tered. The filtrate was washed with ether and acidified with concentrated HCl. The precipitate was washed with water and dried to afford **4** (810 mg, 94%): mp 208–210 °C dec (lit.[15] mp 240–242 °C). Recrystallization from chlorobenzene afforded pure **4**, mp 242–243 °C dec, with quantitative recovery: NMR (acetone-d_6) δ 4.30 (s, 2, CH_2) and 7.80–8.40 (m, 10, aromatic, CO_2H).

3-Oxo-3,4-dihydrocyclopenta[*cd*]pyrene (5). A solution of **4** (800 mg, 3.1 mmol) in liquid HF was stirred for 15 h. The HF was removed under a stream of N_2, and the solid residue was taken up in 250 mL of 1:1 ether–benzene. This solution was washed twice with saturated $NaHCO_3$ solution and water, dried ($MgSO_4$), filtered, and evaporated to dryness. The crude **5** was purified by chromatography on silica gel. Concentration of the benzene fraction afforded pure **5** (650 mg, 87%): mp 216–217 °C dec (lit.[7,8] mp 214 °C; 201–203 °C); NMR δ 3.78 (s, 2, CH_2) and 7.8–8.6 (m, 8, aromatic).

3-Hydroxy-3,4-dihydrocyclopenta[*cd*]pyrene (9). Sodium borohydride (500 mg, 13 mmol) was added to a solution of the ketone **5** (650 mg, 2.7 mmol) in methanol (25 mL), and the resulting solution was stirred at ambient temperature for 2 h. Following evaporation of the solvent, distilled water (25 mL) was added and the product extracted with 2:1 ether–THF. The combined extracts were washed with water, dried, and concentrated to afford **9** (640 mg, 98%): mp 212–214 °C dec (lit.[8] mp 213–215 °C); NMR δ 3.60 (dd, 1 H), 4.20 (dd, 1 H), 6.21 (dd, 1 H), and 7.80–8.50 (m, 8, aromatic).

Cyclopenta[*cd*]pyrene (1). A solution of **9** (500 mg, 2.0 mmol) and *p*-toluenesulfonic acid (1 mg) in benzene (300 mL) was heated at reflux for 30 min and then cooled, washed with dilute aqueous NaOH and water, dried ($MgSO_4$), and evaporated to dryness to afford crude **1**. The latter was purified by chromatography on silica gel. Elution with hexane afforded pure **1** (400 mg, 89%): mp 174–176 °C (lit.[1] mp 174–176 °C); NMR δ 7.15 (d, 1, H_{4or5}), 7.36 (d, 1, H_{4or5}), and 7.85–8.30 (m, 8, aromatic).

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Registry No.—**1**, 27208-37-3; **4**, 22245-55-2; **5**, 69795-70-6; **6**, 1732-13-4; **7**, 1732-25-8; **8a**, 1732-26-9; **8b**, 3353-12-6; **8c**, 69795-71-7; **8d**, 69795-72-8; **9**, 69795-73-9.

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Bridged Biphenyls. Syntheses and Properties of 2,4′-Polymethylenebiphenyls[1]

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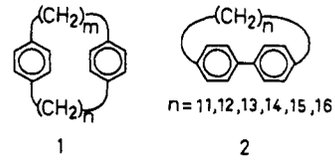
Prelog–Stoll acyloin condensation of the four dimethyl dicarboxylates **12** ($m = 2, p = 3$; $m = p = 3$; $m = 4, p = 3$; and $m = p = 4$), prepared from ethyl *cis*-2-phenylcyclohexylacetate (**9**), afforded the respective acyloins **13**, the Clemmensen reduction of which in turn yielded 2,4′-polymethylenehexahydrobiphenyls **14a–d**. Catalytic dehydrogenation with palladium on carbon converted these hexahydro derivatives into 2,4′-polymethylenebiphenyls **5a–d**, whose spectral properties reveal unusually strained and noncoplanar structures of the biphenyl moiety in the lower homologues.

Our interest in bridged biphenyls was motivated by the fact that while there have been published quite a number of papers from Cram's laboratory reporting the elegant syntheses as well as the exquisite properties of [*m.n*]paracyclophanes (**1**), not much attention had been paid to 4,4′-polymethylenebiphenyls (**2**), which can be regarded as "[*n*.0]paracyclophanes"[2] with $m = 0$ in the general formula **1**. A homologous series of 4,4′-polymethylenebiphenyls (**2**, $n = 11$–16)[3] was eventually prepared in our laboratory, and the electronic,



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NMR, and anion radical ESR spectra[4] all suggested an anomalously strained and coplanar structure for the biphenyl

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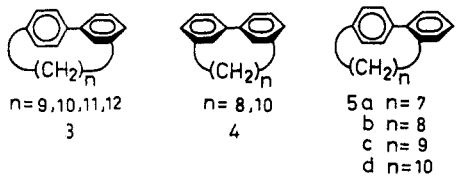
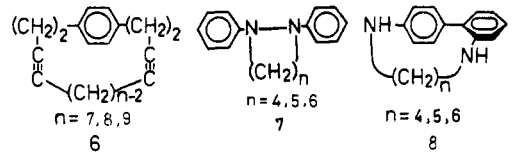
moiety in the lower homologues (n = 11 and 12).

Continuation of our efforts to secure other biphenyl derivatives with the biphenyl moiety held in strained conformations by a polymethylene bridge led to our reported syntheses of 3,4′-polymethylenebiphenyls (**3**, n = 9–12)[5] and 3,3′-polymethylenebiphenyls (**4**, n = 8, 10).[6,7]



Preparation of 2,4′-polymethylenebiphenyls (**5**) was our next logical move, and the present paper describes the syntheses of 2,4′-polymethylenebiphenyls (**5**, n = 7–10) together with their rather unusual spectral properties, reflecting their strained and noncoplanar conformations.

Before reporting our results, it is relevant to give a brief survey of some precedents. Although formation of several members (n = 7–9)[8] of **5** from the diacetylenic paracyclophanes **6** has been suggested on spectroscopic evidence, N,N'-polymethylene-2,4′-diaminobiphenyls (**8**, n = 4–6)[9] (the



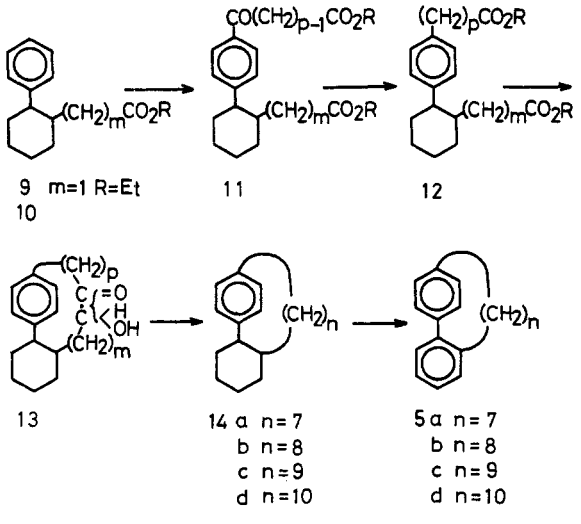
diaza analogues of **5**), prepared from the corresponding N,N'-polymethylenehydrazobenzene (**7**) by benzidine rearrangement, can be cited as the sole previous series of compounds, with an established structure having the 2,4′-bridge across the biphenyl moiety.

Results and Discussion

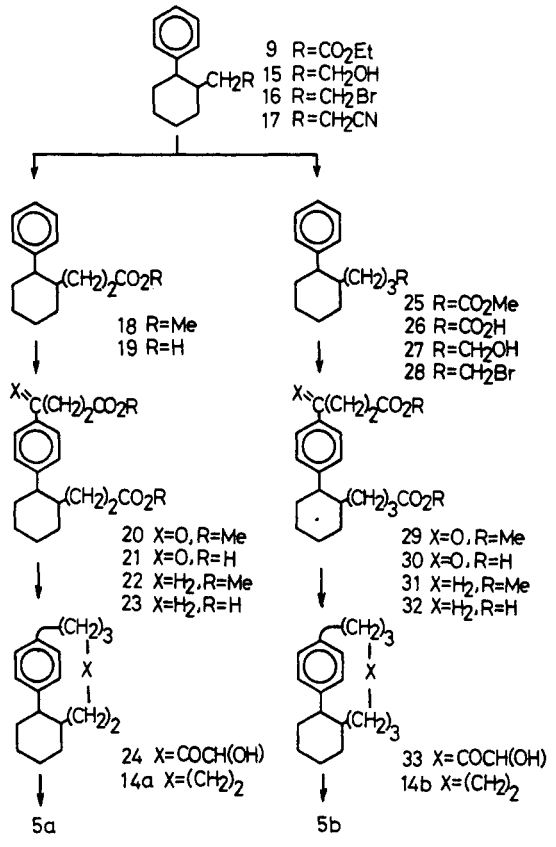
Scheme I illustrates our general synthetic approach to 2,4′-polymethylenebiphenyls (**5**), where the diester **13** having m = 2 p = 3, m = p = 3, m = 4 p = 3, and m = p = 4 led to biphenyls with hepta-, octa-, nona-, and decamethylene bridges between the 2 and 4′ positions.

Modification of ethyl *cis*-2-phenylcyclohexylacetate (**9**)[10] to provide the appropriate homologous monocarboxylates **10** was followed by the Friedel–Crafts acylation with ω-(carbomethoxy)acyl chlorides to introduce side chains at the para position of the benzene ring. After Wolff–Kishner reduction, the resulting dimethyl dicarboxylates **12** were cyclized to

Scheme I



Scheme II

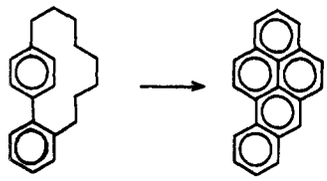


acyloins **13** by a Prelog–Stoll acyloin condensation. Clemmensen reduction of the acyloins gave 2,4′-polymethylenehexahydrobiphenyls (**14**), which were catalytically dehydrogenated with palladium on carbon to yield 2,4′-polymethylenebiphenyls (**5**).

Synthesis of 2,4′-Heptamethylenebiphenyl (5a) (Scheme II). The lowest homologue, **5a**, was prepared following the general Scheme I where m = 2 and p = 3. Lithium aluminum hydride reduction of ethyl *cis*-2-phenylcyclohexylacetate (**9**) furnished the alcohol **15**, which was converted into the cyanide **17** via the bromide **16**. Methanolysis with methanol saturated with hydrogen chloride gave the homologous methyl carboxylate **18**, whose Friedel–Crafts acylation with β-(carbomethoxy)propionyl chloride gave an 87% yield of the keto diester **20**. Permanganate oxidation of the keto diester **20** led to formation of terephthalic acid, and this proved the expected introduction of the acyl group at the para position of the aromatic ring. Wolff–Kishner reduction of **20** followed by esterification afforded the diester **22**, which was then cyclized by a Prelog–Stoll acyloin condensation to furnish the acyloin **24**. Removal of the functional groups was carried out by the Clemmensen reduction to give the 2,4′-bridged hexahydrobiphenyl **14a**. This material was dehydrogenated by heating (230–340 °C) with 10% palladium on carbon to give a 28% yield of 2,4′-heptamethylenebiphenyl (**5a**) as an oil.

Synthesis of 2,4′-Octamethylenebiphenyl (5b) (Scheme II). Scheme I, where m = p = 3, outlines the preparation of the next higher homologue, **5b**. Malonic ester synthesis with the bromide **16** furnished the homologous methyl ester **25**, which was then converted into 2,4′-octamethylenehexahydrobiphenyl (**14b**) by the same sequence of steps described for the preparation of **14a** with comparable yields in each step. Dehydrogenation was carried out by heating with 10% palladium on carbon, and 2,4′-octamethylenebiphenyl (**5b**) was obtained as a crystalline solid. The molecular structure with the octamethylene bridge connecting the 2,4′ positions of hexahydrobiphenyl (Scheme III) permitted formation of

Scheme III



5b 34

benzo[*a*]pyrene (**34**) on dehydrogenation under more drastic conditions.

Synthesis of 2,4′-Nonamethylenebiphenyl (5c) (Scheme IV). The preparation of **5c** followed the general Scheme I where $m = 4$ and $p = 3$. Friedel–Crafts acylation with β-(carbomethoxy)propionyl chloride was carried out on methyl 5-(2-phenylcyclohexyl)valerate (**35**), which had been prepared from the methyl ester **25** via the alcohol **27**, the bromide **28**, and the corresponding cyanide following routine procedures. Heating the 2,4′-bridged hexahydrobiphenyl **14c** with 10% palladium on carbon afforded a 75% yield of 2,4′-nonamethylenebiphenyl (**5c**).

Synthesis of 2,4′-Decamethylenebiphenyl (5d) (Scheme IV). Following the general Scheme I ($m = p = 4$), the Friedel–Crafts acylation was carried out on the methyl ester **35** with γ-(carbomethoxy)butyroyl chloride, and the parallel sequence of conversions described for the lower homologues afforded the 2,4′-decamethylene bridged hexahydrobiphenyl **14d**. Dehydrogenation by heating with palladium on carbon gave 2,4′-decamethylenebiphenyl (**5d**).

NMR Spectra. Except for signals due to the hydrogen atoms on the fused cyclohexane ring in 2,4′-(*n*)methylenehexahydrobiphenyls (**14**), [*n* + 2]paracyclophanes exhibit similar NMR spectra, in which are discernible four groups of signals: aromatic protons (4 H), benzylic protons (3 H), methylene protons (δ 1.0 ~ 2.0), and highly shielded methylene protons (δ −0.5~1.0).

An interesting situation emerges upon conversion to the 2,4′-polymethylenebiphenyl system, where the 2,4′-bridge forces the two benzene rings to have a noncoplanar orientation. The extreme case is to be found in 2,4′-heptamethylenebiphenyl (**5a**), the threshold homologue whose Dreiding molecular model can be constructed without bond angle deformation. Steric effects compell the molecule to be "frozen" in the conformation **51** with nearly a 90° dihedral angle between the benzene rings.

51

In these bridged biphenyls with a noncoplanar conformation in the biphenyl moiety, the diamagnetic shielding of the one benzene ring is expected to be counterbalanced by the paramagnetic shielding effect of the other benzene ring, and this is undoubtedly responsible for the downfield shift observed in all signals in the NMR spectra of 2,4′-polymethylenebiphenyls **5** compared with those of the corresponding hexahydro derivatives **14**. Moreover, it is interesting to observe in the spectra of these 2,4′-bridged biphenyls a distinctly separated pair of benzylic proton signals (around δ 2.9 and 2.3). The signal at higher field can be assigned to the protons of the methylene group located on position 2, where this shielding compensation is expected to be a maximum.

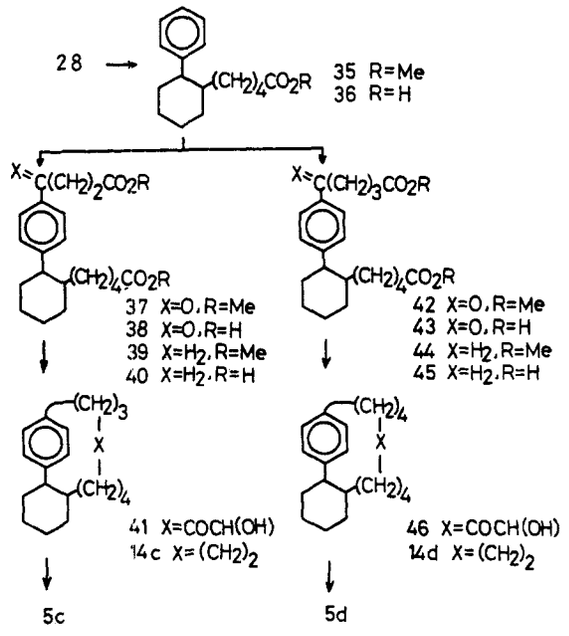
Another conspicuous feature of these NMR spectra is the signal corresponding to moderately shielded protons centered around δ 1.5 (4 H), to which we tentatively assign four protons of the two successive methylene groups (A and B in **51**) next to the 4′-methylene group.

Ultraviolet Absorption Spectra. For the purpose of spectral comparison, 2,4′-di-*n*-butylhexahydrobiphenyl (**49**) and the corresponding biphenyl derivative **50** were prepared from the dimethyl ester **31** (see Scheme V), and Figure 3 (see supplementary material) records the ultraviolet absorption spectra of the four 2,4′-bridged hexahydrobiphenyls as well as that of the reference compound **49**. Similar to the trends observed in [*n*]paracyclophanes, as the bridge length is decreased the absorption maxima move toward longer wavelength, with a significant decrease in the absorption coefficient together with a loss of fine structures.

Figure 4 (supplementary material) records the ultraviolet spectra of 2,4′-polymethylenebiphenyls (**5**) and that of 2,4′-di-*n*-butylbiphenyl (**50**). With a decrease in bridge length, a hypsochromic shift is observed accompanied by a marked drop in extinction coefficient. This is attributable to the resonance inhibition caused by the 2,4′-bridging, which forces the biphenyl moiety to have a noncoplanar conformation.[11]

Lastly, it seems to be pertinent to note here that about a 58° "twist angle" (dihedral angle) was obtained for 2,4′-octamethylenebiphenyl (**5b**) by a simple interpolation into Suzuki's formula,[12] which summerizes the relationship between the dihedral angles and the ultraviolet absorption maxima in various substituted biphenyls.

Scheme IV



Experimental Section

Melting points and boiling points are uncorrected. Infrared spectral data were obtained from a Hitachi EPI-S2 spectrophotometer. Nu-

Scheme V

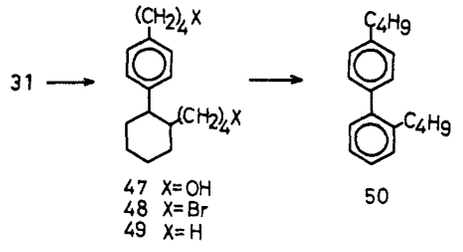


Table I.[a] Characterization Data for Products Obtained by Friedel-Crafts Acylation

product	starting ester	acid chloride used	yield, %	bp, °C (mm)	TR (film) $\nu_{C=O}$, cm^{-1}
20	18	$ClC(=O)(CH_2)_2C(=O)OMe$[f]	87	179–182 (0.1)[b]	1735, 1682
29	25	$ClC(=O)(CH_2)_2C(=O)OMe$	77	183–185 (0.1)[c]	1735, 1680
37	35	$ClC(=O)(CH_2)_2C(=O)OMe$	58	196–200 (0.1)[d]	1736, 1681
42	35	$ClC(=O)(CH_2)_3C(=O)OMe$	53	204–206 (0.1)[e]	1736, 1680

[a] Satisfactory analytical data (±0.4% for C, H) were reported for all new compounds listed in the table. [b] n^{20}_D 1.5255. [c] n^{20}_D 1.5138. [d] n^{20}_D 1.5150. [e] n^{18}_D 1.5173. [f] Registry no., 1490-25-1.

clear magnetic resonance spectra were obtained from 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. Elemental analyses were performed by a Yanagiomoto CHN-Corder Type II.

2-(2-Phenylcyclohexyl)ethanol (15). A solution of ethyl *cis*-2-phenylcyclohexylacetate (**9**;[10] 288 g, 1.41 mol) in ethanol (250 mL), to which copper chromite catalyst (30 g) had been added, was hydrogenated in a steel bomb at 250 atm of hydrogen and at 210–230 °C until the theoretical amount of hydrogen was absorbed. After removal of the catalyst, the filtrate was concentrated under vacuum. The residual oil was distilled to yield **15** (185 g, 77.5%), bp 126–127 °C (2 mm). The alcohol **15** solidified after standing for several hours. Recrystallization from petroleum ether gave mp 57–58 °C; IR (film) 3470 cm^{-1} (OH).

Anal. Calcd for $C_{14}H_{20}O$: C, 82.30; H, 9.87. Found: C, 82.59; H, 10.00.

2′-(2-Bromoethyl)cyclohexylbenzene (16). A mixture of **15** (155 g, 0.76 mol), 47% HBr solution (260 g, 1.50 mol), and concentrated H_2SO_4 (72 g) was refluxed with stirring for 5 h. The reaction mixture was poured into water and extracted with ether. The ether solution was washed with a 3% Na_2CO_3 solution and water and then dried ($CaCl_2$). After removal of the solvent, distillation of the residual oil afforded the bromide **16** (156 g, 78.5%): bp 126–128 °C (2 mm); n^{18}_D 1.5310.

Methyl β-(2-Phenylcyclohexyl)propionate (18). A mixture of **16** (74 g, 0.278 mol), KCN (36 g, 0.55 mol), and 80% ethanol (600 mL) was refluxed with stirring for 24 h. After removal of the ethanol, the reaction mixture was diluted with water and the product was extracted with ether. The ether solution was washed with a 3% KOH solution and water and then dried ($CaCl_2$). Concentration followed by distillation of the residual oil gave the nitrile **17** (38 g, 64%), bp 154–156 °C (8 mm). A solution of **17** (38 g, 0.178 mol) in absolute CH_3OH (100 mL) was saturated with dry HCl. After being allowed to stand for 48 h at room temperature, the reaction mixture was poured into cold water (300 mL) and the resulting solution was heated at 50 °C for 1 h. The separated organic phase was extracted with ether, and the ether solution was washed with a 3% Na_2CO_3 solution and water and dried ($CaCl_2$). The ether was removed, and the residual oil was distilled to give **18** (39.9 g, 91%): bp 139–141 °C (6 mm); n^{16}_D 1.5183; IR (film) 1738 cm^{-1} (C=O).

Hydrolysis of **18** (0.2 g) was accomplished by heating it under reflux for 3 h with KOH (0.5 g) in 70% aqueous ethanol (5 mL). Removal of the ethanol and acidification of the mixture furnished the acid **19** (0.16 g, 84%), which was recrystallized from hexane to give mp 91.5–92.5 °C.

Anal. Calcd for $C_{15}H_{20}O_2$: C, 77.55; H, 8.68. Found: C, 77.75; H, 8.64.

Methyl γ-(2-Phenylcyclohexyl)butyrate (25). To freshly cut sodium (6.7 g, 0.299 g-atom) dissolved in absolute ethanol (500 mL) was added ethyl malonate (93.g, 0.58 mol), and the solution was refluxed for 10 min. A mixture of the bromide **16** (75 g, 0.281 mol) and ethyl malonate (30 g) was added to the sodiomalonate solution during 0.5 h. After being refluxed for 2 h, the reaction mixture was poured into water (1 L) and the separated organic product was extracted with benzene. The benzene extract was washed with water and then dried ($CaCl_2$). The volatile materials were removed by distillation with a final bath temperature of 150 °C (4 mm). Distillation of the residual oil afforded the diester (82.5 g, 85%), bp 172–174 °C (0.1 mm).

The resulting diester was saponified by heating under reflux for 2 h with KOH (480 g) in 80% ethanol (400 mL). After removal of the ethanol, the concentrate was poured into water and acidified with an HCl solution. The separated product was extracted with ether, and the ether solution was dried ($MgSO_4$). Concentration of the ether afforded 45 g of dicarboxylic acid, which was decarboxylated by heating at 185–200 °C for 1 h. The crude monocarboxylic acid **26** was esterified with methanol and concentrated H_2SO_4 in the usual way, and distillation of the product gave **25** (43 g, 70% from **16**): bp 150–152 °C (3 mm); n^{18}_D 1.4979; IR (film) 1738 cm^{-1} (C=O).

Anal. Calcd for $C_{17}H_{24}O_2$: C, 78.42; H, 9.29. Found: C, 78.61; H, 9.21.

Hydrolysis of **25** (0.2 g) with boiling aqueous alcoholic KOH afforded the acid **26** (0.16 g, 85%), which after recrystallization from hexane gave mp 132–133 °C.

Anal. Calcd for $C_{16}H_{22}O_2$: C, 78.01; H, 9.00. Found: C, 78.23; H, 9.06.

4-(2-Phenylcyclohexyl)butanol (27). A solution of **25** (42 g, 0.116 mol) in dry ether (160 mL) was added to a suspension of $LiAlH_4$ (8 g, 0.21 mol) in dry ether (200 mL) during 0.5 h, and the reaction mixture was refluxed for 4 h with stirring. After ethyl acetate was added to destroy the excess reducing agent, the solution was made acidic with dilute HCl and extracted with ether. The ether solution was washed with water and then dried (Na_2SO_4). The ether was removed and the residual liquid distilled to give **27** (34 g, 90.5%): bp 148–150 °C (3 mm); n^{23}_D 1.5093; IR (film) 3450 cm^{-1} (OH).

The phenylurethane derivative of **27** was prepared, and after recrystallization from CCl_4 it gave mp 215–216 °C.

Anal. Calcd for $C_{23}H_{29}NO_2$: C, 78.59; H, 8.29; N, 3.99. Found: C, 78.36; H, 8.46; N, 3.87.

2′-(4-Bromobutyl)cyclohexylbenzene (28). A mixture of **27** (34 g, 0.147 mol), 47% HBr solution (51 g, 0.294 mol), and concentrated H_2SO_4 (16.2 g) was refluxed for 5 h. The same procedure described for the preparation of **16** afforded the bromide **28** (39 g, 90%): bp 160–162 °C (3 mm); n^{16}_D 1.5260.

Methyl δ-(2-Phenylcyclohexyl)valerate (35). In the same manner as described for the preparation of **18** via an alkyl cyanide, the bromide **28** (39 g, 0.142 mol) was converted to the ester **35** (26 g, 71%): bp 136–139 °C (1 mm); n^{19}_D 1.4965; IR (film) 1737 cm^{-1} (C=O).

Anal. Calcd for $C_{18}H_{26}O_2$: C, 78.79; H, 9.55. Found: C, 78.98; H, 9.46.

Saponification of **35** (0.2 g) with boiling aqueous alcoholic KOH afforded the acid **36** (0.16 g, 84%), mp 123–124 °C (from benzene–hexane).

Anal. Calcd for $C_{17}H_{24}O_2$: C, 78.42; H, 9.29. Found: C, 78.36; H, 9.18.

2′-[2-(Carbomethoxy)ethyl]-4-[1-Oxo-3-(carbomethoxy)-propyl]cyclohexylbenzene (20). A mixture of **18** (26 g, 0.106 mol), β-(carbomethoxy)propionyl chloride[13] (16.1 g, 0.108 mol), and $Cl_2CHCHCl_2$ (190 mL) was cooled to 0 °C in a ice–salt bath. Anhydrous $AlCl_3$ (49.5 g, 0.37 mol) was added in six portions to the stirred mixture during 0.5 h, and the resulting mixture was stirred for 3 h at 40–50 °C. The dark solution was poured over ice, and the separated organic phase was washed with a 2 N HCl solution, water, a 3% Na_2CO_3 solution, and water and then dried ($CaCl_2$). After evaporation of the solvent, the residual oil was distilled to give **20** (33 g, 86.7%). Yield, boiling point, n_D, and IR data are presented in Table I.

Saponification of **20** (0.2 g) with methanolic KOH afforded **21**. Yield and melting point data are presented in Table II.

2′-[2-(Carbomethoxy)ethyl]-4-[3-carbomethoxy)propyl]cyclohexylbenzene (22). A mixture of **20** (33 g, 0.092 mol), 80% hydrazine hydrate (28.8 g, 0.46 mol), KOH (35.9 g, 0.64 mol), and triethylene glycol (200 mL) was heated at 150 °C, and then water and excess hydrazine hydrate were allowed to escape until the temperature reached 195 °C. Heating was continued at 210 °C for 10 h, and the reaction mixture was cooled followed by dilution with water (300 mL). This solution was made acidic with concentrated HCl, and the mixture was extracted with $CHCl_3$. The chloroform solution was washed with water and dried ($MgSO_4$). After evaporation of the solvent, the crude acid **23** was esterified by heating for 8 h with CH_3OH (60 mL) containing concentrated H_2SO_4 (5 g). The reaction mixture was poured into cold water and then extracted with ether. The ether solution was washed with water, a 3% Na_2CO_3 solution, and water and was dried ($CaCl_2$). After removal of the ether, distillation of the residual oil gave

Table II.[a] **Physical Properties of the Products**

product	no.	yield, %	bp, °C (mm) [mp, °C]	IR (KBr or film); $\nu_{C=O}$, cm^{-1}
keto diacid	**21**	85	[145–146][b]	1706, 1603
	30	84	[131–132][b]	1705, 1602
	38	83	[150–151][b]	1706, 1683
	43	86	[162–163][b]	1705, 1682
diester	**22**	83	156–159 (0.1)[c]	1735
	31	85	173–175 (0.1)[d]	1736
	39	76	169–172 (0.1)[e]	1735
	44	68	210–213 (0.1)[f]	1737
diacid	**23**	85	[73–74][b]	1703
	32	87	[68–69][b]	1702
	40	82	[67–68][g]	1703
	45	81	[104–105][h]	1702

[a] Satisfactory analytical data (±0.4% for C, H) were reported for all new compounds listed in the table. [b] Recrystallized from benzene. [c] n^{23}_D 1.5152. [d] n^{21}_D 1.5146. [e] n^{20}_D 1.5075. [f] n^{16}_D 1.5135. [g] From benzene–hexane. [h] From aqueous acetic acid.

22. Yield, boiling point, n_D, and IR data are presented in Table II.

Saponification of **22** (0.2 g) with methanolic KOH afforded the acid **23**. Yield and melting point data are presented in Table II.

2′,4-Heptamethylenecyclohexylbenzene (14a). (a) The acyloin cyclization of the diester **22** was carried out using the high dilution method. A solution of **22** (15.7 g, 0.045 mol) in dry xylene (300 mL) was added over 48 h to a vigorously agitated (vibro-mixer) suspension of sodium (3.8 g, 0.173 g-atom) in boiling xylene (370 mL) under a nitrogen atmosphere. Heating and stirring were continued for a further 1.5 h, and the reaction mixture was cooled to 0 °C. After acetic acid (25 mL) was slowly added, insoluble polymer and sodium acetate were removed. The xylene solution was concentrated, and the residual yellow oil was distilled to give the acyloin **24** (5.2 g): bp 171–174 °C (0.1 mm); n^{29}_D 1.5420; IR (film) 3460 (OH), 1710 cm^{-1} (C=O).

(b) Clemmensen reduction of the acyloin **24** was carried out as follows. Amalgamated zinc was prepared by swirling zinc (66 g) with a mixture of mercuric chloride (1.9 g), concentrated HCl (1.4 mL), and water (200 mL). A solution of **24** (5.2 g, 0.0184 mol) in toluene (60 mL) was added to the amalgamated zinc with 200 mL each of concentrated HCl and acetic acid. The mixture was heated under reflux for 48 h, during which time four 50-mL portions of concentrated HCl were added. The reaction mixture was cooled and diluted with water, and then the product was extracted with ether. The ether solution was washed with water, a 3% Na_2CO_3 solution, and water and was dried ($CaCl_2$). After evaporation of the solvent, the resulting oil was chromatographed on neutral alumina (100 g). Elution with hexane gave a colorless oil (2.8 g) which was distilled to afford the hydrocarbon **14a**. Yield, boiling point, n_D, NMR, and UV data are presented in Table III.

2,4′-Heptamethylenebiphenyl (5a). The hydrocarbon **14a** (0.7 g, 2.7 mmol) was mixed with 10% palladium on carbon (70 mg), and the mixture was heated in a salt bath for 4 h, during which the heating temperature was gradually raised from 230 to 340 °C. The hydrogen evolved amounted to 145 mL (25 °C) or 80% of the theoretical amount. Hexane (10 mL) was added to the reaction mixture, and the catalyst was removed. The filtrate was freed of solvent, and the residual colorless oil was chromatographed on neutral alumina. Elution with hexane yielded an oil which was distilled twice to give **5a**. Yield, boiling point, n_D, IR, NMR, and UV data are presented in Table IV.

Benzo[a]pyrene (34). The hydrocarbon **14b** (0.27 g, 1.0 mmol) was dehydrogenated by heating at 250–400 °C for 3 h with 10% palladium on carbon. The product was taken up in benzene, filtered free of catalyst, and recrystallized from benzene to give **34** (0.15 g, 60%), mp 177–178 °C (lit.[14] mp 176–177.5 °C).

Anal. Calcd for $C_{20}H_{12}$: C, 95.21; H, 4.79. Found: C, 95.30; H, 4.74.

The picrate was recrystallized from ethanol to give mp 197–198 °C (lit.[14] mp 197–198 °C).

Table III.[a] **Physical Properties of 2′,4-Polymethylenecyclohexylbenzenes (14)**

product	starting diester	yield,[b] %	bp, °C (mm) [mp, °C]	NMR (100 MHz), δ (CCl_4, Me_4Si)	UV (95% EtOH) λ_{max} (log ε), nm
14a	**22**	22	117–119 (0.1)[c]	−0.5 ~ 0.3 (br, 2 H), 0.3 ~ 1.0 (m, 7 H), 1.0 ~ 2.3 (m, 12 H), 2.6 ~ 3.1 (m, 3 H), 7.0 (s, 4 H)	266 (3.91), 273 (2.45), 279 (2.51)
14b	**31**	35.5	146–148 (0.1)[d]	−0.1 ~ 0.3 (br, 2 H), 0.3 ~ 0.6 (m, 7 H), 0.8 ~ 2.1 (m, 14 H), 2.4 ~ 2.8 (m, 3 H), 7.0 (s, 4 H)	223 (3.92), 262 (2.45), 269 (2.57), 277 (2.51)
14c	**39**	23.5	[48–49][e]	0.3 ~ 1.3 (m, 15 H), 1.3 ~ 2.1 (m, 10 H), 2.4 ~ 2.8 (m, 3 H), 7.0 (s, 4 H)	222 (3.92), 262 (2.46), 269 (2.58), 277 (2.52)
14d	**44**	20	[54–55][f]	0.4 ~ 1.2 (m, 15 H), 1.2 ~ 2.0 (m, 12 H), 2.4 ~ 2.9 (m, 3 H), 7.0 (s, 4 H)	221 (3.92), 260 (2.48), 268 (2.61), 276 (2.56)

[a] Satisfactory analytical data (±0.4% for C, H) were reported for all new compounds listed in the table. [b] From starting diester. [c] n^{28}_D 1.5505. [d] n^{20}_D 1.5475. [e] Recrystallized from aqueous ethanol. [f] From ethanol.

Table IV.[a] **Physical Properties of 2,4′-Polymethylenebiphenyls (5)**

product	yield, %	bp, °C (mm) [mp, °C]	IR (film or KBr), cm^{-1}	NMR (100 MHz), δ (CCl_4, Me_4Si)	UV (95% EtOH) λ_{max} (log ε), nm
5a	28	106–108 (0.1)[b]	3060, 3030, 2935, 2873, 1960, 1600, 1513, 1472, 1460, 1444, 1050, 937, 854, 814	0.3 ~ 0.5 (br, 1 H), 0.5 ~ 0.8 (m, 5 H), 1.3 ~ 1.6 (t, 4 H), 2.1 ~ 2.4 (t, 2 H), 2.7 ~ 3.0 (t, 2 H), 6.9 ~ 7.4 (m, 8 H)	233 sh (3.97)
5b	82	[86–87][c]	3060, 3030, 2910, 2860, 1923, 1516, 1480, 1460, 1440, 1407, 1108, 1004, 837, 826, 764, 747, 733, 708	0.7 ~ 1.3 (m, 8 H), 1.0 ~ 1.9 (t, 4 H), 2.2 ~ 2.5 (t, 2 H), 2.8 ~ 3.1 (t, 2 H), 6.9 ~ 7.4 (m, 8 H)	235 (4.04)
5c	75	[60–61][c]	3060, 3028, 2922, 2860, 1920, 1515, 1478, 1461, 1438, 1407, 1182, 1106, 1004, 898, 824, 812, 759, 747, 733, 707	0.6 ~ 1.0 (m, 10 H), 1.3 ~ 1.5 (t, 2 H), 1.6 ~ 1.8 (t, 2 H), 2.3 ~ 2.5 (t, 2 H), 2.8 ~ 3.0 (t, 2 H), 7.0 ~ 7.4 (m, 8 H)	238 (4.08)
5d	85	171–172 (0.1)[d]	3080, 3022, 2935, 2865, 1920, 1530, 1483, 1460, 1445, 1407, 1005, 825, 758, 752, 750, 736, 722, 707	0.7 ~ 0.9 (br, 2 H), 0.9 ~ 1.4 (m, 10 H), 1.7 ~ 2.0 (t, 4 H), 2.4 ~ 2.6 (t, 2 H), 2.7 ~ 2.9 (t, 2 H), 7.0 ~ 7.4 (m, 8 H)	238 (4.10)

[a] Satisfactory analytical data (±0.4% for C, H) were reported for all new compounds listed in the table. [b] n^{21}_D 1.5845. [c] Recrystallized from ethanol. [d] n^{20}_D 1.5655.

Anal. Calcd for $C_{26}H_{15}N_3O_7$: C, 64.86; H, 3 14; N, 8.73. Found: C, 65.32; H, 3.45; N, 8.57.

2',4-Bis(4-hydroxybutyl)cyclohexylbenzene (47). The preparation of **47** was carried out by the same method described for the preparation of **27**, utilizing the diester **31** (3.6 g, 10 mmol), $LiAlH_4$ (0.4 g, 10 mmol), and dry ether (30 mL). The product was distilled to give **47** (2.7 g, 90%): bp 204–206 °C (0.1 mm); n^{21}_D 1.5118; IR (film) 3450 cm^{-1} (OH).

2',4-Bis(4-bromobutyl)cyclohexylbenzene (48). The preparation of **48** was carried out by the same method described for the preparation of **16**, utilizing **47** (2.5 g, 8.2 mmol), 47% HBr solution (5.2 g, 31 mmol), and concentrated H_2SO_4 (1 g). Distillation of the product gave the bromide **48** (2.7 g, 75%(: bp 193–195 °C (0.1 mm); n^{16}_D 1.5499.

2',4-Di-*n*-butylcyclohexylbenzene (49). A solution of **48** (1.0 g, 2.3 mmol) in dry tetrahydrofuran (5 mL) was added dropwise to a suspension of $LiAlH_4$ (0.4 g, 10 mmol) in dry tetrahydrofuran (8 mL) during 15 min. The reaction mixture was refluxed with stirring for 10 h, and the excess reducing agent was decomposed with ethyl acetate. After the mixture was acidified with diluted HCl solution, the organic phase was extracted with ether. After workup in the usual manner, the product was distilled to give **49** (0.5 g, 80%): bp 148–150 °C (1.0 mm); n^{20}_D 1.5121.

Anal. Calcd for $C_{20}H_{32}$: C, 88.16; H, 11.84. Found: C, 88.24; H, 11.79.

2,4'-Di-*n*-butylbiphenyl (50). The hydrocarbon **49** (0.4 g, 1.47 mmol) was dehydrogenated by heating at 250–280 °C for 1 h with 10% palladium on carbon (40 mg). Distillation of the oily product gave **50** (3.5 g, 90%): bp 112–114 °C (0.5 mm); n^{19}_D 1.5198.

Anal. Calcd for $C_{20}H_{26}$: C, 90.16; H, 9.84. Found: C, 90.20; H, 9.81.

Registry No.—**5a,** 69597-38-2; **5b,** 792-28-9; **5c,** 69597-39-3; **5d,** 899-75-2; **9,** 69597-22-4; **14a,** 69597-20-2; **14b,** 69651-44-1; **14c,** 69597-21-3; **14d,** 69651-19-0; **15,** 69597-23-5; **16,** 69597-24-6; **17,** 69597-25-7; **18,** 69597-05-3; **19,** 4099-77-8; **20,** 69597-01-9; **21,** 69597-08-6; **22,** 69597-12-2; **23,** 69597-16-6; **24,** 69597-26-8; **25,** 69597-06-4; **26,** 69597-27-9; **27,** 69597-28-0; **27** phenylurethane, 69597-29-1; **28,** 69597-30-4; **29,** 69597-02-0; **30,** 69597-09-7; **31,** 69597-13-3; **32,** 69597-17-7; **34,** 50-32-8; **34** picrate, 5929-01-1; **35,** 69597-07-5; **36,** 69597-31-5; **37,** 69597-03-1; **38,** 69597-10-0; **39,** 69597-14-4; **40,** 69597-18-8; **42,** 69597-04-2; **43,** 69597-11-1; **44,** 69597-15-5; **45,** 69597-19-9; **47,** 69597-32-6; **48,** 69597-33-7; **49,** 69597-34-8; **50,** 69597-35-9; diethyl [2(2-phenylcyclohexyl)ethyl]-propanedioate, 69597-36-0; [2-(2-phenylcyclohexyl)ethyl]propenedioic acid, 69597-37-1; sodium ethylmalonate, 996-82-7.

Supplementary Material Available: Figure 1, showing the NMR spectra of 2'-4-polymethylenecyclohexylbenzenes, Figure 2, showing the NMR spectra of 2,4'-polymethylenebiphenyls, Figure 3, showing the UV spectra of 2',4-polymethylenecyclohexylbenzenes, and Figure 4, showing the UV spectra of 2,4'-polymethylenebiphenyls (4 pages). Ordering information is given on any current masthead page.

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Determination of Enantiomeric Purity of Chiral Lactones. A General Method Using Nuclear Magnetic Resonance[1]

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A general method is described for determining enantiomeric purities of chiral lactones, regardless of their ring size. The approach involves treatment of a lactone with methyllithium, followed by NMR examination of the diol produced in the presence of a chiral shift reagent such as $Eu(tfc)_3$. The method is broadly applicable to a wide range of variously substituted γ-, δ-, and ϵ-lactones. Its accuracy for enantiomeric excess determinations is ±3%. This has been confirmed using selected optically active lactones of established optical purities.

The development of asymmetric syntheses of chiral lactones, for use as synthons and as target molecules, is receiving increasing attention from both the chemical[2,3] and enzymic[4] directions. As a result, a pressing need has arisen for accurate and convenient methods for evaluating their enantiomeric purities. Optical rotation criteria have been used almost exclusively until very recently, despite the fact that the unreliability of optical methods is well documented.[5] However, although direct enantiomeric excess (ee) determination techniques are recognized as being much preferred, neither of the two lactone ee determination methods[6,7] reported so far is generally applicable. The GLC approach,[6] involving conversion of the lactone to an orthoester with (2*R*,3*R*)-2,3-butanediol, works well with δ-lactones. However, all attempts to extend it to γ-lactone analyses have been unsatisfactory.[8] The NMR method,[7] which utilizes chiral solvating agents, has been applied to both γ- and δ-lactones. For geometric reasons, it is most effective for γ-lactone structures.

Direct methods for ee determination are becoming increasingly dominated by chiral NMR shift reagent techniques.[10] These methods have proven spectacularly successful with chiral molecules possessing a broad range of functional groups. Disappointingly, although chiral shift reagent analyses of esters are well documented,[3b,10b,11] optical purities of lactones cannot be measured using the chiral shift reagents currently available.[1,3b] This problem has now been overcome by reacting the lactones (**1**) with methyllithium (Scheme I) followed by NMR examination of the resulting diols (**2**) in the

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