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Syntheses of the Optically Active Multilayered [2.2]Paracyclophanes with Known Absolute Configurations[1]

Masao Nakazaki,* Koji Yamamoto, Sigeo Tanaka, and Hideyuki Kametani

Department of Chemistry, Faculty of Engineering Science, Osaka University, Toyonaka, Osaka, Japan

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Starting from (*R*)-(−)-4-methyl[2.2]paracyclophane, a series of optically active, multilayered [2.2]paracyclophanes (**10**, **11**, **14**, and **15**) with known absolute configurations were synthesized; the "chiral recognition" principle was applied for the preparation of (*R,R,R*)-(−)-five-layered [2.2]paracyclophane (**14**). The chiroptical properties of these compounds are described.

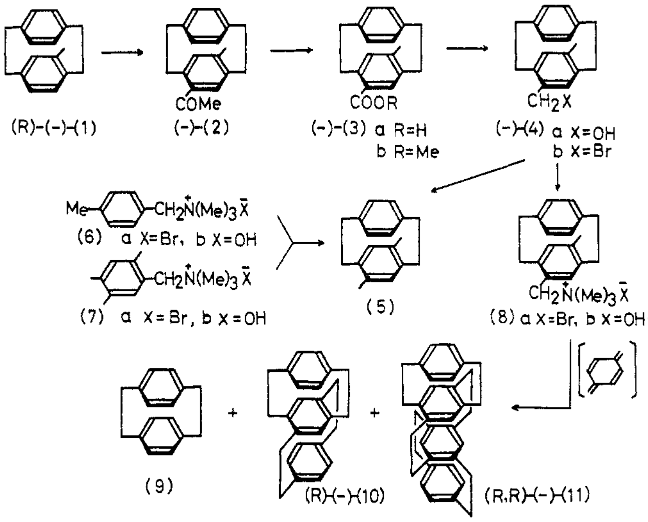
Interesting features about the multilayered [2.2]paracyclophanes with benzene rings closely packed together by means of a *p*-ethano bridge are the distortion of the benzene rings and the transannular interaction caused by the closely spaced face-to-face arrangement of the aromatic rings. Recently, racemic modifications of such multilayered compounds were synthesized and their unusual physical and chemical properties were reported.[2]

In an earlier paper,[3] we reported the preparation of [8][8]- and [8][10]paracyclophanes which have two para bridges spanning the benzene ring giving rise to D_2 and C_2 symmetry, respectively. Upon building up multilayered [2.2]paracyclophanes by Longone's method[2a,b] we also encounter molecules with C_2 or D_2 symmetry, because steric hindrance should cause the formation of molecules with these symmetries to be more favorable. We have been interested in the preparation of these "gyrochiral"[4] compounds with C_2 or D_2 symmetry as well as the chiroptical properties inherent to their helical structures. This contribution is concerned with the synthesis of a series of optically active, multilayered [2.2]paracyclophanes with known absolute configurations.

Results and Discussion

(*R*)-(−)-[3]Chochin (10) and (*R,R*)-(−)-[4]Chochin (11).[5] Our general scheme for the preparation of optically active multilayered [2.2]paracyclophanes can be seen in Scheme I, which illustrates the synthetic route to the two- and three-layered [2.2]paracyclophanes, **10** and **11**.

Scheme I



(*R*)-(−)-4-Methyl[2.2]paracyclophane (**1**),[6] whose absolute configuration had been determined, served as our starting material as well as a liaison compound relating the stereochemistry of the [2.2]paracyclophane series to that of our multilayered compounds. Acetylation of **1** with acetyl chloride and anhydrous aluminum chloride afforded the acetyl derivative **2**, which was further converted by a haloform reaction into (*R*)-(−)-carboxylic acid (**3a**), mp 205–206 °C, $[\alpha]^{21}\mathrm{D}$ −224°. The methyl ester **3b** of this acid was reduced with lithium aluminum hydride to the alcohol **4a** which was converted into the quaternary ammonium bromide **8a**, mp 213–215 °C, $[\alpha]^{20}\mathrm{D}$ −94°, via the bromide **4b**. Since the bromide **4b** is a crucial compound for the following transformations, we established its structure before continuation of our synthesis. Upon lithium aluminum hydride reduction, the bromide **4b** gave a (−)-4,7-dimethyl derivative (**5**), the structure of which was confirmed by the independent synthesis of its racemic modification involving the "cross cou-

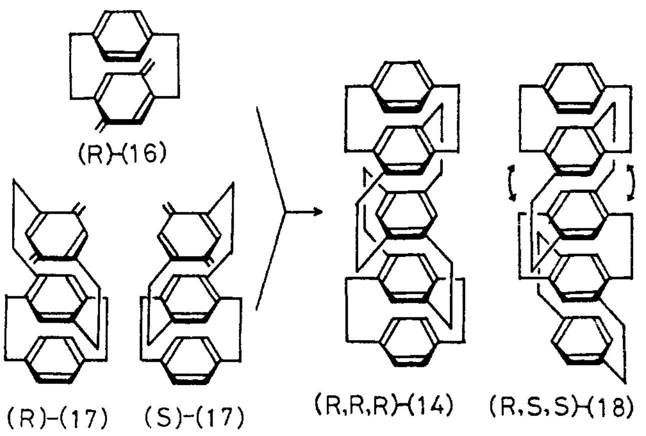
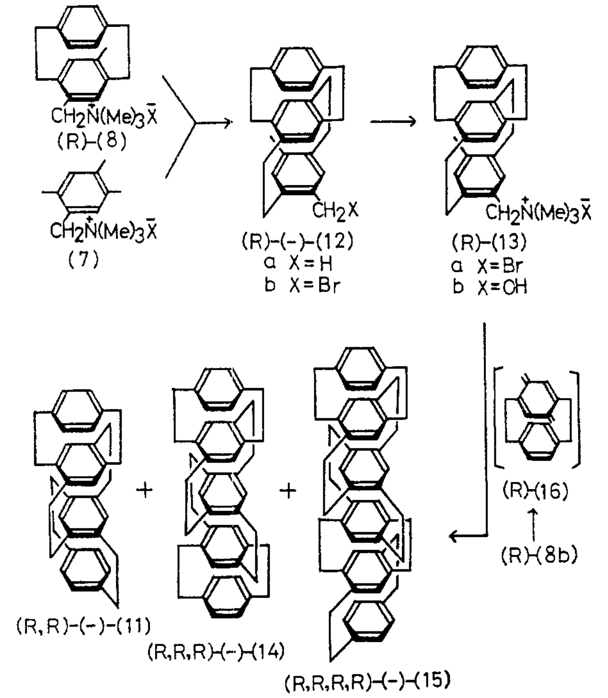


Figure 1. Chirality growth of [n]chochin.

pling"[7] between the two Hofmann bases, **6b** and **7b**, derived from *p*-xylene and durene, respectively. Thus having prepared intermediate **4b** with known structure, we could proceed with our synthetic sequence. A mixture of (*R*)-(−) quaternary salt (**8a**) and *p*-xylyltrimethylammonium bromide (**6a**) (1:1) was treated with silver oxide to furnish a mixture of the Hofmann bases which was then pyrolyzed in boiling toluene. Evolution of trimethylamine occurred smoothly, and the resulting reaction mixture was fractionated by chromatography on neutral alumina to give [2.2]paracyclophane (**9**, 7%), (*R*)-(−)-triple-layered [2.2]paracyclophane (**10**, 5%), mp 170–171 °C, and (*R,R*)-(−)-quadruple-layered compound (**11**, 4%), mp 230–231 °C.

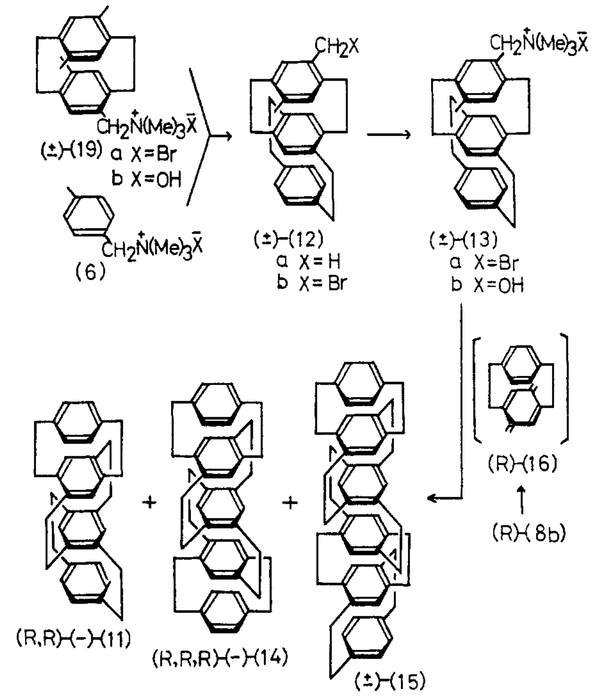
(*R,R,R*)-(−)-[5]Chochin (14) and (*R,R,R,R*)-(−)-[6]-Chochin (15). As the key intermediate for the synthesis of optically active six-layered [2.2]paracyclophane, we selected (−)-triple-layered [2.2]paracyclophane (**12**) (Scheme II) which possesses C_2 symmetry and which could be prepared by cross-coupling between previously mentioned (*R*)-(−)-**8** and 2,4,5-trimethylbenzyltrimethylammonium base (**7**). Monobromination with *N*-bromosuccinimide followed by quaternization with trimethylamine converted the dimethyl derivative **12a** into (−)-ammonium bromide **13a** which was again cross-coupled with (*R*)-(−)-**8a**. The reaction mixture, after chromatography, afforded the following sequence of components: (*R,R*)-(−)-quadruple-layered [2.2]paracyclophane (**11**, 6%), (*R,R,R*)-(−)-five-layered compound (**14**, 3%), mp >300 °C, and (*R,R,R,R*)-(−)-six-layered compound (**15**, 1.4%), mp >300 °C.

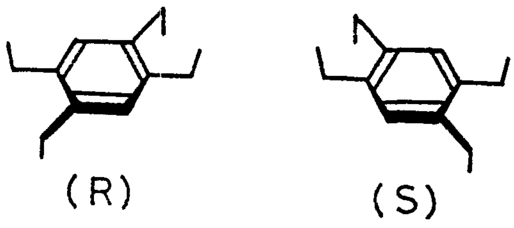
Scheme II



Preparation of (*R,R,R*)-(−)-[5]Chochin (14) by the Chiral Recognition Principle. So far our guiding principle for constructing optically active multilayered [2.2]paracyclophanes has been such that an optically active intermediate with known absolute configuration was dimerized or coupled with an achiral precursor such as **7b**. We now divert attention from the above approach to a second one which involves the coupling of the optically active two-layered intermediate **16** with the racemic triple-layered intermediate **17** (Figure 1). A priori two diastereomers, **14** and **18**, could be expected; however, inspection of a molecular model indicates that the one (**18**) with *R,S,S* configuration has an "eclipsed" interaction between two ethano bridges as indicated by the curved arrows in Figure 1. This would make diastereomer **18** less stable than diastereomer **14** with helical D_2 symmetry, explaining the predominance of **14** in the product mixture. The synthetic scheme for this "chirality recognition" approach is shown in Scheme III. The (±)-triple-layered dimethyl[2.2]paracyclophane (**12a**) prepared from the (±)-double-layered Hofmann base (**19b**) and **6b**, was treated with *N*-bromosuccinimide to furnish the (±)-monobromide **12b** which in turn was converted into the (±)-triple-layered quaternary ammonium salt (**13a**) according to Longone's procedure.[2a,b] Cross-breeding pyrolysis of a mixture of this racemic Hofmann base **13b** and the optically active double-layered Hofmann's base (*R*)-**8b** afforded, as was expected, (*R,R,R*)-(−)-five-layered [2.2]-paracyclophane (**14**, 3%), mp >300 °C, $[\alpha]^{22}\mathrm{D}$ −362°, as the cross-coupling product, and (*R,R*)-(−)-quadruple-layered [2.2]paracyclophane (**11**, 7%) as the product of self coupling of the optically active two-layered starting material. Since isolation of the (*R,R,R*)-five-layered compound (**14**) meant that the double-layered xylylene derivative (*R*)-(**16**) from the optically active intermediate (*R*)-(**8b**) coupled preferentially with (*R*)-(**17**) over its enantiomer (*S*)-(**17**), there must be left behind a mixture of (*R*)-(**17**) and (*S*)-(**17**) slightly rich in the

Scheme III





(20) **(21)**

Figure 2. Planar chirality of the inner benzene rings in [*n*]chochin.

Table I. Number of Stereoisomers of [*n*]Chochin

n	*N*	D_2 isomer	C_{2h} isomer	C_2 isomer
3	2	2		
4	3	2	1	
5	6	4		2
6	10	4	2	4
7	20	8		12
8	36	8	4	24

latter. We anticipated the isolation of (*S,S,S,S*)-(+)-six-layered paracyclophane from the reaction mixture, but so far we have been unable to isolate this optically active six-layered compound, the only isolable six-layered compound being the racemic modification (**15**, 0.5%).

Nomenclature. Having succeeded in the preparation of optically active multilayered [2.2]paracyclophanes, it seems pertinent to discuss their nomenclature in which special emphasis is placed upon designation of stereochemistry. Vögtle's nomenclature[8] considerably simplifies the cumbersome IUPAC names; e.g., the quadruple-layered [2.2]paracyclophane (**11**) would be named as [2.2](1,4)(1,4)[2.2](2,5)(1,4)-[2.2](2,5)(1,4)cyclophane. In spite of its logical approach, the names derived from this system are still long and especially inconvenient for describing stereochemistry. To remedy these difficulties, we would like to propose a genetic name "[*n*]-chochin"[9] for the family of multilayered compounds constructed solely from [2.2]paracyclophane units, where *n* represents the number of layers. Furthermore, the stereochemistry of an [*n*]chochin may be expressed by specifying the planar chirality[10] of each of the inner benzene rings. Figures 1 and 2 illustrate the application of this nomenclature. The symmetry inherent to an [*n*]chochin permits us to derive the following formula which will give the total number (*N*) of stereoisomers, where *n* is the number of layers. Since the repeating element is a [2.2]paracyclophane, whole stereoisomers have at least C_2 symmetry; when *n* is odd, the stereoisomers of [*n*]chochin are all chiral belonging to either D_2 or C_2 point groups; when *n* is even, there can arise achiral meso compounds which have C_{2h} symmetry. Table I tabulates the number of the stereoisomers for successive members (*n* = 3–8) of [*n*]chochin calculated by means of the formulas below.

n odd ($n \geqq 3$)

$$N = 2^{n-3} + 2^{(n-3)/2}$$

$$D_2 \text{ isomers: } 2^{(n-1)/2}$$

$$C_2 \text{ isomers: } 2^{n-3} - 2^{(n-3)/2}$$

n even ($n \geqq 4$)

$$N = 2^{n-3} + 2^{(n-4)/2}$$

$$D_2 \text{ isomers: } 2^{(n-2)/2}$$

$$C_2 \text{ isomers: } 2^{n-3} - 2^{(n-2)/2}$$

$$C_{2h} \text{ isomers: } 2^{(n-4)/2} \text{ (meso)}$$

Chiroptical Properties. Figure 3 records the circular dichroism curves in isooctane of (*R*)-(−)-4,7-dimethyl[2.2]-paracyclophane (**5**), (*R*)-(−)-**10**, (*R,R*)-(−)-**11**, (*R,R,R*)-(−)-**14**, and (*R,R,R,R*)-(−)-**15**. A common stereochemical feature among these compounds is the presence of the benzene ring(s) with the *R* planar chirality (**20**). As has been established by x-ray diffraction,[10] these benzene rings are not planar but instead distorted, having puckered conformations with approximate D_2 symmetry.

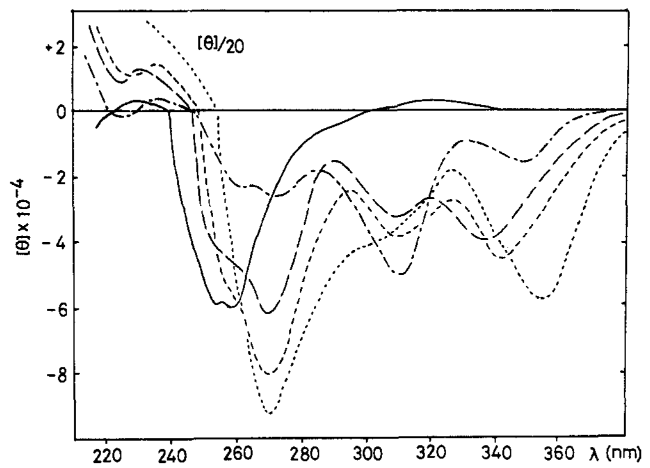
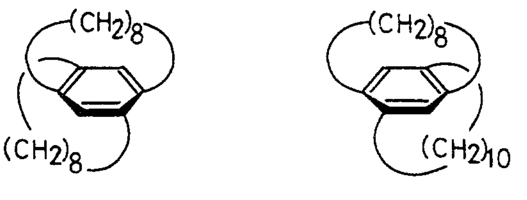


Figure 3. CD spectra of (*R*)-(−)-(**5**) (—), (*R*)-(−)-(**10**) (— — —), (*R,R*)-(−)-(**11**) (– –), (*R,R,R*)-(−)-(**14**) (- - - -), and (*R,R,R,R*)-(−)-(**15**) (· · ·) in isooctane.

(*MPM*)$_2$ D_2-twist benzene
(−)-Cotton effect
(240~360 nm)
(22)

(*PMP*)$_2$ D_2-twist benzene
(+)-Cotton effect
(240~360 nm)
(23)

Figure 4. Chirality of D_2-twist benzene.



(S)-(+)-(**24**) (R)-(−)-(**25**)

Figure 5.

The Cahn–Ingold–Prelog nomenclature[11] for conformational chirality can be extended to specify the chiralities of the enantiomeric D_2-twist benzenes as shown in Figure 4: (*MPM*)$_2$ D_2-twist benzene (**22**) and (*PMP*)$_2$ D_2-twist benzene (**23**). Inspection of molecular models indicates that the benzene rings in [2.2]paracyclophanes with the *R* planar chirality (**20**) suffer a distortion corresponding to the (*MPM*)$_2$ D_2-twist benzene ring (**22**), whereas the ones with the *S* planar chirality are deformed to have the (*PMP*)$_2$ D_2-twist benzene ring (**23**). The CD spectra (Figure 3) reveal that the compounds with (*MPM*)$_2$ D_2-twist benzene ring (**22**) exhibit negative Cotton effects at 240–360 nm. This generalization is supported by the positive Cotton effect observed in (*S*)-(+)-[8][8]paracyclophane (**24**) [with (*PMP*)$_2$ conformation] and negative Cotton effect observed in (*R*)-(−)-[8][10]paracyclophane (**25**) [with (*MPM*)$_2$ conformation].[12] In contrast to the rather simple CD spectra of these [*m*][*n*]paracyclophanes, the CD spectra of the multilayered [2.2]paracyclophanes are more complex, exhibiting bands which can be grouped roughly into 270, 310, and 340–360 nm regions. Face-to-face interactions between the distorted benzene rings should be responsible for this fine structure.[13] Theoretical analyses of the CD spectra of the multilayered [2.2]paracyclophanes as well as of [*m*][*n*]paracyclophanes are in progress in our laboratory.

Experimental Section

Melting points and boiling points are uncorrected. Infrared spectral data were obtained from a Hitachi EPI-S2 spectrophotometer. Nuclear magnetic resonance spectra were obtained from a JNM-MH-100 spectrometer. Ultraviolet spectra were recorded on a Hitachi EPS-3T spectrometer. Circular dichroism data were measured on a JASCO J-20 spectropolarimeter with CD attachment. Mass spectral data were measured on a Hitachi RMS-4 spectrometer.

(*R*)-(−)-4-Acetyl-7-methyl[2.2]paracyclophane (2). To a solution of anhydrous aluminum chloride (46 g) and acetyl chloride (32 g) in 1,1,2,2-tetrachloroethane (500 ml) at −30 °C was added in one portion (−)-4-methyl[2.2]paracyclophane (**1**,[6] 45 g). The mixture was kept at −15 to −20 °C with stirring for 10 min, and was then poured over ice. The separated organic phase was washed with 2 N hydrochloric acid, water, 3% sodium bicarbonate solution, and again with water, and then dried. After evaporation of the solvent, the solid product was recrystallized from methanol to give **2** (43 g, 81%): mp 142–143 °C; $[\alpha]^{22}\mathrm{D}$ −127° (*c* 0.34, $CHCl_3$); IR (KBr) 1670 (C=O), 1587, 1536, 1496, 1430, 1353, 1264, 948, 908, 876, 802, 723 cm^{-1}; NMR ($CDCl_3$) τ 3.16–3.95 (m, 6 H), 5.85–6.25 (m, 1 H), 6.52–7.55 (m, 7 H), 7.60 (s, 3 H), 7.92 (s, 3 H).

Anal. Calcd for $C_{19}H_{20}O$: C, 86.32; H, 7.63. Found: C, 86.31; H, 7.65.

(*R*)-(−)-4-Carbomethoxy-7-methyl[2.2]paracyclophane (3b). Bromine (60 g) was added during 30 min to a stirred solution of potassium hydroxide (60 g) in water (250 ml) at 0 °C. A solution of (−)-**2** (30 g) in dioxane (500 ml) was added to the hypobromite solution during a period of 1 h with continued cooling and stirring. The mixture was then stirred for 3 h at room temperature. The excess oxidizing reagent was destroyed by adding a solution of sodium bisulfite (2 g) in water (250 ml). After acidification of the solution with dilute hydrochloric acid, the precipitate was collected and dried under vacuum. The resulting crude acid was recrystallized from methanol to yield **3a** (24 g, 80%), mp 205–206 °C, $[\alpha]^{21}\mathrm{D}$ −224° (*c* 0.52, $CHCl_3$).

Anal. Calcd for $C_{18}H_{18}O_2$: C, 81.17; H, 6.81. Found: C, 81.08; H, 6.81.

This acid **3a** was esterified by heating under reflux for 2 h with methanol (200 ml) containing concentated sulfuric acid (10 ml). The cooled solution was then poured into water, and the product was extracted with ether. The ether extracts were washed with water, 3% sodium bicarbonate solution, and again with water, and then dried. After removal of the ether, the product was recrystallized from methanol to give **3b** (22 g, 87%): mp 136–137 °C; $[\alpha]^{22}\mathrm{D}$ −192° (*c* 0.34, $CHCl_3$); IR (KBr) 1670 (C=O), 1590, 1546, 1497, 1436, 1411, 1276, 943, 919, 876, 799, 717 cm^{-1}; NMR ($CDCl_3$) τ 0.2 (broad s, 1 H), 3.12–3.88 (m, 6 H), 5.59–6.06 (m, 1 H), 6.50–7.57 (m, 7 H), 7.88 (s, 3 H).

Anal. Calcd for $C_{19}H_{20}O_2$: C, 81.39; H, 7.19. Found: C, 81.34; H, 7.22.

(*R*)-(−)-4-Hydroxymethyl-7-methyl[2.2]paracyclophane (4a). A solution of **3b** (41 g) in dry tetrahydrofuran (300 ml) was added dropwise to a suspension of lithium aluminum hydride (5.5 g) in dry tetrahydrofuran (200 ml). The mixture was heated under reflux for 6 h, and excess reducing reagent was decomposed by addition of ethyl acetate. After the mixture was acidified with dilute hydrochloric acid, the organic phase was extracted with ether. The ether solution was washed with water, 3% sodium bicarbonate solution, and again with water, and then dried. After evaporation of the ether, the solid material was recrystallized from benzene–hexane to give **4a** (32 g, 91%): mp 100–101 °C; $[\alpha]^{23}\mathrm{D}$ −133° (*c* 0.39, $CHCl_3$); IR (KBr) 3400 (O–H), 1590, 1495, 1450, 1435, 1407, 1064, 1026, 993, 910, 873, 800, 716 cm^{-1}; NMR ($CDCl_3$) τ 3.22–3.78 (m, 6 H), 5.36–5.71 (AB quartet, $J_{AB} = 12.8$ Hz, 2 H), 6.45–7.50 (m, 8 H), 7.93 (s, 3 H), 8.33 (s, 1 H).

Anal. Calcd for $C_{18}H_{20}O$: C, 85.67; H, 7.99. Found: C, 85.87; H, 8.03.

(*R*)-(−)-4-Bromomethyl-7-methyl[2.2]paracyclophane (4b). To a stirred solution of the alcohol **4a** (73 g) in dry ether (2 l.) was added dropwise a solution of phosphorus tribromide (78.3 g) in dry ether (400 ml) at room temperature. The mixture was stirred for 2 h at room temperature, and water (300 ml) was slowly added to the reaction mixture. The separated organic phase was washed with dilute sodium bicarbonate solution and water, and then dried. After removal of the ether, the solid product was recrystallized from carbon tetrachloride to yield **4b** (78 g, 87%): mp 138–139 °C; $[\alpha]^{22}\mathrm{D}$ −23° (*c* 0.76, $CHCl_3$); IR (KRr) 1590, 1495, 1456, 1433, 1409, 1372, 1214, 946, 912, 878, 807, 767, 729, 717 cm^{-1}; NMR ($CDCl_3$) τ 2.97–3.96 (m, 6 H), 5.53–5.83 (AB quartet, $J_{AB} = 10.4$ Hz, 2 H), 6.42–7.94 (m, 8 H), 7.91 (s, 3 H).

Anal. Calcd for $C_{18}H_{19}Br$: C, 68.57; H, 6.09. Found: C, 68.76; H, 5.98.

(*R*)-(−)-4,7-Dimethyl[2.2]paracyclophane (5). A solution of **4b** (0.5 g) in dry tetrahydrofuran (7 ml) was added dropwise to a suspension of lithium aluminum hydride (0.2 g) in dry tetrahydrofuran (10 ml). The mixture was heated under reflux for 10 h, and the excess reducing reagent was decomposed by addition of dilute hydrochloric acid. The aqueous and organic layers were separated and the aqueous layer extracted with ether. The combined organic layers were washed with 3% sodium bicarbonate solution and water and dried. After concentration, the solid material was recrystallized from ethanol to give **5** (0.28 g, 75%): mp 140–141 °C; $[\alpha]^{23}\mathrm{D}$ −155° (*c* 0.73, $CHCl_3$); MS *m/e* 236 (M^+); IR (KBr) 2970, 2880, 2820, 1590, 1445, 1433, 1403, 1383, 1362, 1086, 980, 950, 932, 899, 870, 708 cm^{-1}; NMR ($CDCl_3$) τ 3.31 (dd, $J = 8, 2$ Hz, 2 H), 3.74 (dd, $J = 8, 2$ Hz, 2 H), 4.11 (s, 2 H), 6.62–7.63 (m, 8 H), 7.96 (s, 6 H); CD (isooctane), $[\theta] \times 10^{-4}$ (nm) 0 (223), +13.4 (230.5), 0 (240), −5.67 (251.5), −6.02 (261), −0.75 (287), 0 (299), +0.64 (313.5), 0 (330).

Anal. Calcd for $C_{18}H_{20}$: C, 91.47; H, 8.53. Found; C, 91.45; H, 8.53.

(±)-4,7-Dimethyl[2.2]paracyclophane (5). A mixture of *p*-methylbenzyltrimethylammonium bromide (**6a,** 4.0 g) and duryltrimethylammonium bromide[2] (**7a,** 4.3 g) was dissolved in water (100 ml) and treated with freshly prepared silver oxide. To the resulting mixture of quaternary bases, **6b** and **7b,** was added toluene (100 ml) containing phenothiazine (30 mg), and the mixture was heated with stirring. After removal of water by azeotropic distillation, the reaction mixture was refluxed for 3 h. The insoluble polymer was removed from the reaction mixture and the filtrate was concentrated under vacuum. The resulting solid was chromatographed on neutral alumina. Elution with hexane gave [2.2]paracyclophane (**9**), 4,7-dimethyl[2.2]paracyclophane (**5**), and 4,7,12,15-tetramethyl[2.2]paracyclophane.[14] The compound **5** was recrystallized from hexane, 0.35 g (8.4%), mp 151–152 °C.

Anal. Calcd for $C_{18}H_{20}$: C, 91.47; H, 7.53. Found: C, 91.48; H, 8.51.

(*R*)-(−)-4-Trimethylammoniomethyl-7-methyl[2.2]paracyclophane Bromide (8a). A solution of **4b** (87 g) in ether (2 l.) was treated with excess anhydrous trimethylamine. The resulting salt was collected by filtration, washed with ether, and dried to afford **8a** (99 g, 95%). An analytical sample was recrystallized from ethanol–benzene, mp 213–215 °C, $[\alpha]^{20}\mathrm{D}$ −94° (*c* 0.72, CH_3OH).

Anal. Calcd for $C_{21}H_{28}NBr$: C, 67.37; H, 7.54; N, 3.74; Br, 21.35. Found: C, 67.51; H, 7.62; N, 3.71; Br, 21.46.

(*R*)-(−)-Triple-Layered (10) and (*R,R*)-(−)-Quadruple-Layered [2.2]Paracyclophane (11). A mixture of *p*-methylbenzyltrimethylammonium bromide (**6a,** 2.8 g) and **8a** (4.0 g) was dissolved in water (150 ml) and treated with freshly prepared silver oxide. To the resulting aqueous solution of quaternary bases, **6b** and **8b,** was added toluene (150 ml) containing phenothiazine (50 mg), and the mixture was heated with stirring. After removal of water by azeotropic distillation, the reaction mixture was refluxed for 6 h. The insoluble polymer was removed from the reaction mixture, the resulting filtrate was concentrated to a small volume under vacuum, and the remaining solution was chromatographed on neutral alumina. Elution with hexane–benzene (9:1) gave [2.2]paracyclophane (**9,** 0.11 g, 7%). Further elution with hexane–benzene (5:1) produced (−)-triple-layered [2.2]paracyclophane (**10**) and (−)-quadruple-layered compound (**11**). The compound **10** was recrystallized from hexane: 0.19 g (5%); mp 170–171 °C; $[\alpha]^{28}\mathrm{D}$ −256° (*c* 0.67, $CHCl_3$); IR (KBr) 2960, 2880, 2820, 1580, 1491, 1448, 1424, 1183, 925, 901, 862, 707, 678 cm^{-1}; UV (isooctane) λ_{max} 227 sh, 280, 291 sh, 348 nm (log ϵ 4.21, 4.27, 4.22, 2.41); NMR ($CDCl_3$) τ 3.85 (s, 8 H), 4.65 (s, 2 H), 6.8–7.7 (m, 16 H); CD (isooctane) $[\theta] \times 10^{-4}$ (nm) 0 (222.5), −2.77 (226), 0 (230), +9.67 (236), 0 (250), −2.26 (260), −2.59 (272), −5.15 (309), −1.50 (350), 0 (374); MS *m/e* 338 (M^+).

Anal. Calcd for $C_{26}H_{26}$: C, 92.26; H, 7.74. Found: C, 92.28; H, 7.81.

The compound **11** was recrystallized from hexane–benzene: 0.1 g (4%); mp 230–231 °C; $[\alpha]^{21}\mathrm{D}$ −285° (*c* 0.39, $CHCl_3$); IR (KBr) 2950, 2880, 2820, 1580, 1492, 1448, 1424, 1184, 924, 880, 866, 788, 707, 685, 668 cm^{-1}; UV (isooctane) λ_{max} 230 sh, 267 sh, 310 nm (log ϵ 4.20, 3.61, 3.27, 2.86); NMR ($CDCl_3$) τ 3.98 (s, 4 H), 4.65 (s, 2 H), 6.8–7.7 (m, 24 H); CD (isooctane) $[\theta] \times 10^{-4}$ (nm) 0 (211), +31.2 (217.5), +26.3 (232.5), 0 (249), −4.59 (260), −6.26 (272), −3.30 (311), −3.97 (339), −2.62 (355), 0 (385); MS *m/e* 468 (M^+).

Anal. Calcd for $C_{36}H_{36}$: C, 92.26; H, 7.74. Found: C, 92.27; H, 7.76.

(±)-Dimethyl Derivative of Triple-Layered [2.2]Paracyclophane (12a). A mixture of quaternary ammonium bromide (**19a**,[12] 50 g), methylbenzyltrimethylammonium bromide (**6a**, 160 g), and water (2 l.) was converted to the hydroxides, **6b** and **19b**, in the usual manner using silver oxide. After removal of the solids, the aqueous solution was evaporated to 500 ml under vacuum. The resulting solution was mixed with toluene (1.3 l.) containing phenothiazine (2 g), and heated to reflux. Water was removed by azeotropic distillation, and the reaction mixture was refluxed for 3 h. After the insoluble polymer was removed from the reaction mixture, the filtrate was concentrated to 200 ml under vacuum. Insoluble polymer and [2.2]paracyclophane were filtered off, and the filtrate was concentrated. The concentrate was chromatographed on neutral alumina with hexane. The resulting product was recrystallized from hexane to give (±)-**12a** (14 g, 33%): mp 175–176 °C; IR (KBr) 2950, 2880, 2820, 1584, 1496, 1453, 1432, 944, 906, 877, 801, 730, 721, 703, 682 cm^{-1}; UV (isooctane) λ_{max} 233 sh, 286 sh, 344 nm (log ϵ 4.11, 3.38, 2.08); NMR ($CDCl_3$) τ 3.80 (s, 4 H), 4.33 (s, 2 H), 4.37 (s, 2 H), 6.80–7.91 (m, 16 H), 8.14 (s, 6 H); MS *m/e* 366 (M$^+$).

Anal. Calcd for $C_{28}H_{30}$: C, 91.75; H, 8.25. Found: C, 91.71; H, 8.26.

(*R*)-(−)-Dimethyl Derivative of Triple-Layered [2.2]Paracyclophane (12a). The preparation of (−)-**12a** was carried out by the same method described for the preparation of (±)-**12a**, utilizing the quaternary ammonium bromides, **8a** (45 g) and **7a** (120 g). (−)-Dimethyl compound **12a** was purified by column chromatography on neutral alumina and recrystallized from hexane, affording 12.2 g (28%), mp 170–171 °C, $[\alpha]^{21}D$ −241° (*c* 0.46 $CHCl_3$).

Anal. Calcd for $C_{28}H_{30}$: C, 91.75; H, 8.25. Found: C, 91.71; H, 8.27.

(±)-Quaternary Ammonium Bromide (13a). A mixture of (±)-**12a** (13.5 g), *N*-bromosuccinimide (3.5 g), benzoyl peroxide (20 mg), and carbon tetrachloride (300 ml) was heated to reflux for 4 h. After removal of succinimide, the filtrate was concentrated under vacuum. The concentrate was taken up in ether and treated with excess anhydrous trimethylamine to give (±)-**13a** (7.5 g, 82% based on *N*-bromosuccinimide). An analytical sample was recrystallized from water to give the monohydrate, mp >300 °C.

Anal. Calcd for $C_{31}H_{38}NBr \cdot H_2O$: C, 72.65; H, 5.90; N, 2.73; Br, 15.59. Found: C, 72.86; H, 5.96; N, 2.66; Br, 15.71.

(*R*)-(−)-Quaternary Ammonium Bromide (13a). The optically active ammonium bromide **13a** (6.8 g, 82% based on *N*-bromosuccinimide) was prepared from (−)-**12a** (12 g) following the method described for the preparation of racemic **13a**. An analytical sample was recrystallized from water to give the monohydrate, mp >300 °C, $[\alpha]^{21}D$ −148° (*c* 0.63, $CHCl_3$).

Anal. Calcd for $C_{31}H_{38}NBr \cdot H_2O$: C, 72.65; H, 5.90; N, 2.73; Br, 15.59. Found: C, 72.78; H, 5.93; N, 2.79; Br, 15.69.

(*R,R,R*)-(−)-Quintuple-Layered [2.2]Paracyclophane (14) and (*R,R,R,R*)-(−)-Sextuple-Layered [2.2]Paracyclophane (15). The aqueous hydroxide solution, derived from a mixture of (−)-**13a** (6 g) and (−)-**8a** (4 g), was mixed with toluene (200 ml) and phenothiazine (0.2 g), and then pyrolyzed as described for the preparation of (−)-**10** and (−)-**11**. Insoluble polymers were removed from the mixture and the filtrate was concentrated under vacuum. The resulting solid was chromatographed on neutral alumina. Elution of the column with hexane–benzene (9:1) provided (−)-**11** (0.5 g, 6%). Further elution with hexane–benzene (5:1) produced (−)-**14** (0.13 g, 3%), which when recrystallized from hexane–benzene gave mp >300 °C; $[\alpha]^{22}D$ −362° (*c* 0.22, $CHCl_3$); IR (KBr) 2940, 2890, 2830, 1582, 1497, 1477, 1450, 1425, 1182, 946, 894, 870, 796, 716, 673 cm^{-1}; UV (isooctane) λ_{max} 271 sh, 350 nm (log ϵ 3.90, 2.70); NMR ($CDCl_3$) τ 3.90 (s, 8 H), 4.85 (s, 4 H), 5.00 (s, 2 H), 6.1–8.1 (m, 32 H); CD (isooctane) $[\theta] \times 10^{-4}$ (nm) 0 (211), +42.6 (218), +28.5 (234), 0 (252), −8.11 (271.5), −3.74 (312), −4.47 (343), 0 (390); MS *m/e* 598 (M$^+$).

Anal. Calcd for $C_{46}H_{46}$: C, 92.26; H, 7.74. Found: C, 92.25; H, 7.76.

Elution with hexane–benzene (1:1) afforded (−)-**15** (0.05 g, 1.4%), which when recrystallized from benzene gave mp >300 °C; $[\alpha]^{16}D$ −420° (*c* 0.24, $CHCl_3$); IR (KBr) 2940, 2890, 2830, 1582, 1495, 1477, 1453, 1425, 1182, 893, 749, 711, 672 cm^{-1}; UV (isooctane) λ_{max} 275 sh, 355 sh nm (log ϵ 3.93, 3.09); NMR ($CDCl_3$) τ 3.94 (s, 8 H), 4.95 (s, 4 H), 5.15 (s, 4 H), 7.0–8.2 (m, 40 H); CD (isooctane) $[\theta] \times 10^{-4}$ (nm) 0 (257), −9.28 (274), −3.97 (310), −5.80 (355), 0 (400); MS *m/e* 728 (M$^+$).

Anal. Calcd for $C_{56}H_{56}$: C, 92.26; H, 7.74. Found: C, 92.29; H, 7.71.

Preparation of (*R,R,R*)-(−)-[5]Chochin (14) by "Chiral Recognition". The hydroxide solution (100 ml) derived from a mixture of quaternary ammonium bromides, (±)-**13a** (8.8 g) and (−)-**8a** (9.1 g), was pyrolyzed in the usual manner. After removal of the insoluble polymers, the filtrate was concentrated under vacuum and the residual oil was chromatographed on neutral alumina. Elution with hexane–benzene (9:1) gave (−)-**11** (0.4 g, 7%). Further elution with hexane–benzene (5:1) produced (−)-**14** (0.3 g, 3%), mp >300 °C, $[\alpha]^{21}D$ −349° (*c* 0.20, $CHCl_3$). Elution with benzene provided (±)-**15** (30 mg, 0.5%) as sparingly soluble prisms, which when recrystallized from xylene gave mp >300 °C.

Anal. Calcd for $C_{56}H_{56}$: C, 92.26; H, 7.74. Found: C, 92.28; H, 7.73.

Registry No.—**1**, 24351-81-3; **2**, 60582-60-7; **3a**, 32212-95-6; **3b**, 60582-61-8; **4a**, 36325-22-1; **4b**, 36325-23-2; (−)-**5**, 32212-91-2; (±)-**5**, 60582-62-9; **6a**, 16814-21-4; **7a**, 27742-95-6; **8a**, 36659-06-0; **10**, 36757-08-1; **11**, 60619-06-9; (±)-**12a**, 60619-07-0; (−)-**12a**, 60619-08-1; (±)-**13a**, 60619-09-2; (−)-**13a**, 60619-10-5; **14**, 60619-11-6; (−)-**15**, 60619-12-7; (±)-**15**, 60619-13-8; **19a**, 60619-14-9.

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