BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 46, 263—265 (1973)

Macro Rings. V.[1] Syntheses of Tetraoxaparacyclophanes Containing Two Biphenyl Nuclei

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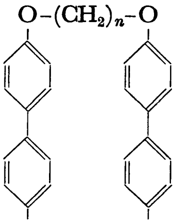
(Received May 25, 1972)

Three new tetraoxaparacyclophanes containing two biphenyl nuclei connected with oxypolymethyleneoxy bridges in the respective 4,4′-positions, such as 1,5,18,22-tetraoxa[5.0.5.0]paracyclophane I_3, 1,6,19,24-tetraoxa[6.0.6.0]paracyclophane I_4, and 1,7,20,26-tetraoxa[7.0.7.0]paracyclophane I_5, were synthesized. The UV, IR, and NMR spectra of these paracyclophanes were compared with those of the corresponding open-chain compound, IV_3.

Three paracyclophanes, I_3, I_4, and I_5, in which the 4,4′-positions of two biphenyl molecules are connected with five-, six-, and seven-membered bridges respectively, were synthesized. The IR, UV, and NMR spectral properties of these compounds, I′s, and of the corresponding open-chain compounds, IV_3, will be discussed.



I_3: $n=3$, I_4: $n=4$, I_5: $n=5$.

Fig. 1. Tetraoxaparacyclophanes

The synthetic routes are shown in Schemes 1, 2, and 3. Three portions of a potassium salt of 4,4′-biphenyldiol were treated, respectively, with ethylene-, trimethylene-, and tetramethylene-chlorohydrins to give diols, II′s, which were then treated with phosphorous tribromide to give dibromides, III′s. The dibromides, III′s, were also prepared in considerable yields by the condensation of 4,4′-biphenyldiol with polymethylene dibromides in the presence of potassium carbonate.[3] The dibromides, III′s, were reduced with lithium aluminum hydride to IV′ compounds. These compounds were synthesized as reference compounds, which served as open-chain models of the cyclic compounds, I′s, in a comparison of their spectra.

Most macrocyclic ethers, known as ansa compounds, are diethers which are generally prepared by the intramolecular condensation of compounds with a

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[1] Part IV of this series: Y. Urushigawa, T. Inazu, and T. Yoshino, This Bulletin, **44,** 2546 (1971).

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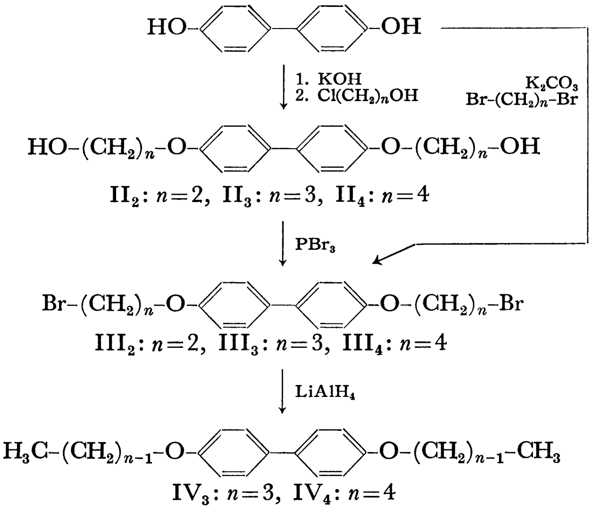
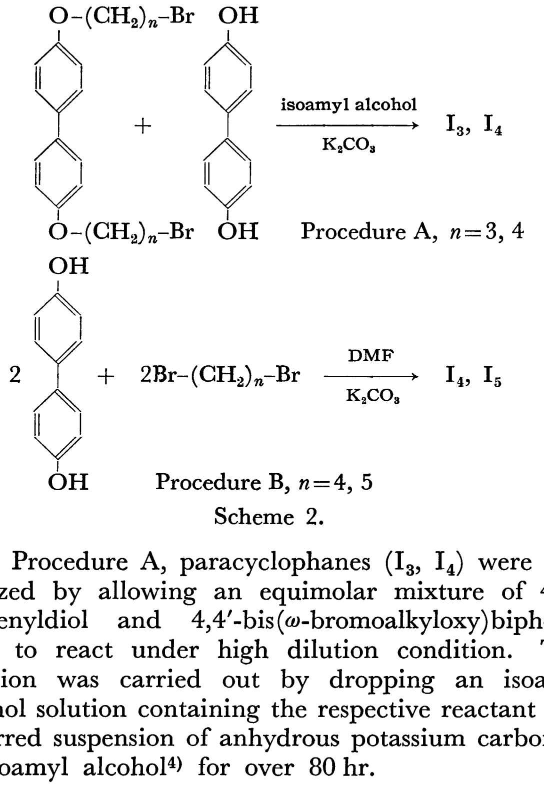
[3] R. Adams and L. N. Whitehill, *J. Amer. Chem. Soc.*, **63,** 2073 (1941).



Scheme 1.

phenolic hydroxyl group and a long-chain ω-haloalkyloxy group.[3] Since the compounds to be synthesized in this investigation are tetraethers, though, it was difficult to use this method without alteration in the syntheses of tetraethers. Therefore, as is shown in Scheme 2, the intermolecular double condensation (Procedure A) and the one-step quadruple condensation (Procedure B) were adopted.

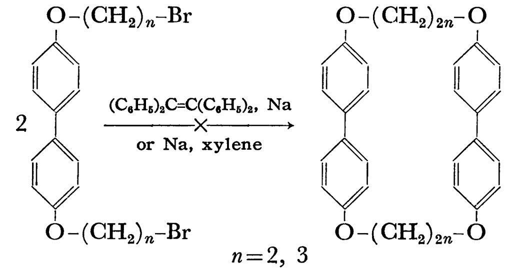


Scheme 2.

In Procedure A, paracyclophanes (I_3, I_4) were synthesized by allowing an equimolar mixture of 4,4′-biphenyldiol and 4,4′-bis(ω-bromoalkyloxy)biphenyl III′s to react under high dilution condition. This reaction was carried out by dropping an isoamyl alcohol solution containing the respective reactant into a stirred suspension of anhydrous potassium carbonate in isoamyl alcohol[4] for over 80 hr.

In Procedure B, paracyclophanes (I_4, I_5) were synthesized by dropping, over a 30 hr period, a dimethylformamide solution containing 4,4′-biphenyldiol and polymethylene dibromide into a stirred mixture of anhydrous potassium carbonate in dimethylformamide; the products were thus obtained as crystalline solids. The yields of the cyclic compounds in both procedures were very low, but, unexpectedly, the yields of the products in the procedure B were appreciably higher than those in Procedure A.

In the hope of obtaining the tetraoxa[6.0.6.0]- and tetraoxa[8.0.8.0]paracyclophanes shown in Scheme 3, the intermolecular Wurtz reaction of 4,4′-bis(ω-bromoalkyloxy)biphenyl (III_3, III_4) was attempted under a nitrogen atmosphere both in the presence of a sodium adduct of tetraphenylethylene in tetrahydrofuran at room temperature and in the presence of molten sodium in boiling xylene, but no paracyclophane was obtained in either case.



Scheme 3.

The cyclic structures of I_3, I_4, and I_5 were confirmed by their IR, UV, and NMR spectra, by elementary analyses, and by a molecular-weight determination. In the infrared spectra, the absorptions of the cyclic compounds, I′s, were more complicated than that of the open-chain model, IV_3, in the 800—900 cm^{-1} region. These bands were used as a diagnosis[5] for the cyclic structure.

The NMR spectra suggest that the conformation of the two biphenyl nuclei in the macro ring may not be fixed rigidly, but may be flexible in a solution at room temperature. The peaks for benzene protons were found to shift upfield by 0.2—0.6 ppm from those of open-chain models, IV′s. Among the paracyclophanes, I_3, I_4, and I_5, the peaks for benzene protons exhibited to shift to a higher field with a decrease in the methylene numbers in the oxypolymethyleneoxy bridges. These upfield shifts are due to the shielding by the biphenyl nuclei on the opposite side of the macro ring. The close resemblance of UV spectra of paracyclophanes, I′s, to those of the corresponding open-chain models, IV′s, reveals that the aromatic rings of I′s are planar and that there is no strain in the macro rings.

The problem whether or not other small molecules are included in the empty space of the macrocyclic rings is also interesting; studies of these adducts are now in progress.

Experimental

All the melting points are uncorrected. The ultraviolet spectra were measured on a Hitachi ESP-3T spectrophotometer. The infrared spectra were measured on a Hitachi EPI-S2 spectrophotometer. The NMR spectra were recorded on Hitachi R-20 photometer, using tetramethyl silane as the internal standard and deuterochloroform as the solvent.

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4) H. Stetter and E. E. Roos, *Chem. Ber.*, **87**, 566 (1954).

5) D. J. Cram and H. Steinberg, *J. Amer. Chem. Soc.*, **73**, 5961 (1951).

The molecular weights were measured by means of a Hitachi Perkin-Elmer 115 molecular weight apparatus, using benzene as the solvent.

4,4′-Bis(2-bromoethoxy)biphenyl, III$_2$. A mixture of 2 g (0.011 mol) of 4,4′-biphenyldiol, 8.27 g (0.044 mol) of ethylene bromide, 20 ml of acetone, 2 ml of water, and 5 g of potassium carbonate was refluxed with stirring on a steam-bath for 15 hr, after which an additional 1.75 g of potassium carbonate was added and stirring and refluxing was continued for 20 hr. The acetone was then distilled off with stirring to prevent bumping. The reaction mixture was then washed with water and recrystallized from a dioxane–ethanol mixture. White needles, mp 175—176°C; yield, 1.0 g (24%). Found: C, 48.22; H, 4.14%. Calcd for $C_{16}H_{16}Br_2O_2$: C, 48.03; H, 4.03%.

4,4′-Bis(3-bromopropoxy)biphenyl, III$_3$. A mixture of 10 g (0.054 mol) of 4,4′-biphenyldiol, 50 g (0.270 mol) of trimethylene dibromide, 40 ml of acetone, 6.7 ml of water, and 36 g of potassium carbonate was stirred and refluxed on a steam-bath for 40 hr. At the end of this period, the acetone was removed, and the reaction mixture was shaken with water. The product was recrystallized from a dioxane–ethanol mixture; white crystals, mp 127—128°C; yield, 13.8 g (60%). Found: C, 52.47; H, 4.94%. Calcd for $C_{18}H_{20}Br_2O_2$: C, 50.49; H, 4.67%.

4,4′-Bis(4-bromobutoxy)biphenyl, III$_4$. This was prepared in the same way as the corresponding 4,4′-bis(3-bromopropoxy)biphenyl, III$_3$. From 5 g (0.027 mol) of 4,4′-biphenyldiol, 25 g (0.107 mol) of tetramethylene dibromide, 15 ml of acetone, 3.4 ml of water, and 18 g of potassium carbonate, 8 g (65%) of a product was obtained; white crystals, mp 136°C. Found: C, 52.37; H, 5.26%. Calcd for $C_{20}H_{24}Br_2O_2$: C, 52.66; H, 5.30%.

4,4′-Dipropoxybiphenyl, IV$_3$. A suspension of 500 mg of the III$_2$ dibromide in 100 ml tetrahydrofuran was stirred, and then the solution was added, drop by drop, into a mixture of excess lithium aluminum hydride in 50 ml of tetrahydrofuran at room temperature; after stirring for an additional 1.5 hr, the mixture was refluxed for 6 hr. After cooling, the mixture was treated with water and extracted with benzene. The removal of the benzene under reduced pressure gave a white powder, which was recrystallized from an ethanol–benzene mixture to give 170 mg (55% yield) of a white crystalline powder; mp 156—158°C. NMR; 7.23 ppm (8H, quartet, aromatic), 3.955 (4H, triplet, O-$\mathbf{CH_2}$), 1.85 (4H, quintet, O-CH_2-$\mathbf{CH_2}$-CH_3), 1.05 (6H, triplet, O-CH_2-CH_2-$\mathbf{CH_3}$). IR; 1609 cm^{-1} (m, ν_{ip} C=C), 1501 (s, ν_{ip} C=C), 1242 (s, ν_{as} C-O-C), 824 (s, δ_{op} H-C_{arom}). UV; λ_{max} 267 nm, $\varepsilon_{max}=5.9\times10^3$.

4,4′-Dibutoxybiphenyl, IV$_4$. This compound was prepared in exactly the same manner as the 4,4′-dipropoxybiphenyl, IV$_3$. The product was white crystals; mp 145—146°C. Yield, 60%.

1,5,18,22-Tetraoxa[5.0.5.0]paracyclophane, I$_3$. Into a 3 liter, four-necked reaction flask of the high-dilution apparatus, we placed 650 ml of dry isoamyl alcohol and 8 g of finely-powdered, anhydrous potassium carbonate which had been heated in an open dish over a free flame for 30 min. A solution of 2.997 g (0.007 mol) of 4,4′-bis(3-bromopropoxy)biphenyl III$_3$ and 1.303 g (0.007 mol) of 4,4′-biphenyldiol in 850 ml of dry isoamyl alcohol was then introduced into a boiling alcohol–potassium carbonate mixture over an 85 hr period. A current of nitrogen was run through the circulatory system in order to minimize any oxidation of the 4,4′-biphenyldiol which might take place. After having been stirred and heated for an additional hour, the reaction mixture was allowed to cool, filtered to remove the inorganic salts present, and evaporated under diminished pressure on a water pump until only traces of the isoamyl alcohol remained. The dark, viscous material remaining was placed in a Soxhlet extractor and partially extracted with petroleum ether for 18 hr. A pale yellow mass remaining in the Soxhlet extractor was recrystallized form benzene to give white needles. Mp above 280°C; yield, 22 mg (0.7%). NMR; 6.80 ppm (16H, quartet, aromatic), 4.25 (8H, triplet, O-$\mathbf{CH_2}$), 2.05 (4H, multiplet, O-CH_2-$\mathbf{CH_2}$-CH_2-O). IR; 1609 cm^{-1} (m, ν_{ip} C=C), 1497 (s, ν_{ip} C=C), 1224 (s, ν_{as} C-O-C), 817 (s, δ_{op} H-C_{arom}). UV; λ_{max} 263 nm, $\varepsilon_{max}=1.1\times10^4$. Found: C, 79.76; H, 6.37%; mol wt, 452.1. Calcd for $C_{30}H_{28}O_4$: C, 79.62; H, 6.24%; mol wt, 452.5.

1,6,19,24-Tetraoxa[6.0.6.0]paracyclophane, I$_4$. *Method A*: This compound was prepared in the same way as the corresponding cyclic ether, I$_3$. In the reaction flask we placed 650 ml of dry isoamyl alcohol and 7 g of powdered potassium carbonate which had been heated to a red heat for 30 min. A solution of 3.194 g (0.007 mol) of 4,4′-bis(4-bromobutoxy)biphenyl, III$_4$, and 1.303 g (0.007 mol) of 4,4′-biphenyldiol in 850 ml of dry isoamyl alcohol was then added to the boiling alcohol–potassium carbonate mixture over an 80 hr period. The product consisted of white prisms. Mp 235—236°C; yield, 13 mg (0.4%). NMR; 6.87 ppm (16H, quartet, aromatic), 4.16 (8H, multiplet, O-$\mathbf{CH_2}$), 1.90 (8H, multiplet, O-CH_2-$\mathbf{CH_2}$-$\mathbf{CH_2}$-CH_2-O). IR; 1607 cm^{-1} (m, ν_{ip} C=C), 1496 (s, ν_{ip} C=C), 1245 (s, ν_{as} C-O-C), 820 (s, δ_{op} H-C_{arom}). UV; λ_{max} 264 nm, $\varepsilon_{max}=1.3\times10^4$. Found: C, 79.96; H, 6.74%; mol wt, 488.8. Calcd for $C_{32}H_{32}O_4$: C, 79.97; H, 6.71%; mol wt, 480.6.

Method B: A solution of 3.30 g (0.018 mol) of 4,4′-biphenyldiol and 3.82 g (0.018 mol) of tetramethylene dibromide in 800 ml of dimethylformamide was added, from a dropping funnel and over a 30 hr period, to a suspension of 30 g of potassium carbonate in 600 ml of dimethylformamide, the temperature being kept at 130°C. After stirring and heating for an additional hour, the reaction mixture was cooled, filtered to remove the inorganic salts, and then concentrated to about 400 ml. It was then placed in an ice box and allowed to stand overnight. Crystals were deposited. The material was crystallized from dimethylformamide to give white prisms. Yield, 320 mg (3.8%). The IR and NMR spectra of this compound were in accord with those of the cyclic compound, I$_4$, prepared by Method A.

1,7,20,26-Tetraoxa[7.0.7.0]paracyclophane, I$_5$. A solution of 4.66 g (0.0025 mol) of 4,4′-biphenyldiol and 5.75 g (0.025 mol) of pentamethylene dibromide in 800 ml of dimethylformamide was added, through a dropping funnel and over a 30 hr period, to a suspension of 30 g of potassium carbonate in 700 ml of dimethylformamide, the temperature being kept at 130°C. After stirring and heating for an additional hour, the reaction mixture was cooled, filtered to remove the inorganic salts, and concentrated to about 400 ml. It was then placed in the ice box and allowed to stand overnight. Crystals were deposited. The material was crystallized from dimethylformamide to give white needles. Mp 236°C; yield, 200 mg (3.1%). NMR: 6.98 ppm (16H, quartet, aromatic), 4.05 (8H, multiplet, O-$\mathbf{CH_2}$), 1.75 (12H, multiplet, O-CH_2-$\mathbf{CH_2}$-$\mathbf{CH_2}$-$\mathbf{CH_2}$-CH_2-O). IR; 1600 cm^{-1} (m, ν_{ip} C=C), 1495 (s, ν_{ip} C=C), 1227 (s, ν_{as} C-O-C), 812 (s, δ_{op} H-C_{arom}). UV; λ_{max} 265 nm, $\varepsilon_{max}=1.4\times10^4$. Found: C, 80.70; H, 7.30%; mol wt, 471.8. Calcd for $C_{34}H_{36}O_4$: C, 80.28; H, 7.13%; mol wt, 508.6.

This work was supported in part by a grant of the Ministry of Education and a grant of Takeda Science Foundation.