Table V. Crystal Data for $C_{15}H_{22}O_3$

a = 21.322 (7)	$\alpha = \beta = \gamma = 90°$
b = 7.593 (2)	
c = 8.387 (1)	
Space group $P2_12_12_1$	$Z = 4$
ρ_c = 1.217 g cm^{-3}	ρ_{meas} = 1.203 g cm^{-3}
μ(Cu Kα) = 6.76 cm^{-1}	

employed to collect intensity data out to a 2θ of 120° using automatic θ–2θ step scans. Of a total 1204 reflections scanned, 1053 were considered observed by the criteria $I > 3\sigma(I)$ and were included in structure refinement. Lorentz and polarization factors were applied in the normal manner,[10] and the data were corrected for absorption by the method of Tompa.[11] Weights were calculated by the method of Stout and Jensen:[12] $w(F) = [(K/4Lp\ I)(\sigma^2(I) + (0.03I)^2)]^{-1}$. Scattering factors used were as follows: for nonhydrogen atoms from Cromer and Mann;[13] and for hydrogen from Stewart, Davidson, and Simpson.[14]

The structure was solved by direct methods using the program MULTAN.[10] Positions of all nonhydrogen atoms were refined, first isotropically, then anisotropically, by full-matrix least squares minimizing $\Sigma w\Delta F^2$, and all hydrogen atoms were located from a subsequent difference Fourier map. Further refinement of positional parameters for all atoms and anisotropic temperature factors for the nonhydrogen atoms resulted in a final R factor of 4.7% ($R = \Sigma||F_o| - |F_c||/\Sigma|F_o|$). The R factor for all data, including unobserved reflections, was 5.7%; the weighted R_w ($R_w = [\Sigma w\Delta F^2]^{1/2}/[\Sigma wF_o^2]^{1/2}$) was 5.9%; and the largest shift divided by the standard deviation was 0.27 at the end of refinement. A $\delta(R)$ normal probability plot[15] was calculated and was essentially linear with a slope of 2.11 and an intercept of 0.14. A final difference Fourier showed no peaks greater than ±0.2 eÅ^{-3}. Absolute configuration could not be determined from the data.

Acknowledgments. P.W.J., J.C.H., S.K.R., A.H., and P.L. gratefully acknowledge financial support from Grant GM-AM 19783 of the National Institute of Health, the Montana Heart Association, and the National Science Foundation for partial support for purchase of an HA-100 NMR spectrometer. C.N.C. and R.L. wish to thank Montana State University for a grant of computing time. Finally, Dr. W. Waters and Mr. Tantivanich of the University of Montana are acknowledged for their assistance in obtaining the optical rotation data.

Registry No.—I, 52279-13-7; II, 60410-89-1; III, 35101-40-7.

Supplementary Material Available. Dihedral angles, equations of planes, positional and thermal parameters, and standard deviations (2 pages). Ordering information is given on any current masthead page.

References and Notes

(1) Abstracted in part from the Ph.D. Theses of J.C.H., 1972, Montana State University.
(2) F. Bohlmann, C. Zdero, and M. Grenz, *Chem. Ber.*, **107**, 2730–2759 (1974); F. Bohlmann and C. Zdero, *ibid.*, **107**, 2912–2922 (1974); F. Bohlmann, C. Zdero, and M. Grenz, *ibid.*, **107**, 3928–3945 (1974); F. Bohlmann and N. Rao, *Tetrahedron Lett.*, 613–616 (1973).
(3) H. Nagano, Y. Tanahashi, Y. Moriyama, and T. Takahashi, *Bull. Chem. Soc. Jpn.*, **46**, 2840–2845 (1973).
(4) M. Tada, Y. Moriyama, Y. Tanahashi, and T. Takahashi, *Tetrahedron Lett.*, 4007–4010 (1971).
(5) H. Ishii, T. Tozyo, and H. Minato, *Tetrahedron*, **21**, 2605–2610 (1965); H. Ishii, T. Tozyo, and H. Minato, *J. Chem. Soc. C*, 1545 (1966); H. Ishii, T. Tozyo, M. Nakamura, and H. Minato, *Tetrahedron*, 2911–2918 (1970).
(6) Y. Moriyama, T. Sato, H. Nagano, Y. Tanahashi, and T. Takahashi, *Chem. Lett.*, 637–640 (1972).
(7) P. W. Jennings, S. K. Reeder, J. C. Hurley, C. N. Caughlan, and G. D. Smith, *J. Org. Chem.*, **39**, 3392 (1974).
(8) The melting point of III has been shown to be a function of heating rate or when you place it on the heating device. If heated slowly, it will decompose over a 5 °C range around 122 °C. However, if placed in the heating chamber which is already at 130–132 °C, III will melt at 144–145 °C.
(9) In ref 7 the assignments were inadvertently reversed.
(10) Computer programs used were by F. R. Ahmed and co-workers (NRC-2, Data Reduction; NRC-8, Fourier for Distorted and Undistorted Nets; and NRC-12, Scan of Interatomic Distances and Angles; National Research Council, Ottawa, Ontario, Canada), Busing and Levy (ORFLS), Carrol K. Johnson (ORTEP), and Germaine, Main, and Woolfson (MULTAN, 1972 version). These programs were locally modified for use with the XDS Sigma 7 computer. Other programs were written locally by G. D. Smith, C. N. Caughlan, and R. D. Larsen.
(11) J. DeMeulemaer and J. Tompa, *Acta Crystallogr.*, **19**, 1014 (1965).
(12) G. H. Stout and L. H. Jensen, "X-Ray Structure Determination", Macmillan, New York, N.Y., 1968, p 457.
(13) D. T. Cromer and J. B. Mann, *Acta Crystallogr., Sect. A*, **24**, 321 (1968).
(14) R. F. Stewart, E. R. Davidson, and W. T. Simpson, *J. Chem. Phys.*, **42**, 3175 (1965).
(15) S. C. Abrahams and E. T. Keve, *Acta Crystallogr., Sect. A*, **27**, 157 (1971).

Syntheses of [8][8]- and [8][10]Paracyclophanes[1]

Masao Nakazaki,* Koji Yamamoto, and Sigeo Tanaka

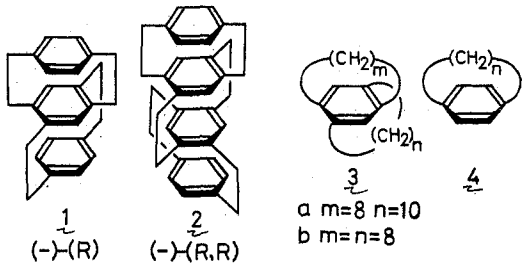
Department of Chemistry, Faculty of Engineering Science, Osaka University, Toyonaka, Osaka, Japan

Received May 20, 1976

Coupling of 2,5-dimethylene-2,5-dihydrofuran with the *p*-xylylene derivative (**16b**) prepared from 10-bromomethyl-13-methyl[8]paracyclophane (**8b**) yielded the benzene–furan "hybrid" [2.2]paracyclophane (**18b**) whose furan moiety was converted to a tetramethylene chain affording [8][8]paracyclophane (**3b**). The same sequence of reactions applied to 12-bromomethyl-15-methyl[10]paracyclophane (**8a**) furnished [8][10]paracyclophane (**3a**). The uv and NMR spectra of these [*n*][*n*]- and [*m*][*n*]paracyclophanes reveal their unusually twisted benzene rings.

Preparations of the optically active triple- and quadruple-layered [2.2]paracyclophanes **1** and **2** with known absolute configurations have been reported from our laboratory;[2] these compounds have D_2 symmetry and are gyrochiral.[3] While substitution of both the outer benzene nuclei of **1** with equivalent polymethylene chains leads to **3b** with D_2 symmetry, substitution with different polymethylene chains gives **3a** with C_2 symmetry. Although the names of [*n*][*n*]- and [*m*][*n*]-paracyclophanes were proposed by Smith[4] for these types of compounds, none of them have yet been prepared. By analysis[5] of the uv spectra of [*n*]paracyclophanes **4** with short para

Chart I



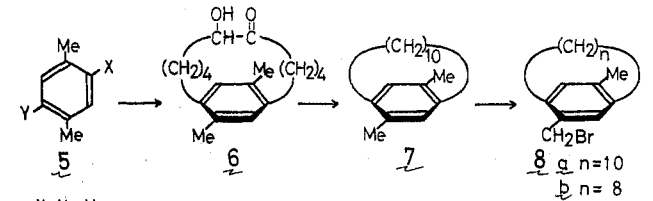
bridges, Allinger has suggested that the benzene nuclei exist in a highly strained boat form (C_{2v} symmetry). [m][n]Paracyclophanes (3) with short polymethylene bridges are accordingly expected to possess benzene nuclei with twist-boat conformations (D_2 symmetry, $m = n$; C_2 symmetry, $m \neq n$). This contribution is concerned with the syntheses of [8][8]- and [8][10]paracyclophanes (**3b, 3a**).

Results and Discussion

Our general approach (see Scheme III) to [8][8]- and [8][10]paracyclophanes, **3b** and **3a,** involved coupling of the para-bridged *p*-xylylene derivatives **16a** and **16b** with 2,5-dimethylene-2,5-dihydrofuran[6] to furnish respectively the benzene–furan "hybrid" [2.2]paracyclophanes **18a** and **18b** whose furan moieties were transformed to give octamethylene bridges.

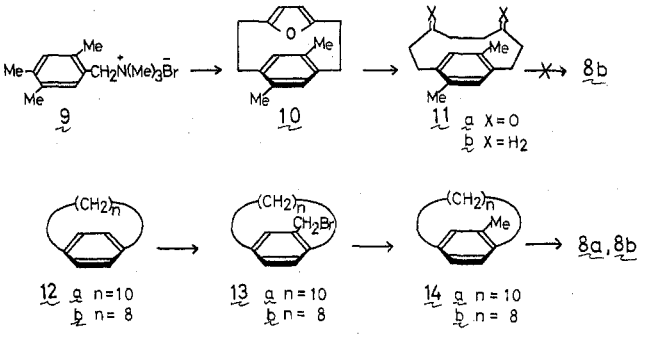
Preparations of 10-Bromomethyl-13-methyl[8]paracyclophane (8b) and 12-Bromomethyl-15-methyl[10]paracyclophane (8a). Schemes I and II summarize the

Scheme I



a X=Y=H
b X=H, Y=CO(CH2)3CO2Me
c X=H, Y=(CH2)4CO2H
d X=H, Y=(CH2)4CO2Me
e X=CO(CH2)3CO2Me, Y=(CH2)4CO2Me
f X=Y=(CH2)4CO2H
g X=Y=(CH2)4CO2Me

Scheme II



synthetic sequences to 10-bromomethyl-13-methyl[8]paracyclophane (**8b**) and 12-bromomethyl-15-methyl[10]paracyclophane (**8a**), the precursors of *p*-xylylenes **16b** and **16a.**

Friedel–Crafts acylation of *p*-xylene (**5a**) with γ-carbomethoxybutyryl chloride followed by the Wolff–Kishner reduction led to formation of the acid **5c,** which was then converted to the methyl ester **5d.** After the second γ-carbomethoxybutyl group was introduced to the methyl ester **5d,** the resulting keto ester **5e** was converted to the dimethyl ester **5g** by the Wolff–Kishner reduction followed by esterification. The dimethyl ester **5g** was submitted to acyloin condensation under high-dilution conditions to give the para-bridged acyloin **6** (64% yield) which afforded 12,15-dimethyl[10]paracyclophane (**7**) after Clemmensen reduction. Bromination of **7** in carbon tetrachloride at room temperature gave a 45% yield of the bromide **8a.**

The preparation of the bromide **8b** was first attempted by bromination of 10,13-dimethyl[8]paracyclophane (**11b**) whose synthesis was carried out by Cram's method[6] applied on duryltrimethylammonium bromide **9.**[7] "Hybrid" coupling between 2,5-dimethylene-3,5-dihydrofuran and the *p*-xylylene derivative prepared from the quaternary ammonium salt **9** gave a 21% yield of the benzene–furan "hybrid" [2.2]paracyclophane **10.** Although the desired 10,13-dimethyl[8]paracyclophane (**11b**) was accessible in a 70% yield from the "hybrid" [2.2]paracyclophane **10,** via the diketone **11a,** no clean-cut monobromination product was obtained on the direct bromination of **11b.** We divert attention from this fruitless approach to the second one which starts from [8]paracyclophane (**12b**).[6] Heating of [8]paracyclophane (**12b**) with paraformaldehyde in 47% hydrobromic acid–acetic acid solution[8] led to formation of the bromomethyl product **13b,** which was treated with lithium aluminum hydride to afford 10-methyl[8]paracyclophane (**14b**) in 55% yield based on **12b.** The second bromomethylation of the 10-methyl derivative **14b** gave the desired bromomethyl compound **8b** (74% yield). Conversion of **8b** with lithium aluminum hydride to 10,13-dimethyl[8]paracyclophane (**11b**) confirmed the para relationship of the newly introduced bromomethyl group to the original methyl group. The sequence of steps designed to lead from **12b** to **8b** was applied to [10]paracyclophane(**12a**)[9] affording 12-bromomethyl-15-methyl[10]paracyclophane (**8a**) in 55% yield based on **12a.**

[8][8]Paracyclophane (3b). An equimolecular mixture of 5-methylfurfuryltrimethylammonium iodide and the quaternary ammonium bromide **15c** obtained from the [8] para-bridged bromide **8b** was treated with silver oxide to furnish a mixture of the two Hofmann's bases which was pyrolyzed by refluxing in toluene. Chromatography of the coupling product yielded (in the order of elution) (1) the doubly [8]para-bridged [2.2]paracyclophane[10] (**19b**) (3%), (2) the benzene–furan "hybrid" [2.2]paracyclophane (**18b**) (8%), (3) [2.2]furanophane[12] (**17**) (12%). Since the furan–benzene "hybrid" [2.2]paracyclophane (**18b**) was found to be unstable, it was hydrolyzed with 10% sulfuric acid in acetic acid without further purification to afford the diketone **20c.** Treatment with ethanedithiol–boron trifluoride converted the diketone **20c** into the bisthioketal **20d** which was refluxed in ethyl acetate solution with Raney nickel to yield [8][8]paracyclophane (**3b**) (in 63% yield from the diketone **20c**).

Scheme III

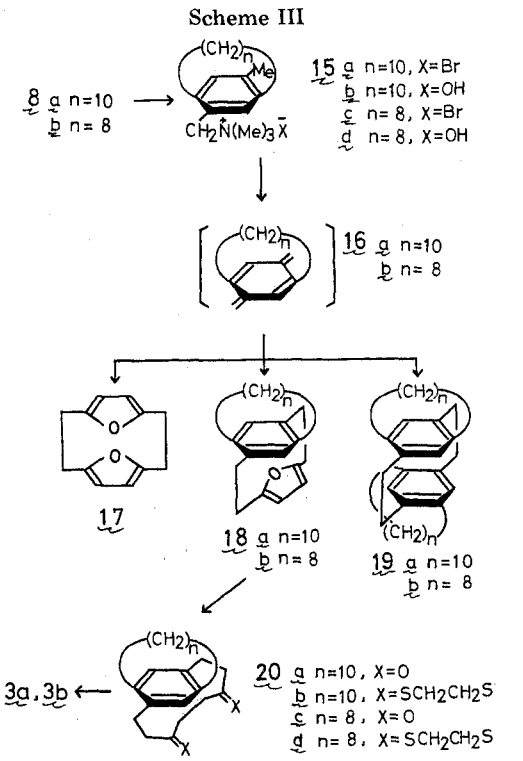


Table I. Ultraviolet Absorption Data in Isooctane

Compd	λ_{max}, nm (log ϵ)			
3a	240 (3.81)	280 (2.51)	289_{sh} (2.41)	
3b	255 (3.80)		291_{sh} (2.54)	
11b	234 (3.85)	283 (2.56)	288_{sh} (2.53)	
19a	233 (4.23)	241 (4.19)	295_{sh} (2.57)	318_{sh} (2.20)
19b	236 (4.17)	251 (4.12)	306_{sh} (2.68)	
4,7,12,15-Tetramethyl-[2.2]paracyclophane	226 (4.26)	250_{sh} (3.57)	308_{sh} (2.10)	

[8][10]Paracyclophane (3a). Coupling of the [10]para-bridged xylylene derivative **16a** with 2,5-dimethylene-2,5-dihydrofuran led to a mixture of reaction products which was submitted to chromatography to yield (in the order of elution) (1) the doubly [10]para-bridged [2.2]paracyclophane (**19a**) (12%), (2) the benzene–furan "hybrid" [2.2]paracyclophane (**18a**) (11%), (3) [2.2]furanophane (**17**) (8%). Hydrolysis followed by bisthioketalization and desulfurization with Raney nickel converted the benzene–furan "hybrid" coupling product **18a** into [8][10]paracyclophane **3a** in 49% yield from **18a.**

Uv Spectra. The uv spectra of [8][8]- and [8][10]paracyclophanes are reproduced in Figure 1 and summarized in

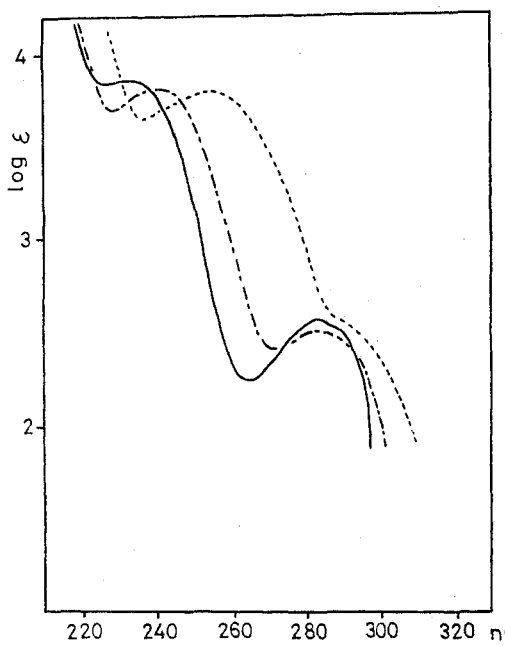


Figure 1. Uv spectra of **3a** (– – – –), **3b** (- - - -), and **11b** (—) in isooctane.

Table I. Allinger analyzed[5] the uv spectra of [*n*]paracyclophanes (**4**) to indicate that the benzene ring of [8]paracyclophane (**4**, $n = 8$) is puckered, the carbon atoms of the benzene ring bearing the methylene bridge being bent out of the plane of the other four carbon atoms, the angle of distortion amounting to about 20°. Should this distortion apply to [8][8]paracyclophane (**3b**), the benzene ring must be deformed to a twist-boat conformation (D_2 symmetry) which is revealed in its rather unusual uv absorption. Compared with the uv spectrum of the open chain model compound **11b,** the maxima tend to move toward longer wavelengths and lower intensities. The similar trends with lesser degree are also evident in the uv spectrum of [8][10]paracyclophane (**3a**). Figure 2 records the uv spectra of the doubly para-bridged [2.2]paracyclophanes **19a** and **19b** as well as 4,7,12,15-tetramethyl[2.2]-paracyclophane.[7] Here also the [8]para-bridged compounds

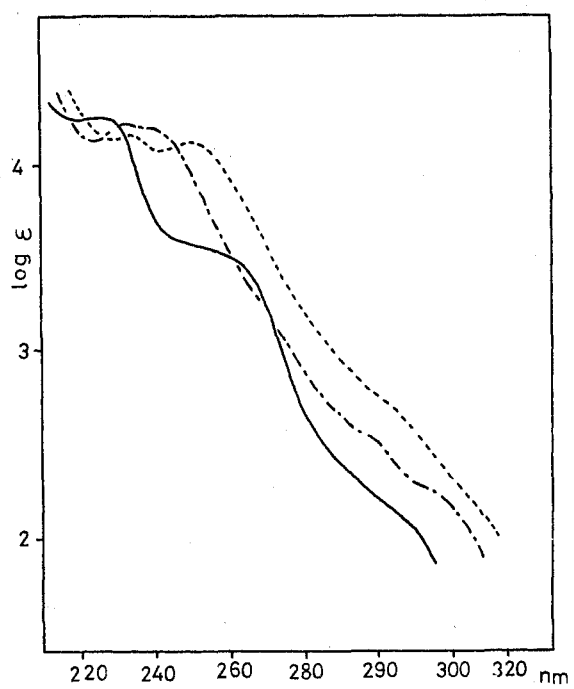


Figure 2. Uv spectra of **19a** (– – – –), **19b** (- - - -), and 4,7,12,15-tetramethyl[2.2]paracyclophane (—) in isooctane.

exhibit marked bathochromic shifts with lowering intensities.

NMR Spectra. Table II summarizes the NMR data of the doubly para-bridged [2.2]paracyclophanes (**19**) and those of [8]- and [10]paracyclophanes as reference compounds. Although general feature of the spectrum of [8][8]paracyclophane are close to that of [8]paracyclophane, the high-field band due to the heavily shielded four methylene protons of [8][8]paracyclophane appears to move toward slightly higher field.

Chemical Topology. It is pertinent to note here some considerations important to chemical topology inherent to these [*n*][*n*]- and [*m*][*n*]paracyclophanes. Inspection of the molecular models of [8][8]- and [8][10]paracyclophanes reveals that their polymethylene bridges should be on the opposite sides of the central benzene ring, and this is supported by the observation that they were unable to form a molecular complex with tetracyanoethylene. However, when the polymethylene chains become long enough, we can expect to have anti (D_2 symmetry) **21** and syn (C_2 symmetry) **22** geometrical isomers for [*n*][*n*]paracyclophane, and one anti (C_2 symmetry) **23** and two syn forms (C_1 symmetry) **24, 25** for [*m*][*n*]paracyclophane depending upon which chain comes nearer to the benzene ring (Chart II).

Experimental Section

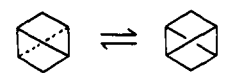
Melting points and boiling points are uncorrected. Infrared spectral data were obtained from a Hitachi EPI-S2 spectrophotometer. Nuclear magnetic resonance spectra were obtained from a JNM-MH-100 spectrometer. Ultraviolet spectra were recorded on a Hitachi EPS-3T

Table II. 100-MHz ^{1}H NMR Data in CCl_4 (τ)

Compd	Aromatic protons	Benzylic protons	Methyl protons	Methylene protons
3a	3.26 (2 H)	6.77–7.23 (4 H)		8.09–8.74 (8 H)
		7.87–7.91 (4 H)		8.74–9.14 (8 H)
				9.14–9.84 (10 H)
				9.84–10.42 (2 H)
3b	3.22 (2 H)	6.70–7.11 (4 H)		8.18–9.04 (14 H)
		7.37–7.85 (4 H)		9.15–9.75 (6 H)
				9.83–10.52 (4 H)
7	3.23 (2 H)	7.02–7.29 (2 H)	7.76 (6 H)	8.40–8.64 (4 H)
		7.46–7.87 (2 H)		8.79–9.12 (4 H)
				9.18–9.72 (8 H)
11b	3.27 (2 H)	6.86–7.15 (2 H)	7.75 (6 H)	8.20–9.00 (6 H)
		7.48–8.04 (2 H)		9.10–9.65 (4 H)
				10.02–10.44 (2 H)
19a	3.95 (4 H)	6.61–6.83 (4 H)		8.48–8.84 (8 H)
		6.93–7.48 (8 H)		8.95–9.27 (8 H)
		7.62–7.94 (4 H)		9.35–9.92 (16 H)
19b	3.85 (4 H)	6.55–6.90 (4 H)		8.35–9.29 (12 H)
		6.90–7.29 (8 H)		9.35–10.10 (8 H)
		7.76–8.10 (4 H)		10.22–10.94 (4 H)

Chart II

[n] [n] Paracyclopane



21 22

[m] [n] Paracyclopane

23 24 25

spectrometer. Mass spectral data were measured on a Hitachi RMS-4 spectrometer. Elemental analyses were determined by Yanagimoto CHN-Corder type II.

Methyl γ-(2,5-Dimethylbenzoyl)butyrate (5b). A mixture of *p*-xylene (**5a**, 54 g, 0.51 mol), γ-carbomethoxybutyryl chloride (83 g, 0.51 mol), and *s*-tetrachloroethane (300 ml) was cooled to −10 °C. Anhydrous aluminum chloride (200 g, 1.5 mol) was added to the stirred mixture in six portions during 2 h, and the reaction mixture was stirred for 3 h at 0 °C. The resulting dark solution was poured over ice, and the separted organic phase was washed with 2 N hydrochloric acid, water, 3% sodium bicarbonate solution, and again water, and then dried. After evaporation of the solvent, the residual oil was distilled to give **5b** (87 g, 73%), bp 177–179 °C (4 mm), n^{18}D 1.5201.

Methyl δ-(2,5-Dimethylphenyl)valerate (5d). A mixture of **5b** (76 g, 0.327 mol), 80% hydrazine hydrate (100 g, 1.6 mol), potassium hydroxide (106 g, 1.9 mol), and triethylene glycol (300 ml) was heated at 140 °C, and then water and excess hydrazine hydrate was allowed to distill until the temperature reached 200 °C. The reaction mixture was heated for 10 h at 200–210 °C, and cooled, and then diluted with water (500 ml). The aqueous solution was neutralized with concentrated hydrochloric acid and the resulting precipitate was extracted with chloroform. The chloroform solution was washed with water, dried, and then evaporated. The crude acid (**5c**) was esterified by heating for 3 h in methanol (300 ml) containing concentrated sulfuric acid (15 g), and the reaction mixture was poured into cold water and then extracted with ether. The ether solution was washed with water, 5% sodium bicarbonate solution, and again with water, and then dried. After removal of the solvent, distillation of the residue gave **5d** (63 g, 87.6%), bp 148–149 °C (6 mm), n^{17}D 1.5043.

Methyl γ-4-(ω-Carbomethoxybutyl)-2,5-dimethylbenzoylbutyrate (5e). Friedel–Crafts acylation of **5d** was carried out by the same method described for the preparation of **5b**, utilizing **5d** (63 g, 0.286 mol), γ-carbomethoxybutyryl chloride (49 g, 0.3 mol), *s*-tetrachloroethane (220 ml), and anhydrous aluminum chloride (122 g, 0.9 mol). The reaction mixture was worked up to give **5e** (77 g, 77.3%), bp 191–193 °C (0.01 mm). Recrystallization of this material from methanol–water gave mp 53–54 °C.

Anal. Calcd for $C_{20}H_{28}O_5$: C, 68.94; H, 8.10. Found: C, 69.01; H, 8.06.

1,4-Bis(ω-carbomethoxybutyl)-2,5-dimethylbenzene (5g). Wolff–Kishner reduction of **5e** was carried out by the same method described for the preparation of **5d**, utilizing **5e** (77 g, 0.221 mol), 80% hydrazine hydrate (69 g, 1.11 mol), potassium hydroxide (83 g, 1.5 mol), and triethylene glycol (350 ml). The crude acid **5f** was esterified in the usual manner to give **5g** (6.5 g, 88%), bp 183–185 °C (0.01 mm). Recrystallization of this ester from methanol–water gave mp 29–30 °C.

Anal. Calcd for $C_{20}H_{30}O_4$: C, 71.82; H, 9.04. Found: C, 71.77; H, 9.10.

Saponification of **5g** with methanolic potassium hydroxide afforded the acid **5f**, and recrystallization of this from methanol gave mp 148–149 °C.

Anal. Calcd for $C_{18}H_{26}O_4$: C, 70.56; H, 8.55. Found: C, 70.51; H, 8.56.

12,15-Dimethyl[10]paracyclophane (7). Preparation of the hydrocarbon **7** was carried out ccording to the usual sequence involving acyloin condensation and Clemmensen reduction.[13]

A. Acyloin Condensation of the Diester 5g. To a suspension of sodium (3.2 g, 0.144 mol) in dry xylene (400 ml) was added during 36 h a solution of **5g** (12 g, 0.036 mol) in dry xylene (300 ml). After an additional 1 h of heating and stirring, the reaction mixture was cooled to 0 °C, and acetic acid (10 ml) was slowly added. The polymer and sodium acetate were removed, and the resulting filtrate was concentrated under vacuum. Distillation of the residual oil gave the acyloin **6** (6.3 g, 64%), bp 152–153 °C (0.1 mm), n^{27}D 1.5412.

B. Clemmensen Reduction of the Acyloin 6. Amalgamated zinc was prepared by swirling zinc (66 g) with a solution of mercuric chloride (1.9 g) in water (200 ml) which contained concentrated hydrochloric acid (1.4 ml). A solution of **6** (6.3 g, 0.023 mol) in toluene (50 ml) was added to the amalgamated zinc with 200 ml each of concentrated hdyrochloric acid and acetic acid. The mixture was heated to reflux for 48 h, during which four 30-ml portions of concentrated hydrochloric acid were added. The reaction mixture was cooled and diluted with water, and then extracted with ether. The ether solution was washed with water, 5% sodium bicarbonate solution, and again with water, and then dried. After evaporation of the solvent, the residual solid was recrystallized from methanol to give **7** (3.7 g, 67%): mp 42–43 °C; ir (KBr) 2970, 2880, 2830, 1495, 1452, 1443, 1338, 1285, 1088, 1027, 910, 894, 835, 781, 711, 703 cm^{-1}; uv (isooctane) λ_{max} 262.5, 272.5, 281.7 nm (log ε 2.48, 2.75, 2.78); NMR (CCl_4) τ 3.23 (s, 2 H), 7.02–7.29 (m, 2 H), 7.46–7.87 (m, 2 H), 7.76 (s, 6 H), 8.40–8.64 (m, 4 H), 8.79–9.12 (m, 4 H), 9.18–9.72 (m, 8 H); MS *m/e* 244 (M^+).

Anal. Calcd for $C_{18}H_{28}$: C, 88.45; H, 11.55. Found: C, 88.51; H, 11.49.

Benzene–Furan Hybrid [2.2]Paracyclophane (10). A solution of duryltrimethylammonium bromide (**9**,[7] 60 g, 0.19 mol) in distilled

water (1.5 l.) was passed through a column containing Amberlite IRA-400 (30–100 mesh, 200 g) which had been converted to the OH form by passing 2 N sodium hydroxide solution (3 l.). The elute was combined with the quaternary ammonium hydroxide prepared from 5-methylfurfurylammonium iodide[6] (53 g, 0.19 mol) following the procedure described above, and the solution was concentrated to 500 ml under vacuum. The concentrate was heated with toluene (1 l.) containing phenothiazine (1 g), and water was removed by azeotropic distillation. After refluxing with stirring for 5 h, the solution was allowed to cool, and insoluble polymers were removed. Concentration to 200 ml under vacuum again gave some polymers which were filtered off. The filtrate was chromatographed on neutral alumina and eluted with hexane. The elution afforded the following sequence of compounds: the hybrid [2.2]paracyclophane **10** (9 g, 21%), 4,7,12,15-tetramethyl[2.2]paracyclophane[7] (4.5 g, 11%), and [2.2]furanophane[12] (4.3 g, 10%). After recrystallization from hexane, the hybrid [2.2]paracyclophane **10** melted at 65–66 °C; ir (KBr) 2970, 2920, 2860, 1600, 1536, 1490, 1446, 1425, 1393, 1365, 1318, 1210, 1162, 1131, 1008, 943, 892, 773, 721, 707 cm^{-1}; NMR (CCl_4) τ 3.63 (s, 2 H), 4.50 (s, 2 H), 6.77–7.12 (m, 2 H), 7.25–7.65 (m, 6 H), 7.90 (s, 6 H).

Anal. Calcd for $C_{16}H_{18}O$: C, 84.91; H, 8.02. Found: C, 85.07; H, 7.96.

3,6-Diketo-10,13-dimethyl[8]paracyclophane (11a). A mixture of **10** (8.8 g, 0.0388 mol), acetic acid (11 ml), water (6 ml), and 10% sulfuric acid (3 ml) was refluxed for 10 h. The solution was poured into water (300 ml) and extracted with chloroform. The organic solution was washed with water, 5% sodium bicarbonate solution, and again with water, and then dried. Removal of the solvent yielded 9.4 g of yellow solid which on recrystallization from benzene–hexane gave **11a** (8.1 g, 85%): mp 189–190 °C; ir (KBr) 2997, 2925, 2880, 1697, 1500, 1458, 1404, 1352, 1288, 1151, 1104, 1083, 895 cm^{-1}; NMR ($CDCl_3$) τ 3.24 (s, 2 H), 6.70–7.85 (m, 8 H), 7.70 (s, 6 H), 8.16–8.78 (m, 4 H).

Anal. Calcd for $C_{16}H_{20}O_2$: C, 78.65; H, 8.25. Found: C, 78.68; H, 8.15.

10,13-Dimethyl[8]paracyclophane (11b). A mixture of **11a** (8 g, 0.0328 mol), 100% hydrazine hydrate (5 g, 0.1 mol), potassium hydroxide (7 g, 0.125 mol), and diethylene glycol (40 ml) was refluxed for 10 h. The reaction mixture was cooled and poured into water, and the product was extracted with ether. After evaporation of the solvent, the residual oil was distilled to give **11b** (5.8 g, 82%): bp 132–134 °c (4 mm); $n^{15}D$ 1.5406; ir (film) 2980, 2930, 2860, 1498, 1458, 1446, 1372, 882, 803, 721, 687 cm^{-1}; NMR (CCl_4) τ 3.27 (s, 2 H), 6.86–7.15 (m, 2 H), 7.48–8.04 (m, 2 H), 7.75 (s, 6 H), 8.20–9.00 (m, 6 H), 9.10–9.65 (m, 4 H), 10.02–10.44 (m, 2 H); MS *m/e* 216 (M^+).

Anal. Calcd for $C_{16}H_{24}$: C, 88.82, H, 11.18. Found: C, 88.86; H, 10.92.

12-Bromomethyl[10]paracyclophane (13a). A mixture of **12a** (28 g, 0.13 mol), paraformaldehyde (7.8 g, 0.26 mol of formaldehyde), acetic acid (60 ml), 85% phosphoric acid (20 ml), and 47% hydrobromic acid (20 ml) was refluxed with stirring for 40 min. The cooled mixture was poured into cold water and extracted with ether. The ethereal solution was washed with water, 5% sodium bicarbonate solution, again with water, and then dried. The solvent was evaporated and distillation of the residue gave **13a** (22.8 g, 81.4%): bp 154–156 °C (1.0 mm); $n^{24}D$ 1.5747; NMR (CCl_4) τ 2.82–3.11 (m, 3 H), 5.52 (q, J = 10.5, 24 Hz, 2 H), 6.68–7.80 (m, 4 H), 7.95–9.98 (m, 16 H).

10-Bromomethyl[8]paracyclophane (13b). The bromomethylation of **12b** was carried out by the same method described for the preparation of **13a,** utilizing **12b** (9 g, 0.048 mol), paraformaldehyde (4.3 g, 0.144 mol of formaldehyde), acetic acid (32 ml), 85% phosphoric acid (10 ml), and 47% hydrobromic acid. The reaction mixture was worked up to give **13b** (8.8 g, 65%): bp 148–150 °C (0.6 mm); $n^{24}D$ 1.5781; NMR (CCl_4) τ 2.84–3.12 (m, 3 H), 6.12 (q, J = 14, 22 Hz, 2 H), 6.82–8.02 (m, 4 H), 8.14–10.35 (m, 12 H).

12-Methyl[10]paracyclophane (14a). A solution of **13a** (20 g, 0.064 mol) in dry tetrahydrofuran (80 ml) was added dropwise to a suspension of lithium aluminum hydride (5 g, 0.18 mol) in dry tetrahydrofuran (180 ml). The mixture was refluxed with stirring for 6 h, and excess reducing reagent was decomposed by addition of ethyl acetate. After acidifying the mixture with dilute hydrochloric acid, the organic phase was extracted with ether. The ether solution was washed with water, 5% sodium bicarbonate solution, and again with water. After evaporation of the solvent, the residual oil was distilled to give **14a** (12 g, 81%): bp 152–154 °C (4 mm); $n^{18}D$ 1.5336; MS *m/e* 230 (M^+); NMR (CCl_4) τ 3.16–3.22 (m, 3 H), 6.82–7.88 (m, 4 H), 7.76 (s, 3 H), 8.24–9.72 (m, 16 H).

Anal. Calcd for $C_{17}H_{26}$: C, 88.62; H, 11.38. Found: C, 88.66; H, 11.40.

10-Methyl[8]paracyclophane (14b). The reduction of **13b** was carried out by the same method described for the preparation of **14a,** utilizing **13b** (8 g, 0.028 mol) and lithium aluminum hydride (2 g, 0.053 mol). Distillation of the product gave **14b** (4.8 g, 85%): bp 124–126 °C (4 mm); $n^{27}D$ 1.5352; MS *m/e* 202 (M^+); NMR (CCl_4) τ 3.12–3.18 (m, 3 H), 6.77–7.93 (m, 4 H), 7.68 (s, 3 H), 8.27–10.45 (m, 12 H).

Anal. Calcd for $C_{15}H_{22}$: C, 89.04; H, 10.96. Found: C, 89.02; H, 10.93.

12-Bromomethyl-15-methyl[10]paracyclophane (8a). A. A mixture of **14a** (10 g, 0.043 ml), paraformaldehyde (2.1 g, 0.07 mol of formaldehyde), acetic acid (15 ml), 85% phosphoric acid (6 ml), and 47% hydrobromic acid (15 ml) was refluxed with stirring for 1 h. After the same treatment described for the preparation of **13a,** distillation of the product gave **8a** (11.7 g, 84%): bp 142–144 °C (1.0 mm); $n^{19}D$ 1.5776; NMR (CCl_4) τ 3.14 (s, 1 H), 3.45 (s, 1 H), 5.62 (q, J = 10, 24 Hz, 2 H), 7.8 (s, 3 H), 6.9–8.0 (m, 4 H), 8.1–9.7 (m, 16 H); MS *m/e* 323 (M^+).

Anal. Calcd for $C_{18}H_{27}Br$: C, 66.86; H, 8.42; Br, 24.72. Found: C, 66.77; H, 8.36; Br, 24.82.

B. A solution of bromine (3 g, 0.018 mol) in carbon tetrachloride (20 ml) was added during 4 h to a stirring solution of **7** (3.7 g, 0.015 mol) in carbon tetrachloride (20 ml) at room temperature. After an additional 5 h of stirring, the reaction mixture was poured into cold water and extracted with ether. The ether solution was washed with water, 5% sodium bicarbonate solution, again with water, and then dried. After evaporation of the solvent, the product was distilled to give **8a** (2.1 g, 45%).

10-Bromomethyl-13-methyl[8]paracyclophane (8b). The bromomethylation of **14b** was carried out by the same method described for the preparation of **8a,** utilizing **14b** (8.5 g, 0.042 mol), paraformaldehyde (1.64 g, 0.054 mol of formaldehyde), acetic acid (14 ml), 85% phosphoric acid (5.5 ml), and 47% hydrobromic acid (14 ml). Distillation of the product gave **8b** (9.2 g, 74%): bp 146–148 °C (2 mm); $n^{24}D$ 1.5778; NMR (CCl_4) τ 3.25 (s, 1 H), 3.44 (s, 1 H), 6.13 (q, J = 14, 23 Hz, 2 H), 6.8–7.2 (m, 2 H), 7.4–7.9 (m, 2 H), 7.71 (s, 3 H), 8.2–9.7 (m, 10 H), 10.0–10.3 (m, 2 H); MS *m/e* 295 (M^+).

Anal. Calcd for $C_{16}H_{23}Br$: C, 65.08; H, 7.85; Br, 27.07. Found: C, 64.96; H, 7.76; Br, 27.18.

12-Dimethylaminomethyl-15-methyl[10]paracyclophane Methanobromide (15a). A solution of **8a** (11.5 g, 0.035 mol) in ether (100 ml) was treated with excess anhydrous trimethylamine. The resulting salt was collected by filtration, washed with ether, and dried to afford **15a** (12.3 g, 92%). An analytical sample was recrystallized from ethanol, mp 224–226 °C.

Anal. Calcd for $C_{21}H_{36}NBr$: C, 65.95; H, 9.49; N, 3.66; Br, 20.90. Found: C, 65.95; H, 9.48; Br, 20.97.

10-Dimethylaminomethyl-13-methyl[8]paracyclophane Methanobromide (15c). A solution of **8b** (9 g, 0.031 mol) in ether (100 ml) was treated with excess anhydrous trimethylamine. The resulting salt was removed by filtration, washed with ether, and dried to afford **15c** (10.1 g, 95%). An analytical sample was recrystallized from ethanol, mp 198–200 °C dec.

Anal. Calcd for $C_{19}H_{32}NBr$: C, 64.39; H, 9.10; N, 3.95; Br, 22.55. Found: C, 64.48; H, 9.15; N, 3.91; Br, 22.42.

Benzene–Furan Hybrid [2.2]Paracyclophane (18a) and Doubly Bridged [2.2]Paracyclophane (19a). A mixture of **15a** (8.0 g, 0.021 mol) and 5-methylfurfuryltrimethylammonium iodide (6.0 g, 0.021 mol) was dissolved in water (300 ml) and converted to the hydroxide **15b** with freshly prepared silver oxide. The resulting aqueous solution was mixed with toluene (300 ml) and phenothiazine (0.1 g), and heated with stirring. After removal of water by azeotropic distillation, the reaction mixture was refluxed for 5 h and allowed to cool. The insoluble polymer was removed and the filtrate was concentrated under vacuum. The concentrate was extracted with hot hexane, and the hexane-soluble portion was chromatographed on neutral alumina in a cold room. Elution of the column with hexane afforded **19a** (0.9 g, 12%), which, when recrystallized from ethanol, gave mp 240–241 °C; ir (KBr) 2960, 2880, 2830, 1597, 1482, 1452, 1440, 1427, 886, 722, 708 cm^{-1}; MS *m/e* (rel intensity) 484 (18), 241 (53), 227 (56), 159 (57), 145 (100), 132 (87), 119 (56), 105 (27).

Anal. Calcd for $C_{36}H_{52}$: C, 89.19; H, 10.81. Found: C, 89.10; H, 10.80.

Further elution with hexane–benzene (9:1) furnished **18a** (1.23 g, 11%), which when recrystallized from ethanol gave mp 74–75°; ir (KBr) 2960, 2880, 2835, 1596, 1536, 1482, 1455, 1437, 1422, 1211, 1174, 1162, 1130, 1008, 946, 892, 773, 723, 707, 670 cm^{-1}; NMR (CCl_4) τ 3.6 (s, 2 H), 4.52 (s, 2 H), 6.6–7.9 (m, 12 H), 8.4–9.9 (m, 16 H); MS *m/e* 336 (M^+).

Anal. Calcd for $C_{24}H_{32}O$: C, 85.66; H, 9.59. Found: C, 85.27; H, 9.69.

Elution with hexane–benzene (5:1) gave [2.2]furanophane (**17**,[12] 0.32 g, 8%), mp 180–181 °C.

Benzene–Furan Hybrid [2.2]Paracyclophane (18b) and Doubly Bridged [2.2]Paracyclophane (19b). A solution (300 ml) of the mixed quaternary ammonium hydroxides derived from a mixture of **15c** (12 g, 0.0034 mol) and 5-methylfurfuryltrimethylammonium iodide (9.5 g, 0.0034 mol) in the usual manner was mixed with toluene (400 ml) and phenothiazine (0.5 g), and then pyrolyzed. Insoluble polymers were removed from the reaction mixture and the filtrate was chromatographed on neutral alumina. Elution with hexane provided **19b** (0.32 g, 3%), which, when recrystallized from ethanol, gave mp 229–231 °C; ir (KBr) 2960, 2875, 2820, 1587, 1478, 1440, 1428, 1045, 1003, 882, 805, 710, 687 cm^{-1}; MS *m/e* (rel intensity) 428 (70), 214 (100), 199 (80), 171 (37), 159 (37), 145 (50), 132 (83), 119 (43).

Anal. Calcd for $C_{32}H_{44}$: C, 89.65; H, 10.35. Found: C, 89.49; H, 10.39.

Further elution with hexane–benzene (9:1) produced **18b** (0.91 g, 8%). Because of instability of **18b**, the oily product could not be purified further: MS *m/e* 308 (M^+).

Elution with hexane–benzene (5:1) gave **17** (0.75 g, 12%).

3,6-Diketo[8][10]paracyclophane (20a). A mixture of **18a** (0.5 g, 1.5 mmol), water (0.5 ml), acetic acid (10 ml), and 10% sulfuric acid (0.3 ml) was heated at 65 °C with stirring for 1 h. The reaction mixture was poured into water (50 ml) and extracted with dichloromethane. The organic layer was washed with water, 5% sodium bicarbonate solution, and again with water, and then dried. After removal of the solvent, the residue was chromatographed on neutral alumina. Elution with dichloromethane afforded **20a** (0.47 g, 89%), which when recrystallized from hexane gave mp 161–162 °C; ir (KBr) 2970, 2890, 2830, 1700, 1593, 1488, 1452, 1435, 1408, 1318, 1287, 1170, 1145, 1000, 1077, 999, 770, 744, 732, 705 cm^{-1}; NMR (CCl_4) τ 3.33 (s, 2 H), 6.65–7.95 (m, 12 H), 8.15–8.60 (m, 8 H), 8.80–9.10 (m, 4 H), 9.15–9.70 (m, 8 H); MS *m/e* 354 (M^+).

Anal. Calcd for $C_{24}H_{34}O_2$: C, 81.31; H, 9.65. Found: C, 81.27; H, 9.70.

3,6-Diketo[8][8]paracyclophane (20c). Hydrolysis of **18b** was carried out by the method described for the preparation of **20a**, utilizing **18b** (0.4 g, 1.3 mmol), water (0.4 ml), acetic acid (10 ml), and 10% sulfuric acid (0.3 ml). The resulting product was chromatographed on neutral alumina. Elution with dichloromethane produced **20c** (0.24 g, 57%), which, when recrystallized from hexane, gave mp 156–157 °C; ir (KBr) 2970, 2890, 2840, 1700, 1595, 1484, 1454, 1431, 1408, 1317, 1287, 1168, 1143, 1098, 1075, 898, 734, 720, 687 cm^{-1}; NMR (CCl_4) τ 3.21 (s, 2 H), 6.82–7.93 (m, 12 H), 8.16–9.13 (m, 10 H), 9.17–9.65 (m, 4 H), 9.90–10.32 (m, 2 H); MS *m/e* 326 (M^+).

Anal. Calcd for $C_{22}H_{30}O_2$: C, 80.93; H, 9.26. Found: C, 80.62; H, 9.18.

Bisethanedithioketal 20b. A solution of **20a** (0.35 g, 1.0 mmol) in glacial acetic acid (20 ml) was mixed with a solution of ethanedithiol (0.2 g, 20 mmol) in glacial acetic acid (6 ml) which contained 47% boron trifluoride etherate (2 ml). After standing for 2 days at room temperature, the reaction mixture was poured into water (100 ml). The product was extracted with chloroform and washed with water and then dried. Removal of the solvent yielded the white solid product which on crystallization from ethanol gave **20b** (0.34 g, 87%), mp 153–154 °C.

Anal. Calcd for $C_{28}H_{42}S_4$: C, 82.97; H, 10.40. Found: C, 83.01; H, 10.36.

[8][10]Paracyclophane (3a). To a solution of **20b** (0.25 g, 0.6 mmol) in ethyl acetate (10 ml) was added W-5 Raney nickel (2 g), and the mixture was refluxed for 1.5 h. After being cooled and filtered, the resulting solution was concentrated under vacuum. The residual oil was chromatographed on neutral alumina. Elution with hexane afforded a colorless oil, which was distilled to give **3a** (0.13 g, 65%): bp 179–181 °C (2.0 mm); $n^{24}D$ 1.5472; ir (film) 2960, 2880, 2860, 2675, 1602, 1485, 1451, 1436, 1336, 1207, 1056, 1005, 883, 833, 730, 705, 687 cm^{-1}; MS *m/e* (rel intensity) 326 (100), 241 (28), 227 (38), 145 (30), 131 (30), 119 (26), 105 (24).

Anal. Calcd for $C_{24}H_{38}$: C, 88.27; H, 11.73. Found: C, 88.29; H, 11.74.

[8][8]Paracyclophane (3b). A solution of **20c** (0.15 g, 0.5 mmol) in glacial acetic acid (10 ml) was mixed with a solution of ethanedithiol (0.2 g, 20 mmol) in glacial acetic acid (5 ml). After 47% boron trifluoride etherate (2 ml) was added, the mixture was kept in a tightly sealed bottle and allowed to stand for 2 days at room temperature. Then the mixture was poured into water (100 ml). The product was extracted with chloroform, washed with 3% sodium bicarbonate solution and water, and then dried. After evaporation of the solvent, the crude thioketal **20d** was directly desulfurized as follows. To a solution of the crude thioketal **20d** (0.16 g) in ethyl acetate (10 ml) was added W-5 Raney nickel (1 g). The mixture was refluxed for 1 h, cooled, and filtered. After concentration of the filtrate, the oily product was subjected to alumina column chromatgraphy. Elution with hexane gave **3b** (0.09 g, 63%), which, when recrystallized from ethanol, gave mp 60–61 °C; ir (KBr) 2970, 2900, 2840, 2670, 1598, 1483, 1452, 1437, 1337, 1203, 1050, 1007, 876, 836, 726, 715, 707, 686 cm^{-1}; MS *m/e* (rel intensity) 298 (100), 199 (35), 185 (48), 145 (36), 131 (35), 119 (34), 105 (27).

Anal. Calcd for $C_{22}H_{34}$: C, 88.52; H, 11.48. Found: C, 88.46; H, 11.48.

Registry No.—**3a**, 34106-24-6; **3b**, 32543-09-2; **5a**, 106-42-3; **5b**, 60438-86-0; **5c**, 30098-17-0; **5d**, 60438-87-1; **5e**, 60438-88-2; **5f**, 60438-89-3; **5g**, 60438-90-6; **6**, 60438-91-7; **7**, 32543-11-6; **8a**, 32543-10-5; **8b**, 32543-03-6; **9**, 27742-95-6; **10**, 33357-05-0; **11a**, 60438-92-8; **11b**, 60438-93-9; **12a**, 5649-96-7; **12b**, 4685-74-9; **13a**, 26878-19-3; **13b**, 60438-94-0; **14a**, 60438-95-1; **14b**, 60438-96-2; **15a**, 32543-12-7; **15b**, 60438-97-3; **15c**, 32691-02-4; **17**, 5088-46-0; **18a**, 32540-67-3; **18b**, 32543-04-7; **19a**, 32585-31-2; **19b**, 32543-05-8; **20a**, 60438-98-4; **20b**, 60438-99-5; **20c**, 32543-07-0; **20d**, 32543-08-1; γ-carbomethoxybutyryl chloride, 1501-26-4; hydrobromic acid, 24959-67-9; 5-methylfurfuryltrimethylammonium iodide, 1197-60-0.

References and Notes

(1) Presented at the 24th Annual Meeting of the Chemical Society of Japan, Osaka, April 1971, Preprint, Vol. III, p 1293. M. Nakazaki, K. Yamamoto, and S. Tanaka, *Tetrahedron Lett.*, 341 (1971).
(2) M. Nakazaki, K. Yamamoto, and S. Tanaka, *J. Chem. Soc., Chem. Commun.*, 433 (1972).
(3) M. Nakazaki, "Syntheses and Stereochemistry of Twisted Organic Compounds", Invited Lecture at 30th National Meeting of the Chemical Society of Japan, Osaka, April 1974.
(4) D. H. Smith, "Bridged Aromatic Compounds", Academic Press, New York, N.Y. 1964, p 13.
(5) N. L. Allinger, L. A. Freiberg, R. B. Hermann, and M. A. Miller, *J. Am. Chem. Soc.*, **85**, 1171 (1963).
(6) D. J. Cram, C. S. Montgomery, and G. R. Knox, *J. Am. Chem. Soc.*, **88**, 515 (1966).
(7) D. T. Longone and C. L. Warren, *J. Am. Chem. Soc.*, **84**, 1507 (1962); D. T. Longone and F. P. Boettcher, *ibid.*, **85**, 3436 (1963).
(8) A. T. Blomquist and B. H. Smith, *J. Am. Chem. Soc.*, **82**, 2073 (1960); A. T. Blomquist, R. E. Stahl, Y. C. Meinwald, and B. H. Smith, *J. Org. Chem.*, **26**, 1687 (1961).
(9) D. J. Cram and H. U. Daeniker, *J. Am. Chem. Soc.*, **76**, 2743 (1954).
(10) Stereochemical consideration suggests the chiral trans configuration (D_2 symmetry) to this doubly [8]para-bridged [2.2]paracyclophane (**19b**), which was supported by comparison of racemic **19b** with the optically active **19b**[11] recently prepared from the optically active **15c**.
(11) K. Yamamoto and M. Nakazaki, *Chem. Lett.*, 1051 (1974).
(12) H. E. Weiberg, F. S. Fawcett, W. E. Mochel, and C. W. Theobald, *J. Am. Chem. Soc.*, **82**, 1428 (1960).
(13) D. J. Cram, N. L. Allinger, and H. Steinberg, *J. Am. Chem. Soc.*, **76**, 6132 (1954).