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Preparation of (−)-(*M*)-[2.2]Paracyclophanohexahelicene from (−)-(*M*)-1,4-Dimethylhexahelicene and the Absolute Configuration of 4-Substituted [2.2]Paracyclophanes

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Photocyclization of a cis–trans mixture of the 1,2-diarylethylene precursor **9** gives 1,4-dimethylhexahelicene (**10**). The levorotatory enantiomer of **10** with *M* helicity is converted to (−)-(*M*)-[2.2]paracyclophanohexahelicene (**6**), which confirms the *R* configuration previously assigned to (−)-[2.2]paracyclophanecarbaldehyde (**5**).

Our continuing interest in chiroptical properties of twisted π-electron systems has led us to prepare the trans doubly bridged ethylene **1**,[1] [8][8]paracyclophane (**2**),[2] and the multilayered [2.2]paracyclophane (**3**)[3] in optically active modification (Chart I).

In our assignment of *S* and *S,S,S,S* configurations to (+)-**2** and (+)-**3**, optically active [2.2]paracyclophanecarboxylic acid (**4**) played an important role as a stereochemical liaison compound.

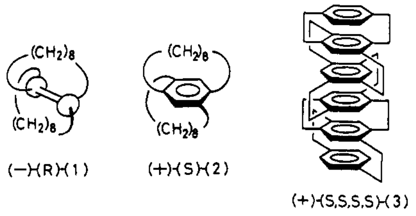
Among various chemical methods[4-8] previously reported for assignment of an *R* configuration to carboxylic acid **4**, Martin and co-worker's synthetic approach[8] (Scheme I) has been most convincing.

In their experiment, which was originally designed to elucidate the absolute configuration of (−)-hexahelicene (**11**) by correlating it with the "established" *R* configuration[9] of (−)-**4**, they converted (−)-**4**, via the (−)-aldehyde **5**, to the (−) doubly layered hexahelicene **6**.

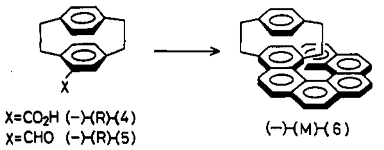
The unique stereochemistry inherent to the [2.2]paracyclophane system **5** with *R* configuration should force the layered hexahelicene **6** to assume a configuration with *M* helicity, and comparison of the ORD curves of (−)-**6** and (−)-hexahelicene (**11**) eventually enabled them to assign *M* helicity to (−)-**11**.

Since there has been accumulated ample experimental evidence[10] to support the *M* helicity of (−)-hexahelicene (**11**), their approach can rather be regarded, contrary to their original intention, as a most reliable chemical correlation to give the *R* configuration to the (−)-aldehyde **5**.

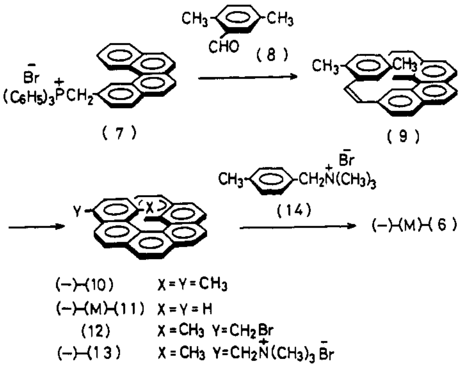
Chart I



Scheme I



Scheme II



It is unfortunate, however, that their final product **6** was apparently impure (reportedly exhibits a blue fluorescence) and has been poorly characterized, seemingly because of its alleged instability.

Recently, we have reported the microbial reduction of [2.2]metacyclophane derivatives and revised the absolute configuration[11] of 4-substituted [2.2]metacyclophanes closely related to **4**. This prompted us to reexamine Martin's work along the opposite direction of their original approach, i.e., preparation of the optically active [2.2]paracyclophanohexahelicene (**6**) from 1,4-dimethylhexahelicene (**10**) with known absolute configuration (Scheme II).

Results and Discussion

Preparation of (−)-[2.2]Paracyclophanohexahelicene (6) from (−)-1,4-Dimethylhexahelicene (10, Scheme II). The Wittig reaction between 2,5-dimethyl-

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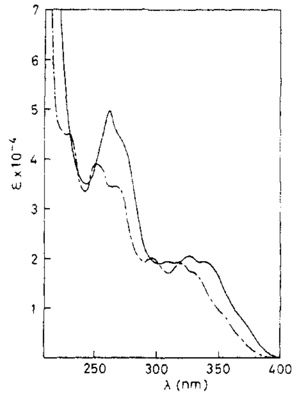

Figure 1. UV spectra of (−)-1,4-dimethylhexahelicene (**10**, -·-) and the (−) doubly layered hexahelicene **6** (—) (in hexane).

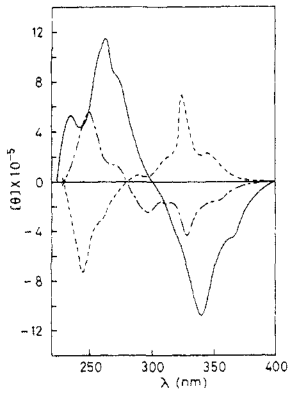

Figure 2. CD spectra of (+)-(*P*)-hexahelicene (**11**, ---), (−)-1,4-dimethylhexahelicene (**10**, -·-), and the (−) doubly layered hexahelicene **6** (—) (in hexane).

benzaldehyde (**8**) and [(2-benzo[*c*]phenanthryl)methyl]triphenylphosphonium bromide (**7**) gave a ca. 1:1 mixture of cis–trans isomers of the 1,2-diarylethylene **9** whose recrystallization from hexane–benzene furnished a 31% yield of the trans isomer, mp 129–130 °C. The cis–trans mixture of **9** was dissovled in benzene containing a small amount of iodine and was irradiated with a medium-pressure mercury lamp for 4 h. Column chromatography gave 1,4-dimethylhexahelicene (**10**; 64% yield; mp 252–253 °C) which was characterized by its two CH_3 NMR signals at δ 0.54 and 2.42, corresponding to the inner and outer methyl groups. Optical resolution was accomplished by column chromatography over chiral poly(triphenylmethyl methacrylate),[12] and elution with hexane afforded a specimen of (−)-**10** (mp 241–243 °C; $[\alpha]_{577}$ −432°) whose ca. 12% optical purity was estimated from the reported value of $[\alpha]_{578}$ −3756°[13] of (−)-hexahelicene (**11**).

Photochemical NBS bromination in CCl_4 converted (−)-**10** into the bromide **12**, which was directly treated with trimethylamine in ether to produce the (−) ammonium bromide **13**, $[\alpha]_D$ −465°. From a 2:1 molar equiv mixture of *p*-xylyltrimethylammonium bromide (**14**) and (−)-**13**, Cram's *coupling*[14] *afforded a complex mixture of* doubly layered cyclophanes. Column chromatography of the product over SiO_2 gel gave crude, layered hexahelicene **6** whose preparative TLC (SiO_2) followed by recrystallization from ethyl acetate yielded (−)-[2.2]paracyclophanohexahelicene (**6**) as yellow prisms: 4% yield; mp 236–237 °C; $[\alpha]_{577}$ −662°. Our final product **6** was found to be quite stable in the solid state as well as in various solutions and exhibits almost no detectable fluorescence under diffused room light or on UV irradiation.

Table I

fraction	weight, mg	$[\alpha]^{28}_D$ ($CHCl_3$), deg
1	33	−690
2	129	−310
3	164	−30
4	39	+630
5	10	+1700
6	7	+2656

Chiroptical Properties and Absolute Configuration. Comparison of the UV spectra of (−)-1,4-dimethylhexahelicene (**10**) and the (−) doubly layered hexahelicene **6** (Figure 1) shows that introduction of a [2.2]paracyclophane moiety markedly enhances absorption in the 240–280-nm region with a slight bathocromic shift, and this is also reflected in its CD spectrum (Figure 2).

Our estimation of ca. 12% optical purity for the starting optically active **10** allowed us to calculate an absolute rotation $[\alpha]_{577}$ −5520°[15] for the (−) doubly layered hexahelicene **6**. Inspection of Figure 2 should provide convincing evidence to support (−)-1,4-dimethylhexahelicene (**10**) as having *M* helicity, opposite that of (+)-(*P*)-hexahelicene (**11**),[10] and this conclusion automatically assigns the same *M* helicity to the (−) doubly layered hexahelicene **6** prepared from (−)-**10**.

Since this doubly layered (−)-**6** with *M* helicity is the enantiomer originally synthesized from (−)-[2.2]paracyclophanecarbaldehyde (**5**) by Martin, our present experiment assigns the *R* configuration to this (−)-aldehyde **5**, providing complementary evidence to support Martin's previous result.

Experimental Section

All melting points are uncorrected. Infrared spectral data were obtained from a Hitachi 260-10 infrared spectrophotometer. Nuclear magnetic resonance spectra were determined on a JNM MH-100 spectrometer. Ultraviolet spectra were recorded on a Hitachi EPS-3T spectrometer. Mass spectral data were measured on a Hitachi RMS-4 spectrometer. Circular dichroism (CD) spectra were obtained from a JASCO J-40 spectropolarimeter. Elemental analyses were performed by a Yanagimoto CHN-Corder, Type II.

1-(2,5-Dimethylphenyl)-2-(2-benzo[*c*]phenanthryl)ethylene (9). To a stirred solution of [(2-benzo[*c*]phenanthryl)methyl]triphenylphosphonium bromide (**7**;[16] 23.1 g, 0.040 mol) and 2,5-dimethylbenzaldehyde (**8**;[17] 5.9 g, 0.044 mol) in dry DMF (80 mL) was added dropwise a solution of CH_3ONa (7.5 g, 0.14 mol) in dry DMF (60 mL). After being stirred for 3 days at room temperature, the reaction mixture was poured into water (300 mL) and extracted with chloroform. The chloroform extract was washed with water and then dried ($MgSO_4$). After evaporation of the solvent, the residual oil was chromatographed on neutral alumina. Elution with hexane–benzene (5:1) produced a mixture of the cis and trans isomers of **9** (12.8 g). Separation of the pure trans isomer was achieved by recrystallization of the mixture from hexane–benzene, affording 44 g (31% yield) of *trans*-**9**: mp 129–130 °C; IR (KBr) 3040, 3020, 2940, 2920, 2860, 1600, 1500, 1490, 965, 855, 842, 830, 814, 753, 742 cm^{-1}; NMR (CCl_4) δ 2.38 (s, 3 H), 2.42 (s, 3 H), 7.10–8.18 (m, 14 H), 9.06–9.25 (m, 2 H).

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Anal. Calcd for $C_{28}H_{22}$: C, 93.81; H, 6.19. Found: C, 93.64; H, 6.11.

1,4-Dimethylhexahelicene (10). The mixture of the cis–trans olefins **9** (500 mg) was dissolved in benzene (350 mL) containing iodine (4 mg), and the solution was irradiated with a medium-pressure mercury lamp (Toshiba SHL-100UV) in an atmosphere of nitrogen for 4 h. After the solvent was removed, the residue was chromatographed over alumina. Benzene–hexane eluates were collected, and removal of the solvent left a yellow solid, which was recrystallized from ethyl acetate to give **10**: 320 mg (64%); yellow prisms; mp 252–253 °C; IR (KBr) 3040, 3020, 2960, 2930, 2920, 2880, 1600, 1476, 1440, 1430, 820, 812, 802, 743 cm^{-1}; NMR ($CDCl_3$) δ 0.54 (s, CH_3, 3 H), 2.42 (s, CH_3, 3 H), 6.00–8.10 (m, Ar H, 14 H); UV (hexane) λ_{max} 230 nm (log ϵ 4.63), 252 (4.59), 270 (4.53), 297 (4.30), 318 (4.29), 330 (sh, 4.23), 354 (sh, 3.94); mass spectrum, *m/e* 356 (M^+).

Anal. Calcd for $C_{28}H_{20}$: C, 94.08; H, 5.80. Found: C, 94.24; H, 5.76.

Optical Resolution of 1,4-Dimethylhexahelicene (10). A finely ground powder of chiral poly(triphenylmethacrylate)[12] (2.0 g) was swollen with hexane (5 mL) and was packed in a glass tube (12 mm i.d.) to give a 5-cm column. A solution of (±)-dimethylhexahelicene (**10**, 0.4 g) in hexane was introduced into the column, and eluted with hexane to give the 10-mL aliquots (Table I).

The procedure was repeated to process a total of 6.4 g of the 1,4-dimethylhexahelicene (**10**), and the combined first and second fractions gave the (–) enantiomer **10**: 2.3 g; mp 241–243 °C; $[\alpha]^{28}_{\mathrm{D}}$ –404°, $[\alpha]^{28}_{577}$ –432° ($CHCl_3$).

Anal. Calcd for $C_{28}H_{20}$: C, 94.08; H, 5.80. Found: C, 94.29; H, 5.69.

1-Methyl-4-(bromomethyl)hexahelicene (12). A stirred and refluxed solution of (–)-**10** (2.3 g, 6.5 mmol), NBS (1.1 g, 6.5 mmol), and benzoyl peroxide (4 mg) in CCl_4 (50 mL) was irradiated with a tungsten lamp (100 W) for 4 h. The mixture freed of the precipitated succinimide was washed with 3% $NaHCO_3$ and water and then was dried ($MgSO_4$). After removal of the solvent, the residue was column chromatographed over SiO_2 gel (20 g), and elution with benzene gave the bromide **12** as a yellow viscous oil which was converted into the double-layerd helicene **6** without further purification: NMR ($CDCl_3$) δ 4.20 (q, J_{ab} = 12 Hz, CH_2); mass spectrum *m/e* 435 (M^+).

(–)-Quaternary Ammonium Bromide (13). To a chilled solution of the crude bromide **12** (3.0 g) in absolute ether (20 mL) was added trimethylamine (15 mL), and the mixture was stirred at room temperature for 13 h. The precipitate was collected and washed with ether to give a white solid: 1.2 g (38% yield from the dimethyl derivative **10**); $[\alpha]^{28}_{\mathrm{D}}$ –465° ($CHCl_3$).

(–)-[2.2]Paracyclophanohexahelicene (6). A mixture of (–)-**13** (1.1 g, 2.22 mmol) and *p*-xylyltrimethylammonium bromide (**14**;[14] 1.4 g, 5.73 mmol) was dissolved in water (300 mL), and freshly prepared silver oxide (from 5 g of silver nitrate) was added. After the mixture was stirred for 24 h at room temperature, the precipitate was removed by filtration, and the filtrate was concentrated to 100 mL under vacuum. The concentrated hydroxide solution was mixed with toluene (100 mL) containing phenothiazine (20 mg) and heated to reflux. After removal of water by azeotropic distillation, the reaction mixture was refluxed for 4 h. The mixture freed of an isoluble polymer by filtration was concentrated in vacuo, and the residue was chromatographed over SiO_2 gel. While elution with hexane gave [2.2]paracyclophane (110 mg), further elution with hexane–benzene (5:1) produced crude (–)-**6** which was purified by preparative TLC (SiO_2 gel). Elution of hexane yielded (–)-**6** (40 mg, 4%), which was recrystallized from ethyl acetate: mp 236–237 °C ; yellow prisms; $[\alpha]^{28}_{\mathrm{D}}$ –584°, $[\alpha]^{28}_{577}$ –662° ($CHCl_3$); IR (KBr) 3060, 3040, 3010, 2950, 1600, 1580, 840, 812, 800, 790, 763, 739, 712 cm^{-1}; NMR ($CDCl_3$) δ 1.42–2.07 (m, 4 H), 2.76–3.17 (m, 3 H), 3.62–4.00 (m, 1 H), 4.60 (dd, *J* = 8, 2 Hz, 1 H), 5.62 (dd, *J* = 8, 2 Hz, 1 H), 5.82 (d, *J* = 8 Hz, 1 H), 6.15 (t, *J* = 8 Hz, 1 H), 6.22–6.46 (m, 3 H), 6.80–7.08 (m, 2 H), 7.62 (d, *J* = 8 Hz, 1 H), 7.77–8.12 (m, 8 H); UV (hexane) λ_{max} 233 nm (sh, log ϵ 4.62), 263 (4.70), 272 (sh, 4.64), 310 (4.28), 325 (4.32), 340 (4.29), 367 (sh, 3.92); CD (hexane) 10^{-5} $[\Theta]$ (λ, nm) +0.61 (234), +1.35 (263), +0.98 (273), –1.25 (340), –0.51 (367); mass spectrum, *m/e* 458 (M^+).

Anal. Calcd for $C_{36}H_{26}$: C, 94.27; H, 5.65. Found: C, 94.28; H, 5.72.

Registry No. (–)-**6**, 37044-40-9; **7**, 35160-98-6; **8**, 5779-94-2; *cis*-**9**, 76756-20-2; *trans*-**9**, 76756-21-3; (±)-**10**, 76756-22-4; (–)-**10**, 76820-61-6; (+)-**11**, 17486-32-7; **12**, 76756-23-5; (–)-**13**, 76756-24-6; **14**, 16814-21-4.

Reaction of $HCo(CO)_4$ with Methyl 2,3-Diphenyl-2-cyclopropene-1-carboxylate: Synthesis of Methyl *t*,*t*-2,3-Diphenyl-*c*-2-formylcyclopropane-*r*-1-carboxylate

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Reaction of $HCo(CO)_4$ with the diphenylcyclopropene **1** leads to the three possible hydrogenated cyclopropanes but in addition a single hydroformylation product is formed. This aldehyde was synthesized by an unambiguous procedure; it is compound **2**, formed by cis addition of $HCo(CO)_4$ to the more hindered face of the cyclopropene.

Introduction

Although most highly conjugated olefins react with $HCo(CO)_4$ under stoichiometric conditions to give hydrogenated products, we have found that methyl 2,3-diphenyl-2-cyclopropene-1-carboxylate, **1**, undergoes stoichiometric hydroformylation to give an 18–22% yield of a single pure aldehyde with the balance of the material consisting of hydrogenated isomers. The structure of the aldehyde could be one of the four possible aldehydes **2**–**5**. Compounds **2** and **3** would arise from cis addition to either face of **1**, while **4** and **5** would result from trans addition. Because of the paucity of information on the stereochemistry of the stoichiometric hydroformylation (e.g., is the reaction a concerted 1,2-addition, or a stepwise radical or cationic reaction),[1] it was considered important to determine which of the four possible aldehydes is formed in the above reaction.

Results and Discussion

The aldehyde isolated from the stoichiometric hydroformylation of **1** is a nicely crystalline colorless compound, mp 144.5–145.0 °C. Treatment of it with $LiAlH_4$ gives a

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