200 BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 44, 200—203(1971) [Vol. 44, No. 1

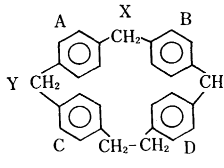
Macro Rings. III[1,2]. The Synthesis of [2. 1. 1. 1]Paracyclophane

Toshio KAWATO,[3] Takahiko INAZU, and Tamotsu YOSHINO
Department of Chemistry, Faculty of Science, Kyushu University, Hakozaki, Fukuoka

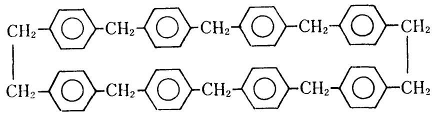
(Received July 20, 1970)

Two new macrocyclic compounds, I and II, which incorporate, respectively, four or eight benzene rings and intervening methylene bridges attached to their *para* positions, were synthesized. The UV, IR, and NMR spectra of these paracyclophanes were compared with a corresponding open-chain compound, III.

Some paracyclophanes have been shown to have interesting characteristics compared with an open-chain analog because of the interaction of the π-electrons of adjacent benzene rings. An interesting characteristic of forming charge-transfer complexes and clathrate compounds may be expected, especially in a cyclophane in which the planes of benzene rings assume such a perpendicular configuration with each other as to form a square prism. The synthesis of [2.1.1.1]paracyclophane I was thus undertaken.



[2.1.1.1]Paracyclophane I
Formula 1

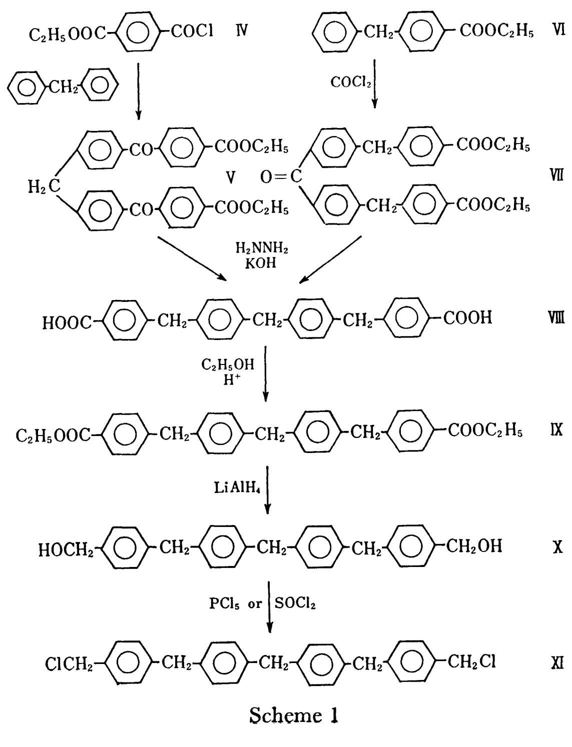


[2.1.1.1.2.1.1.1]Paracyclophane II
Formula 2

As is shown by a Dreiding molecular model of the paracyclophane I, four benzene rings are situated in planes so as to form a slightly deformed square prism whose respective parallel planes are slightly inclined to each other, and four pairs of adjacent benzene rings are connected by an ethylene and three separate methylene bridges, involving a slight strain in the valence angle of each methylene carbon and a slight warp in the planes of the benzene rings. The molecular model also shows that the [2.1.1.1]paracyclophane molecule should exist in the form of two nonsuperposable mirror-image conformers due to the pair of skew conformations of the 1,2-diphenylethane moiety in the macro ring.

A pair of such enantiomeric conformers appear to be interconverted so rapidly at an ordinary temperature by a flip that, because of the equalization of the shielding effects, the signals of the ethylene protons merge into one sharp peak, as will described later, in the NMR spectra. Judging from an inspection of the model of the cyclophane, I, the rocking motion of the benzene ring may be possible, but complete rotation about the para axis is considered to be extremely difficult. In the paracyclophane, II, the situation is quite different. The molecule may be free from strain and the macro ring may be so sufficiently flexible that the benzene rings in it may rotate about the para axis. This difference seems to be associated with the difference between the NMR spectra.

The synthetic routes are shown in Schemes 1 and 2. Diphenylmethane and ethyl *p*-chloroformylbenzoate IV were treated with anhydrous aluminum chloride to give a diketo diester, V. The carbonyl groups of V were then reduced by the Huang-Minlon modification of the Wolff-Kishner reduction to give a dicarboxylic acid, VIII, which was then esterified to give a diester, IX. The diester, IX, was also obtained by the Friedel-Crafts acylation of ethyl *p*-benzylbenzoate and phosgene and by subsequent Wolff-Kishner reduction and esterification. The diester, IX, was reduced with lithium aluminum hydride to a diol, X, which was then treated with phosphorus pentachloride or thionyl chloride to obtain a dichloro compound, XI. The *para*-substituted structures of Compounds V, VIII, IX, X and XI were



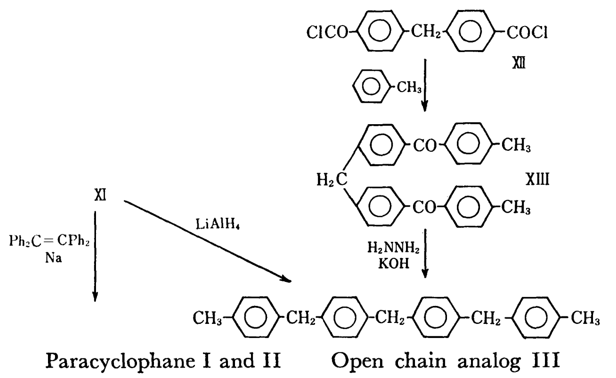
Scheme 1

---

1) Part II of this series: T. Inazu and T. Yoshino, This Bulletin, **41**, 652 (1968).

2) Presented at the 23rd Annual Meeting of the Chemical Society of Japan, Tokyo, April, 1970.

3) Present Address: Laboratory of Chemistry, College of General Education, Kyushu University, Ropponmatsu, Fukuoka.



Scheme 2

shown by their characteristic infrared spectra over the 1650—2000 cm^{-1} range.

The [2.1.1.1]paracyclophane I and the dimeric [2.1.1.1.2.1.1.1]paracyclophane II were prepared by the cyclization of the dichloro compound, XIV, with a sodium adduct of tetraphenylethylene[4] in anhydrous tetrahydrofuran under nitrogen, using the high-dilution technique. The separation of the cyclophanes, I and II, was carried out by fractional crystallization.

An open-chain analog, III, was prepared by the reduction of the dichloro compound, XI, with lithium aluminum hydride or by the Wolff-Kishner reduction of a diketone, which had been produced by the Friedel-Crafts reaction of diphenylmethane-4,4′-dicarbonyl dichloride with toluene.

Between the IR spectra of the cyclophane, I or II, and that of the open-chain analog, III, small and yet characteristic differences were observed. Whereas weak absorption bands were observed in the spectra of the I and II cyclophanes at 1610 and 1575 cm^{-1} (double-bond region), they were not observed for the open-chain analog, III. From this fact, it was assumed that these bands are due to the vibrational transition which is allowed for benzene rings in the macro ring compounds and forbidden for benzene rings in the open-chain analog. A weak absorption band assigned to the symmetric bending of the methyl group was observed at 1380 cm^{-1} for the open-chain analog, III; this band was necessarily absent in the IR spectra of the cyclic compounds. The intensity of the band at 1415 cm^{-1} due to the bending of the methylene groups increased upon ring closure. A similar tendency was observed in the region of the C–H in-plane bending of the benzene rings. In the 800—900 cm^{-1} region of the ring C–H out-of-plane bending vibration, more complicated spectra were observed for the I and II cyclophanes than for the open-chain compound, III. This complication in the spectra by ring closure may be attributable to the appearance of deformation vibrations not allowed for the open-chain compound.

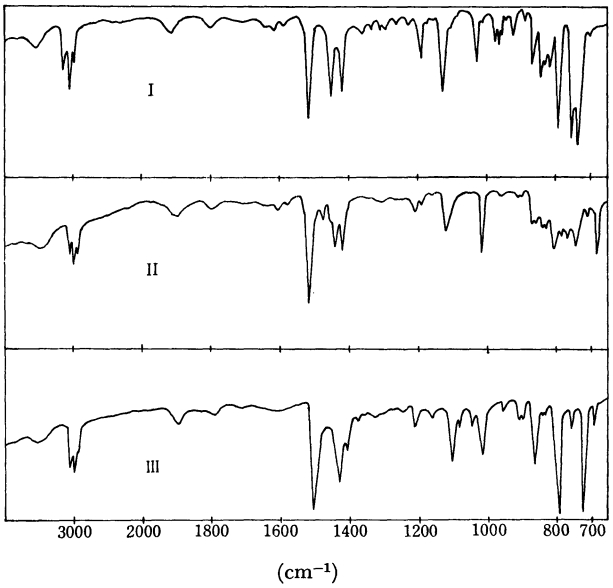


Fig. 1. The IR spectra of compound I, II, and III in KBr disk.

The NMR spectra of the paracyclophanes, I and II, were different from that of the open-chain analog, III, in several respects. In the region of the alkyl protons, the open-chain compound, III, showed a peak due to methyl protons at τ 7.74 and one due to methylene protons at τ 6.16, in an equal area ratio.

On the other hand, the cyclophanes I and II showed no peak due to methyl protons, but, instead, showed a peak indicating the existence of an ethylene bridge resulting from cyclization. The peak of the ethylene protons was at τ 7.21 for the compound I and at τ 7.22 for the compound II. The fact that the peak due to ethylene protons is a singlet means that all the ethylene protons are equivalent. This fact may be readily understandable provided that the pair of conformers due to the two skew conformations of the 1,2-diphenylethane moiety of the macro ring is rapidly interconverted by flip rotation about the C–C axis of the ethylene group, as has been described before.

The singlets at τ 6.25 and 6.33 for the compound I and the singlet at τ 6.13 for Compound II are assigned to methylene protons. In Compound I, on the basis of the area ratio of 1 : 2, the peak at τ 6.25 is assigned to the protons of methylene remote from the ethylene bridge (indicated by X in formula 1), and the peak at τ 6.33, to those of methylenes near the ethylene bridge (indicated by Y and Z). Such a difference in the chemical shift between the methylene protons may be explained by their being shielded unequally by the ring current of the neighboring benzene rings.

The open-chain compound, III, showed a sharp singlet peak of benzene protons at τ 2.97, whereas the cyclophane I and II showed two different peaks. In the cyclophane I, the ring protons exhibit two well-separated peaks, at τ 3.45 and τ 3.10, equal in area. Such a difference in the chemical shift between aryl protons seems to be caused by the same reason as that in the case of methylene protons. From a molecular-model consideration of the cyclophane I, the lower-field peak was assigned to the protons of benzene rings remote from the ethylene bridge (indicated by A and B), and the higher-field peak, to those of benzene rings near the ethylene bridge (indicated by C and D).

In case of the cyclophane II, no such upfield shift of the aryl protons was observed. This fact may be

---

[4] E. Müller and G. Röscheisen, *Chem. Ber.*, **90**, 543 (1957).

explained from an inspection of the molecular model, which shows that the molecule of the cyclophane II may be free from strain and that the macro ring may be so flexible that the benzene rings in it may rotate around the para axis.

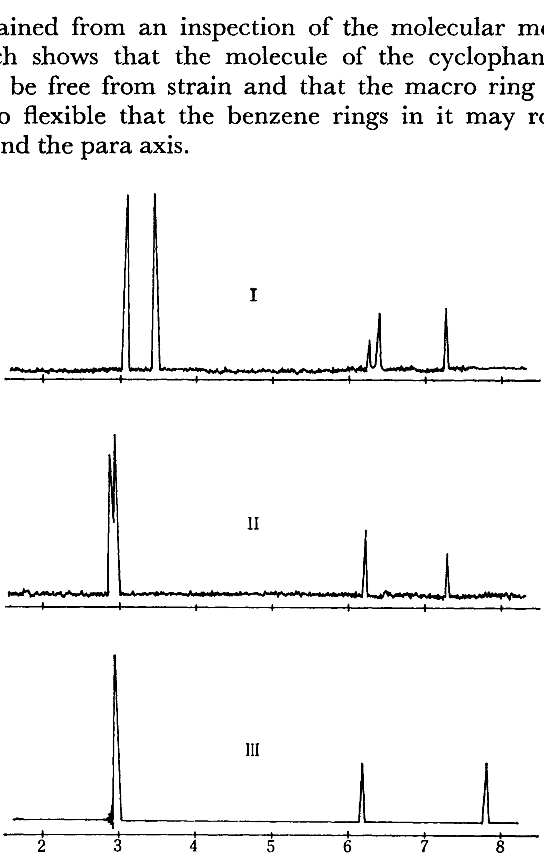


Fig. 2. The NMR spectra of compound I, II, and III in $CDCl_3$.

The UV spectra of the cyclophanes I and II were compared with that of the open-chain compound, III. A loss of the fine structure around 270 mμ in the cyclophane I is noticeable when its spectrum is compared with the spectrum of the open-chain compound, III. This fact is attributable to transannular electronic interactions of the benzene rings. In case of the compound I, compared with the compound III, the major peaks are observed to shift to longer wavelengths and to be weakened in intensity. Furthermore, the fine structure of the peaks becomes less apparent. The new absorption at 242 mμ for I indicates strong transannular electronic interactions of the benzene ring.

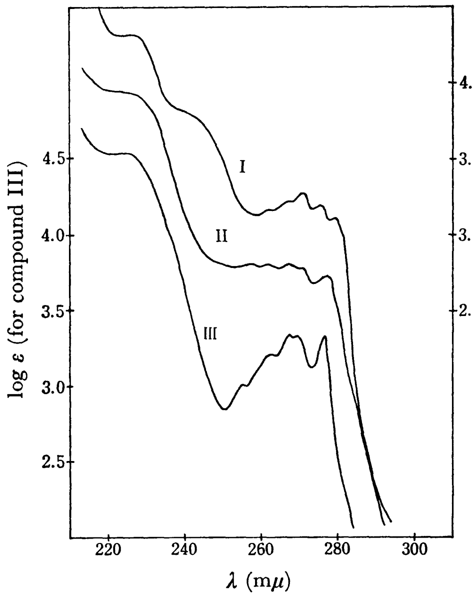


Fig. 3. The UV spectra of compound I, II, and III in ethanol.
I: λ_{max} 269.5 mμ, $\log \varepsilon=3.25$
II: λ_{max} 266.5 mμ, $\log \varepsilon=3.30$
III: λ_{max} 267.0 mμ, $\log \varepsilon=3.32$
The graduation in the ordinate axis for compound II is displaced upward by 0.5 log ε unit increments from that for compound III.

The cyclic structures of the cyclophanes I and II were confirmed by the results of the elementary analysis and by molecular-weight determination, and by the absence of an end methyl group indicated by the IR and NMR spectra, as well as by a comparison of their IR, NMR and UV spectra with that of the open-chain analog, III.

The possibility of the formation of inclusion compounds is now under investigation.

Experimental

All the melting points are uncorrected. The IR spectra were determined in potassium bromide disks or films by means of a Hitachi EPI-S2 spectrophotometer, while the UV spectra were measured in ethanol by means of a Hitachi EPI-3T spectrophotometer. The NMR spectra were recorded at 60 MHz in $CDCl_3$ solution by means of a Varian Associates A-60 photometer. The chemical shifts are quoted as τ values relative to tetramethylsilane. The molecular weights were determined by means of a Hitachi Perkin-Elmer 115 molecular-weight-determination apparatus, using benzene as the solvent.

4,4'-Bis(p-*ethoxycarbonylbenzoyl)diphenylmethane, V.* Into an ice-cooled mixture of 70 g of ethyl *p*-chloroformylbenzoate, IV,[5] and 200 g of powdered anhydrous aluminum chloride in 600 m*l* of carbon disulfide, we stirred, drop by drop, a solution of 27 g of diphenylmethane in 200 m*l* of carbon disulfide at 0°C. The reaction mixture was then refluxed for 5 hr. The removal of carbon disulfide by distillation and the addition of crushed ice and hydrochloric acid yielded a pale yellow powder, which was then crystallized from ethanol to give 60 g (72% yield) of colorless needles; mp 130—130.5°C.

Found: C, 76.20; H, 5.47%. Calcd for $C_{33}H_{28}O_6$: C, 76.14; H, 5.42%.

*4,4'-Bis(*p-*ethoxycarbonylbenzyl)benzophenone, VII.* A mixture of 50 g of ethyl *p*-benzylbenzoate, VI, and 80 g of powdered anhydrous aluminum chloride in 500 m*l* of cabon disulfide was cooled to −15°C, and then 10 g of phosgene were slowly stirred into the mixture at a temperature below −10°C. The temperature was then allowed to rise slowly to room temperature. After a similar treatment of the reaction mixture, 44 g of the keto diester, VII, were obtained as a pale yellow powder, this powder was used without further purification for the preparation of the dicarboxylic acid, VIII.

*4,4'-Bis(*p-*carboxybenzyl)diphenylmethane, VIII.* A mixture of 50 g of the diketo diester, V, 200 g of potassium hydroxide, and 200 m*l* of 85% hydrazine hydrate in 500m*l* of ethylene glycol was refluxed for 1 hr. The water and excess hydrazine were removed by a take-off condenser until the temperature rose to 195—200°C, after which reflux was continued for 6 hr. The cooled solution was diluted with

---

[5] J. B. Cohen and H. S. de Pennington, *J. Chem. Soc.*, **113**, 63 (1918).

water and acidified with concentrated hydrochloric acid. Almost a theoretical amount (42 g) of a white crystalline powder was thus obtained.

The same acid was also obtained by a similar reduction of Compound VII with potassium hydroxide and hydrazine hydrate in ethylene glycol.

*4,4'-Bis(*p*-ethoxycarbonylbenzyl)diphenylmethane, IX.* A mixture of 42 g of the dicarboxylic acid, VIII, 100 g of benzene, and 50 m*l* of concentrated sulfuric acid in 500 m*l* of ethanol was refluxed for 20 hr, the resultant water was removed as a volatile azeotrope composed of benzene, ethanol, and water. After working-up in the usual way, an almost theoretical amount (47 g) of the product was obtained; it was then purified by recrystallization from ethanol to colorless needles with a mp of 120—121.5°C.

Found: C, 80.51; H, 6.61%. Calcd for $C_{33}H_{32}O_4$: C, 80.46; H, 6.55%.

*4,4'-Bis(*p*-hydroxymethylbenzyl)diphenylmethane, X.* A solution of 40 g of the diester, IX, in 400 m*l* of anhydrous tetrahydrofuran was stirred, drop by drop, into a suspension of 5 g of lithium aluminum hydride in 400 m*l* of tetrahydrofuran at room temperature. After being refluxed for 1 hr, the mixture was cooled and treated with water and then with hydrochloric acid. The tetrahydrofuran was removed by distillation, and the resultant precipitate was collected and recrystallized from tetrahydrofuran to give an almost theoretical amount (33 g) of colorless needles; mp 180.5—181°C.

Found: C, 85.25; H, 7.08%. Calcd for $C_{29}H_{28}O_2$: C, 85.26; H, 6.91%.

*4,4'-Bis(*p*-chloromethylbenzyl)diphenylmethane, XI.* A mixture of 30 g of the diol, X, and 35 g of phosphorus pentachloride in 500 m*l* of chloroform was refluxed for 3 hr. After the removal of the solvent and phosphoryl chloride by distillation under reduced pressure, the residue was recrystallized from tetrahydrofuran to give 27 g (83% yield) of colorless needles; mp 164—164.5°C.

Found: C, 78.44; H, 5.98. Calcd for $C_{29}H_{26}Cl_2$: C, 78.20; H, 5.88%.

A mixture of 5 g of the diol, X, and 50 m*l* of thionyl chloride also gave the dichloro compound, XI, in an almost theoretical yield.

*4,4'-Bis(*p*-methylbenzyl)diphenylmethane, III.* To a stirred suspension of 0.03 g of lithium alminum hydride in 30 m*l* of anhydrous tetrahydrofuran, we slowly added a solution of 0.2 g of the dichloro compound, XI, in 20 m*l* of tetrahydrofuran at room temperature. After the usual treatment, 0.17 g (the theoretical amount) of the product was recrystallized from ethanol to give colorless crystals; mp 118—119°C.

Found: C, 92.36; H, 7.65%. Calcd for $C_{29}H_{28}$: C, 92.50; H, 7.50%.

This open-chain model compound was also prepared as follows. By the Friedel-Crafts reaction of 3 g of diphenylmethane-4,4'-dicarbonyl chloride, XII, 2 g of toluene, and 3.5 g of powdered anhydrous aluminum chloride in 70 m*l* of carbon disulfide, 3.1 g (73% yield) of the diketone, XIII, was obtained as pale yellow crystals with a mp of 140°C.

Found: C, 85.95; H, 6.14%. Calcd for $C_{29}H_{24}O_2$: C, 86.11; H, 5.98%.

A mixture of 0.75 g of the above-mentioned diketone, XIII, 3 m*l* of 85% hydrazine hydrate, and 5 g of potassium hydroxide in 50 m*l* of ethylene glycol was refluxed to give 0.7 g (the theoretical amount) of a colorless crystalline product, whose identity was confirmed by a mixed-melting-point determination (118°C) with the sample described above and by a comparison of their IR spectra.

[2.1.1.1]Paracyclophane I and [2.1.1.1.2.1.1.1]Paracyclophane, II. Into a dark-violet solution of 4 g of sodium and 1.5 g of tetraphenylethylene in 400 m*l* of anhydrous tetrahydrofuran, a solution of 5 g of the dichloro compound, XI, in 800 m*l* of anhydrous tetrahydrofuran was stirred, drop by drop, through a modified Hershberg dropping funnel[6] at room temperature under nitrogen over a period of 50 hr. After the careful addition of ethanol, and then water, the removal of the solvent from the mixture gave a white powder; when this powder was washed with water and fractionally crystallized from benzene-ethanol mixture, Compounds I and II were obtained in yields 200 mg and 120 mg respectively.

Compound I was crystallized from ethanol to give colorless crystals; mp 219—220°C.

Found: C, 92.95; H, 7.11%; mol wt, 390. Calcd for $C_{29}H_{26}$: C, 93.00; H, 7.00%; mol wt, 374.5. Compound II was recrystallized from benzene to give colorless needles.

Found: C, 92.87; H, 7.26%; mol wt, 742. Calcd for $C_{58}H_{52}$: C, 93.00; H, 7.00%; mol wt, 749.0.

---

[6] R. E. Benson and B. C. Mukusick, "Organic Syntheses," Coll. Vol. IV, p. 747 (1963).