Hz)	J_{AB} (Hz)	T_c (°C)	E_a (kcal/mol)
(**3a**)	c	20—159	50.5		104	12.8±0.8
	b	18—160	56.0		105	13.2±0.5
(**3b**)	c	19—158	29.7		113	13.1±0.6
	b	20—155	28.0		111	12.6±0.5
(**3c**)	c	21—161	55.0		136	18.5±1.0
(**4a**)	c	16—157	32.4	7.8	76	13.1±0.5
	a	15—160	33.8	8.1	79	13.4±0.4
(**4b**)	c	15—163	7.7	8.5	92	12.2±0.4
	a	14—151	10.8	8.4	91	12.8±0.6
(**4c**)	c	17—160	28.6	9.2	139	18.1±0.8

E_a: Arrhenius activation energy; T_c: coalescence temperature a: hexachloro-1,3-butadiene; b: nitrobenzene-d_5; c: diglyme

Arrhenius plots of these data afforded E_a listed in Table 1, which also lists the chemical-shift differences and coupling constants employed in these calculations. From Table 1, it is clear that each pair of *cis*- and *trans*-isomers shows relatively small differences in their activation energies of internal rotation. Remarkably high activation energies found in the *cis*-diol and *trans*-diol should be ascribed to intermolecular hydrogen bonds.

Experimental

cis-1,12-Dibromo[12]paracyclophane (3a) and trans-1,12-dibromo[12]paracyclophane (4a). A mixture of 5 g of [12]-paracyclophane,[3] 7.7 g of *N*-bromosuccinimide, and 1400 m*l* of carbon tetrachloride was refluxed for 10 hr. The warm solution was filtered to remove succinimide, and evaporated to dryness. The residue was refluxed for 3 hr with 200 m*l* of *n*-hexane, and the undissolved white solide was recrystallized 3 times from *n*-hexane–benzene to give 4.8 g (58%) of the *cis*-dibromide **3a**, mp 172—173°C. Found: C, 53.68; H, 6.50; Br, 39.80%. Calcd for $C_{18}H_{26}Br_2$: C, 53.75; H, 6.51; Br, 39.74%.

Evaporation of mother liquor gave a residue which was

---

[5] These unique AA′BB′ spin systems around a benzene nucleus are peculiar to these rather queer benzene derivatives with C_s and C_2 symmetry respectively.

[6] C. S. Johnson, Jr., *Advan. Magnetic Resonance*, **1**, 35 (1965). These calculated spectra were made up with the aid of a program written for NEAC-2200 Computer, Osaka University Computation Center.

recrystallized 4 times from *n*-hexane to give 0.6 g (7%) of the *trans*-dibromide **4a**, mp 155—156°C. Found: C, 53.61; H, 6.55; Br, 39.83%. Calcd for $C_{18}H_{26}Br_2$: C, 53.75; H, 6.51; Br, 39.74%.

cis-*1,12-Diacetoxy[12]paracyclophane (3b).* A mixture of the *cis*-dibromide **3a** (0.5g), 0.5 g of sodium acetate, and 5 m*l* of acetic acid was refluxed for 16 hr. The warm mixture was filtered to remove sodium bromide, and the filtrate was evaporated *in vacuo*. The residue was cooled, diluted with water, and extracted with ether. The ether layer was washed with water, diluted sodium bicarbonate, and water. The solution was dried, evaporated, and the residue was recrystallized 2 times from *n*-hexane to give 0.33 g (73%) of **3b**, mp 64—65°C. Found: C, 73.18; H, 8.88%. Calcd for $C_{22}H_{32}O_4$: C, 73.30; H, 8.95%.

cis-*1,12-Dihydroxy[12]paracyclophane (3c).* To a solution of 0.7 g of potassium hydroxide in 6 m*l* of ethanol was added 0.25 g of the *cis*-diacetate **3b**, and the mixture was refluxed for 10 hr. The reaction mixture was poured into 20 m*l* of water and extracted with chloroform. The chloroform layer was washed with water, dried and evaporated. The residual solid was recrystallized 3 times from benzene to give 0.11 g (57%) of **3c**, mp 180—181°C. Found: C, 78.08; H, 10.18%. Calcd for $C_{18}H_{28}O_2$: C, 78.21; H, 10.21%.

trans-*1,12-Diacetoxy[12]paracyclophane (4b).* Reaction of the *trans*-dibromide **4a** (0.5 g) with sodium acetate was carried out in a manner similar to that described for the preparation of *cis*-diacetate **3b**. Recrystallization from ethanol gave 0.32 g (71%) of **4b**, mp 82—83°C. Found: C, 73.43; H, 8.92%. Calcd for $C_{22}H_{32}O_4$: C, 73.30; H, 8.95%.

trans-*1,12-Dihydroxy[12]paracyclophane (4c).* Alkaline hydrolysis of 0.25 of the *trans*-diacetate **4b** was carried out in a manner similar to the preparation of *cis*-diol **3c**. Recrystallization from benzene gave 0.12 g (63%) of **4c**, mp 174—175°C. Found: C, 78.11; H, 10.19%. Calcd for $C_{18}H_{28}O_2$: C, 78.21; H, 10.21%.