NOTES

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Synthesis of Three New Azaparacyclophanes Containing Four Benzene Rings

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As a part of studies of paracyclophane chemistry in our laboratory,2) three new azaparacyclophanes containing four benzene rings connected with four bridges in the para-position, such as *N*,*N'*-dimethyl-2,18-dimethyl-2,18-diaza[3.1.3.1]paracyclophane (V), *N*,*N'*-dimethyl-2,19-diaza[3.2.3.2]paracyclophane (IX), and *N*,*N'*,*N''*,*N'''*-tetramethyl-2,11,20,29-tetraaza[3.3.3.3]-paracyclophane (XIII), were synthesized.

The objects of this experiment were to synthesize the azaparacyclophanes with different lengths of bridges, to compare their spectral properties, and to determine whether or not they form an inclusion compound. The synthetic method and results will be described below.

For the synthesis of the above-mentioned compounds, we adopted an amide-formation method in the critical ring-closing step. The azaparacyclophanes, V, IX, and XIII, were prepared by the condensation of each diacid chloride and diamine and by subsequent reduction, while compound V was obtained by the further *N*-methylation of the corresponding cyclic secondary amine, IV.

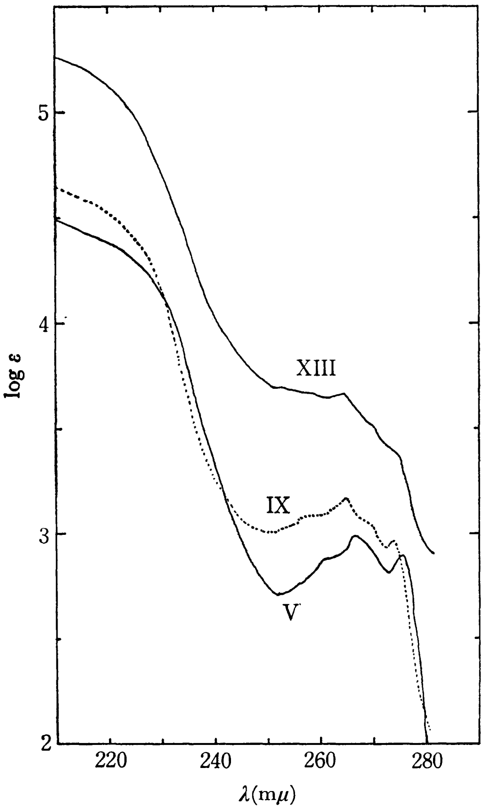

Fig. 1. UV spectra of azaparacyclophane V, IX, and XIII in ethanol.
V: λmax 266.5 mμ, $\log \varepsilon=2.99$
IX: λmax 264.5 mμ, $\log \varepsilon=3.16$
XIII: λmax 264.5 mμ, $\log \varepsilon=3.15$
Curve XIII is displaced upward by 0.5 unit from the two curves below.

Figure 1 records the UV spectra of the azaparacyclophanes, which may be separated into two groups with respect to the length of the bridges. Compounds IX and XIII both contain bridges of more than one methylene unit and have almost equal intensities and wavelengths in λ max. On the other hand, compound V which contains one methylene unit, shows a shift to a slightly longer wavelength and a lower intensity compared to the others. The same effect has been pointed out by Cram3) in a series of diphenylalkanes and related to the proximity of the benzene rings in the diphenylmethane moiety. The above facts may indicate the presence of a transannular electronic effect between benzene rings in V.

The crystallization of the compound XIII from benzene or dioxane gave crystals whose composition corresponded to that of a molecular compound consisting of one molecule of XIII and one molecule of benzene or dioxane. The presence of benzene or dioxane in the isolated substance mentioned above was concluded from the NMR spectra and the composition. In the case of the other paracyclophanes with methylene or ethylene as bridges, no such molecular compound has yet been isolated. It is now under investigation whether or not the benzene or dioxane molecules are included in the empty space of the paracyclophane ring.

Experimental

All melting points are uncorrected; they were measured in a sealed tube filled with nitrogen. The UV spectra were measured on a Hitachi EPI-3T spectrometer in ethanol. The NMR were measured with a Varian A-60 spectrometer in carbon tetrachloride. The molecular weights were measured by means of a Hitachi Perkin-Elmer 115 molecular-weight-determination apparatus, using benzene as the solvent.

2,18-Diaza[3.1.3.1]paracyclophane-3,17-dione (III). The diacid chloride I (3.22 g, 0.011 mol) in 500 m*l* of distilled benzene was subjected to cyclization with the diamine II (5 g, 0.022 mol) in 500 m*l* of distilled benzene over a 10 hr period, in a 5 *l* flask containing 2 *l* of benzene, under refluxing and stirring, according to the procedure of Stetter.4) The still-hot reaction mixture was filtered, and then the solvent was

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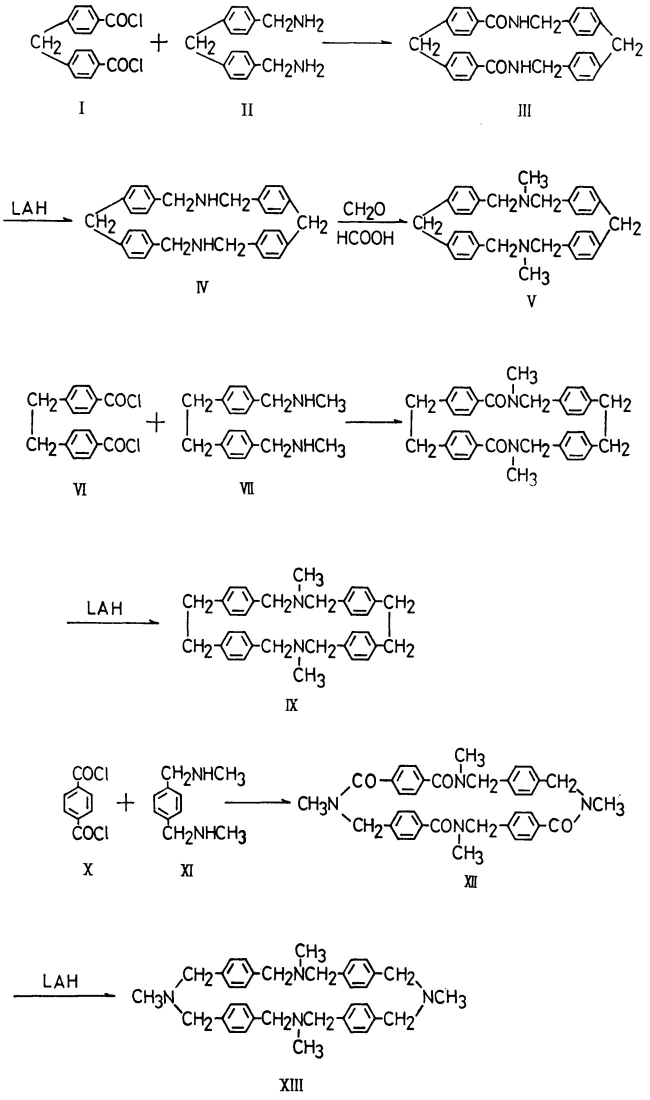
2) See also T. Kawato, T. Inazu, and T. Yoshino, This Bulletin, **44**, 200 (1971).

3) D. J. Cram and M. F. Antar, *J. Amer. Chem. Soc.*, **80**, 3103 (1958).

4) H. Stetter and J. Marx, *Ann. Chem*, **607**, 59 (1957).



evaporated to give 1.2 g of a white precipitate. After crystallization from dioxane, 1 g (20%) of white crystals melting at 312—313°C was obtained. Found: C, 80.56; H, 5.82; N, 6.30%. Calcd for $C_{30}H_{26}N_2O_2$: C, 80.69; H, 5.87; N, 6.27%.

N,N′-*Dimethyl-2, 19-diaza* [*3. 2. 3. 2*]*paracyclophane-3, 18-dione (VIII).* The diacid chloride VI (2.8 g, 0.009 mol), in 500 m*l* of distilled benzene was subjected to cyclization with the diamine VII (4.8 g, 0.018 mol) in 500 m*l* of distilled benzene over a 9 hr period, using the same procedure as was used for compound III. By treating the reaction mixture as above, 3.1 g (65%) of a crystalline product were obtained. A small portion of the product was crystallized from benzene to give white prisms melting at 239—240°C. Found: C, 81.06; H, 6.97; N, 5.26%. Calcd for $C_{34}H_{34}N_2O_2$: C, 81.24; H, 6.82; N, 5.57%.

N,N′,N″,N‴-*Tetramethyl-2, 11, 20, 29-tetraaza* [*3. 3. 3. 3*]*paracyclophane-3,10,21,28-tetraone (XII.)* The diacid chloride (1.5 g, 0.007 mol), in 500 m*l* of distilled benzene, was subjected to cyclization with the diamine XI (2.5 g, 0.015 mol) in 500 m*l* of distilled benzene over a 8 hr period, using the procedure described above. By treating the reaction mixture as above, we obtained 1.45 g (67%) of a white powder which gave white needles decomposing over 380°C by extraction with methanol using a Soxhlet-extractor. Found: C, 73.65; H, 6.29; N, 9.48%. Calcd for $C_{36}H_{36}N_4O_4$: C, 73.45; H, 6.16; N, 9.52%.

2,18-Diaza[*3.1.3.1*]*paracyclophane (IV).* A mixture of 1 g of compound III, 1 g of lithium aluminum hydride, and 150 m*l* of dioxane was refluxed for 64 hr under stirring. After the reaction mixture had then cooled, dilute hydrochloric acid was added to the mixture so that the inorganic substances were dissolved in solution, leaving the amine hydrochloride. After treatment with sodium hydroxide and crystallization from benzene, the hydrochloride gave 660 mg of white needles melting at 210.5—211.5°C (70%). Found: C, 86.49; H, 7.21; N, 6.43%. Calcd for $C_{30}H_{30}N_2$: C, 86.08; H, 7.22; N, 6.69%.

N,N′-*Dimethyl-2,18-diaza*[*3.1.3.1*]*paracyclophane (V).* A mixture of 40 m*l* of formic acid, 660 mg of compound IV, and 3 m*l* of 37% formalin was refluxed for 24 hr. After cooling, 10 m*l* of conc. hydrochloric acid were added, and the excess formalin and formic acid were removed by evaporation. The colorless residue was treated with a sodium hydroxide solution and extracted with benzene. After evaporation, 619 mg of white powder were obtained. White crystals melting at 254—256°C were obtained by crystallization from benzene (550 mg, 78.6%). Found: C, 86.09; H, 7.67; N, 6.00%; mol wt, 439. Calcd for $C_{34}H_{34}N_2$: C, 86.05; H, 7.67; N, 6.27%; mol wt, 446.6.

N,N′-*Dimethyl-2,19-diaza*[*3.2.3.2*]*paracyclophane (IX).* A mixture of 1.35 g of compound VIII, 1 g of lithium aluminum hydride, and 150 m*l* of dioxane was refluxed for 48 hr under stirring. The complex thus formed and the excess lithium aluminum hydride were decomposed by adding methanol and then a sodium sulfate solution. The reaction mixture was warmed and filtered, and the filtrate was concentrated to give white prisms melting at 236—238°C (763 mg, 61.4%). Found: C, 85.95; H, 8.10; N, 5.92%; mol wt 463. Calcd for $C_{34}H_{38}N_2$: C, 86.03; H, 8.07; N, 5.90%; mol wt, 474.6.

N, N′, N″, N‴-*Tetramethyl-2, 11, 20, 29-tetraaza*[*3.3.3.3*]*paracyclophane (XIII).* A mixture of 377 mg of compound XII, 1 g of lithium aluminum hydride, and 100 m*l* of dioxane was refluxed for 72 hr under stirring. To the reaction mixture were added 1 m*l* of a 15% sodium hydroxide solution, and 3 m*l* of water. The mixture was warmed and filtered, and the filtrate was concentrated to give 148 mg (37%) of white needles, XIII-D, which contained dioxane. After heating at 90°C under reduced pressure, XIII-D gave pure XIII: mp 196—198.5°C; NMR (CCl_4) τ 7.68 (12H, singlet, N–CH_3), 6.71 (16H, singlet, PH–CH_2–N), 2.81 (16H, singlet, aromatic); mol wt, 534 (calcd. 532.7); Found: C, 81.28; H, 8.36; N, 10.44%. Calcd for $C_{36}H_{44}N_4$: C, 81.16; H, 8.33; N, 10.52%.

On the other hand, the data of XIII-D were as follows: mp 188—196°C; NMR (CCl_4) τ 6.41 (8H, singlet, dioxane) in addition to the bands of XIII; Found: C, 76.96; H, 8.40; N, 8.89%. Calcd for $C_{36}H_{44}N_4+C_4H_8O_2$: C, 77.38; H, 8.44; N, 9.02%. These results clearly show the presence of dioxane in a ratio of one to one. The crystallization of XIII from benzene also gave the same type of compound containing the benzene: mp 191—197°C; NMR (CCl_4) τ 2.73 (6H, singlet, benzene) in addition to the band of XIII; Found: C, 82.12; H, 8.47; N, 9.07%. Calcd for $C_{36}H_{44}N_4+C_6H_6$: C, 82.58; H, 8.25; N, 9.17%.