Tetrafluoro- and Octafluoro[4.2]paracyclophanes

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Synthetic sequences for the preparation of 6,7,9,10,14,15,17,18-octafluoro[4.2]paracyclophane (**1**) and 6,7,9,10-tetrafluoro[4.2]paracyclophane (**2**) are outlined. The u.v. absorption of compound **1** is hypsochromically shifted more than 20 nm from the long wavelength band (286–291 nm) characteristic of the [2.2]paracyclophanes.

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On décrit les séquences de la synthèse de l'octafluoro 6,7,9,10,14,15,17,18[4.2]paracyclophane (**1**) et du tétrafluoro 6,7,9,10[4.2]paracyclophane. Le spectre d'absorption ultraviolet du composé **1** est déplacé d'une façon hypsochrome par plus de 20 nm par rapport à la bande à longueur d'onde longue (286–291 nm) caractéristique des [2.2]paracyclophanes.

[Traduit par le journal]

In previous papers we described the syntheses and properties of octafluoro[2.2]paracyclophane (1) and tetrafluoro[2.2]paracyclophane (2). We report here the syntheses of 6,7,9,10,14,15,17,18-octafluoro[4.2]paracyclophane (**1**) and its tetrafluoro analog (**2**), as outlined in Schemes 1 and 2, respectively.

While compound **1** was obtained in pure form after an arduous separation from its open-chain analog, p-$CH_3C_6F_4(CH_2)_4C_6F_4CH_3$-$p$, **2** could not be separated cleanly from the corresponding open-chain compound, which was also formed in the final reaction to give a 50:50 mixture (by p.m.r. spectral analysis).

We have discussed previously (2) the influence of polyfluoroaryl rings on the u.v. spectra of [2.2]paracyclophanes and speculated on the possible roles of attractive and repulsive transannular interactions. In the present study we observed the effect of bridge length by comparing the spectra of the octafluoro[2.2]- and [4.2]-paracyclophanes (Fig. 1). When the value of *m* decreases from 4 to 2, a large bathochromic shift (269 nm → 291 nm) occurs, which may reflect enhanced ring distortions with increased proximity of the fluoroaromatic nuclei. This argument requires further scrutiny in light of recent studies on [6]paracyclophane (3). The spectrum of **1** more closely resembles that of its open-chain model (Fig. 1). A similar, though less pronounced, behavior has been observed in the corresponding nonfluorinated analogs (4).

Experimental

All melting points are uncorrected. Infrared spectra were measured on a Perkin-Elmer Model 257 spectrophotometer or a Beckman IR-8 i.r. spectrometer using sodium chloride cells with a path length of 0.1 mm. Ultraviolet spectra in cyclohexane were obtained on a Beckman DK-2 spectrophotometer.

Proton magnetic resonance spectra were obtained on a Varian A-60 n.m.r. spectrometer. Chemical shifts are reported in p.p.m. relative to tetramethylsilane as internal standard. Fluorine magnetic resonance spectra were obtained on a Varian DA-60-IL spectrometer operating at 56.44 MHz in the high resolution mode. Chemical shifts were measured by the sideband technique and are reported in p.p.m. upfield or downfield from hexafluorobenzene as internal standard. Unless otherwise noted, all spectra were obtained at approximately 15% concentration in carbon tetrachloride.

Elemental analyses were conducted by Micro-Tech Laboratories, Inc., Skokie, Illinois and M-H-W Laboratories, Garden City, Michigan.

1,4-Bis(pentafluorophenyl)-2-butene

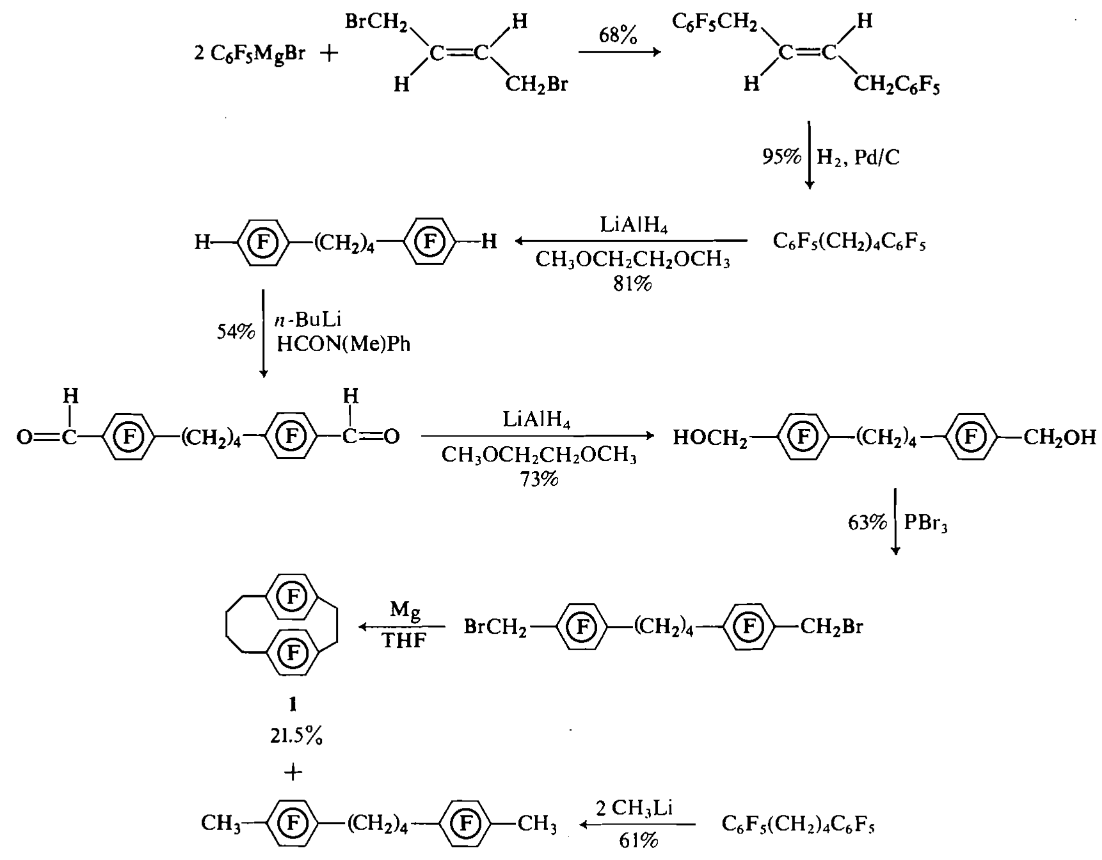
To the solution of pentafluorophenylmagnesium bromide, prepared under nitrogen by treating 6.08 g (0.25 g-atom) of magnesium with 61.8 g (0.25 mol) of bromopentafluorobenzene in 125 ml of anhydrous ether at 15°, was added 26.82 g (0.125 mol) of *trans*-1,4-dibromo-2-butene in 100 ml of anhydrous ether at a moderate rate. The resulting mixture was stirred for 28 h at reflux temperature and hydrolyzed by adding crushed ice and 150 ml of dilute hydrochloric acid. The ether layer was separated, washed with water and a saturated ammonium chloride solution, dried ($MgSO_4$), and evaporated *in vacuo* to give a brown solid. Recrystallization from 95% ethanol with 8 g of activated charcoal afforded 33 g (67.8%) of white needles; m.p. 94–94.5°; n.m.r. (CCl_4): δ 5.64 (m, 2, vinylic) and 3.42 (m, 4, methylene).

1,4-Bis(pentafluorophenyl)butane

Hydrogenation of 1,4-bis(pentafluorophenyl)-2-butene was conducted in ethyl acetate solution in a Parr apparatus using 5% palladium-on-charcoal to give 87% of the desired product, m.p. 71.5–74°.

1,4-Bis(2′,3′,5′,6′-tetrafluorophenyl)butane

To a solution of lithium aluminum hydride (10 g, 0.264 mol) in 240 ml of 1,2-dimethoxyethane, was added slowly



SCHEME 1

at 15°, 30 g (0.075 mol) of the bis(pentafluorophenyl)-butane. The resulting mixture was refluxed for 16 h. After decomposition of excess lithium aluminum hydride by adding a few drops of water followed by hydrolysis with dilute sulfuric acid, the mixture was poured into 2 l of water and a white solid precipitated. After decantation, the water layer was extracted with ether. The ether extract was used to dissolve the white solid, the solution was dried ($MgSO_4$), and evaporated *in vacuo* to give a white solid. Recrystallization from 95% ethanol afforded 22 g (81.3%) of product: m.p. 81.5–83°; n.m.r. δ 6.88 (triplet of triplet, 2, aromatic), 2.81 (m, 4, benzylic), and 1.71 (q, 4, J_{HH} = 3.38 Hz, methylene).

1,4-Bis(4′-formyl-2′,3′,5′,6′-tetrafluorophenyl)butane

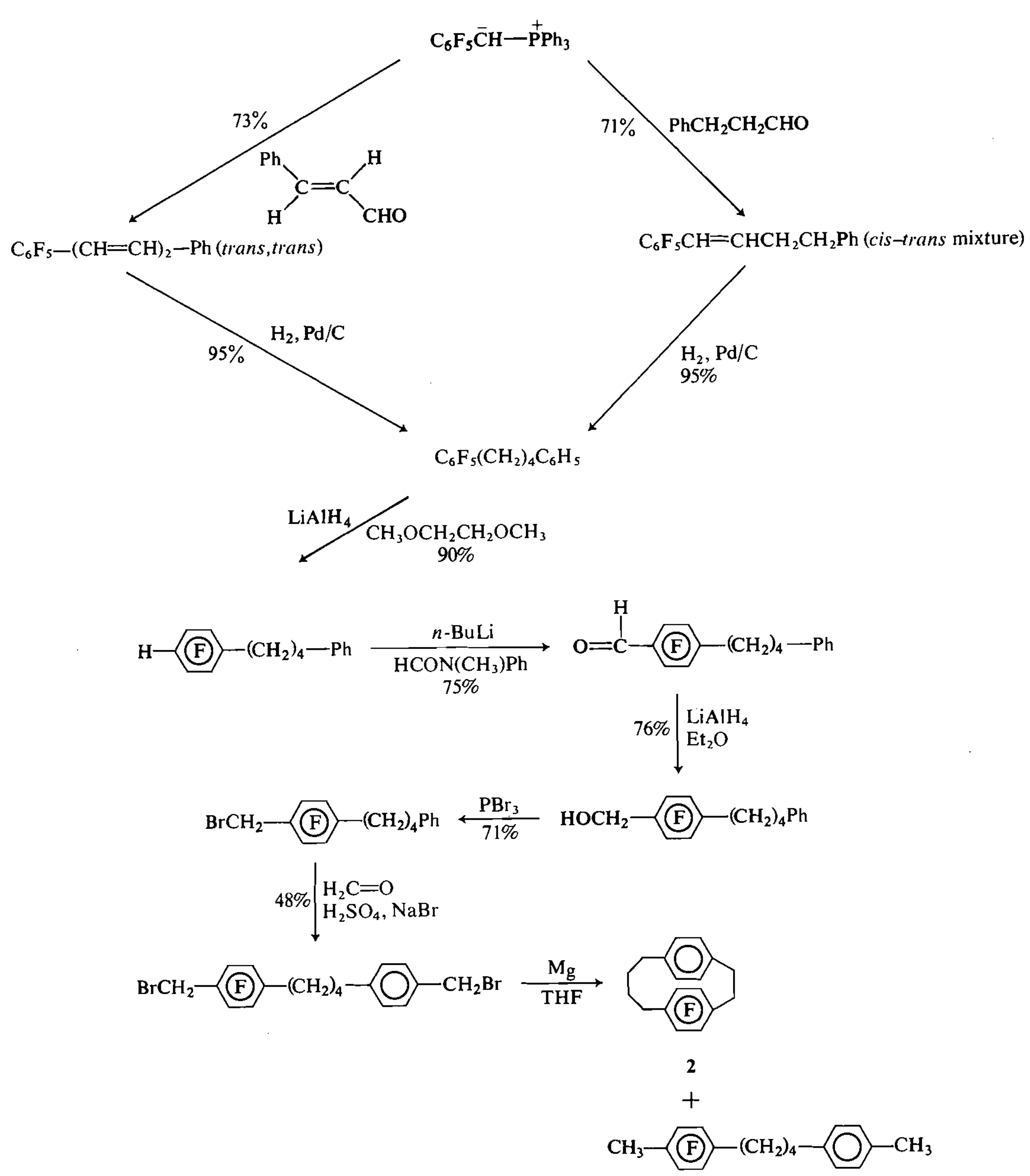
To a solution of 0.12 mol *n*-butyllithium (75.4 ml of 15% *n*-butyllithium in hexane) cooled to −78°, was added slowly 21.2 g (0.06 mol) of the bis(tetrafluorophenyl)-butane in 400 ml of anhydrous ether. The resulting milky solution was allowed to react for 2 h. *N*-Methylformanilide (16.24 g, 0.12 mol) in 160 ml of ether was added and stirred for 3 h. After hydrolyzing with 100 ml of water and 100 ml of 6 *N* hydrochloric acid, the mixture was extracted with 1 l of ether. The ether extract was washed, dried ($MgSO_4$), and evaporated *in vacuo* to give a white solid. Trituration of this solid with 30 ml of ether and filtration gave 13.25 g (53.9%) of the bisaldehyde, m.p. 128–129°; i.r. ($CHCl_3$) 2770 (aldehyde C—H), 1705 (C=O), and 1485 cm^{-1} (polyfluoroaromatic ring); p.m.r. ($CDCl_3$) showed a triplet at δ 10.3, J_{HCCF} = 1.1 Hz (2H, —C_6F_4—CHO), a complex multiplet centered at 2.88 (4H, benzylic protons), and a quintet centered at 1.80, J_{HH} = 3.38 Hz (4H, methylene protons).

1,4-Bis(4′-hydroxymethyl-2′,3′,5′,6′-tetrafluorophenyl)-butane

To a solution of 1.52 g (0.04 mol) of lithium aluminum hydride in 250 ml of 1,2-dimethoxyethane, 20.5 g (0.05 mol) of bisaldehyde in 250 ml of 1,2-dimethoxyethane was added slowly at 15° and the mixture was stirred for 90 min. After addition of 100 ml of dilute hydrochloric acid, the mixture was poured into 3 l of water. The white solid was filtered and washed with water. Recrystallization from benzene gave 15 g (72.5%) of the diol, m.p. 172–174°; i.r. (CCl_4) 3400 and 3330 cm^{-1} (O—H).

1,4-Bis(4′-bromomethyl-2′,3′,5′,6′-tetrafluorophenyl)-butane

A mixture of 23.3 g (0.0563 mol) of bisdiol and 30.54 g (0.1126 mol, 10.71 ml) of phosphorus tribromide was heated at 140° for 5 h and then cooled and poured into 500 ml of water. The yellow solid was filtered, washed successively with water, a 5% sodium carbonate solution, then water, and dried in air. Recrystallization from carbon



SCHEME 2

tetrachloride (400 ml) afforded 19.0 g (62.5%) of product as white needles. Sublimation at 150° (0.1 Torr) gave white crystals, m.p. 163.5–165°.

Anal. Calcd. for $C_{18}H_{12}Br_2F_8$: C, 40.03; H, 2.24. Found: C, 40.34; H, 2.26.

6,7,9,10,14,15,17,18-Octafluoro[4.2]paracyclophane (1)

To one-half of 0.3648 g (0.015 g-atom) of magnesium metal in 5 ml of tetrahydrofuran and a few crystals of iodine in a 250 ml three-necked flask, was added one-half of a tetrahydrofuran solution (105 ml) of 6.6 g (0.0122 mol) of the bisbromomethyl compound. After the mixture was stirred vigorously for 2 h, the Grignard reagent started to form. After two-thirds of the original magnesium had been consumed, the other half of magnesium and the solution of the starting material were added. After stirring for 72 h, 40 ml of tetrahydrofuran was added and the mixture stirred for an additional 60 h. The mixture was acidified with 150 ml of water and 60 ml of dilute hydrochloric acid. Filtration and air drying, followed by sublimation (410° (0.1 Torr)) of the resulting white solid, gave 2.5 g of white sublimate. Analysis of the p.m.r. (CCl_4) spectrum of this sublimate revealed the presence of 16% of starting material, 39% of octafluoro[4.2]paracyclophane (**1**), and 43% of reduction product, 1,4-bis(4′-methyl-2′,3′,5′,6′-tetrafluorophenyl)butane. The yield of **1** was estimated to be 1 g (21.5%). The residue from the sublimation was 2.7 g of polymeric material.

Recrystallization of the sublimate from pentane gave 0.42 g of starting material. The pentane-soluble portion was chromatographed with a 90:10 mixture of pentane–benzene on 1300 g of neutral alumina using a 5 ft column, to give about 1.0 g of material. Recrystallization from 95% ethanol gave 0.42 g of the reduced product, 1,4-bis(4′-methyl-2′,3′,5′,6′-tetrafluorophenyl)butane, m.p. 141–143° (no depression when admixed with an authentic sample); n.m.r. δ 2.27 (t, 6, $^4J_{HF}$ = 2.25 Hz, methyl), 2.75 (4, m, benzylic), and 1.67 (4, m, methylene β to C_6F_5). Evaporation of the ethanol-soluble portion gave a white solid which was recrystallized from 8 ml of 95% ethanol to give 80 mg of reduced product. Evaporation of the ethanol-soluble portion and recrystallization of the residue from 0.75 ml of methylcyclohexane gave 20 mg of white crystals of pure **1**. Sublimation at 125° (0.05 Torr) gave an analytical sample, m.p. 174.5–175.5°; n.m.r. (CCl_4) δ 3.27 (m, 4, —C_6F_4—CH_2CH_2—C_6F_4—), 2.57 (m, 4,—C_6F_4—CH_2—CH_2—CH_2—CH_2—C_6F_4—), and 1.70 (m, 4, —C_6F_4—$CH_2CH_2CH_2CH_2$—C_6F_4—); u.v. λ_{max} (cyclohexane) 222 shoulder and 269 nm (log ε, 3.87 and 3.16); mass spectrum *m*/*e* (relative intensity) 380 (51.3) (m^+), 204 (18.9) (CH_2—C_6F_4—$CH_2CH_2^+$), 176 (100) (CH_2—C_6F_4—CH_2^+), 28 (91) ($CH_2CH_2^+$).

Anal. Calcd. for $C_{18}H_{12}F_8$: C, 56.85; H, 3.18. Found: C, 56.64; H, 3.11.

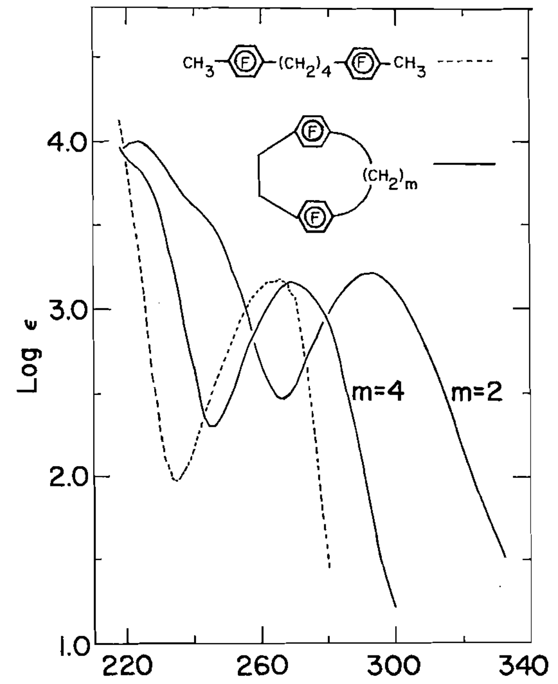


FIG. 1. Ultraviolet spectra of octafluoro[2.2]- and [4.2]paracyclophanes and open-chain model; solvent, cyclohexane.

1,4-Bis(4′-methyl-2′,3′,5′,6′-tetrafluorophenyl)butane

To an ethereal solution (20 ml) of 5 g (0.0128 mol) of 1,4-bis(pentafluorophenyl)butane, 15.85 ml of 5% methyllithium in ether was added sufficiently slowly to allow a gentle reflux under nitrogen. The resulting mixture turned light yellow, was stirred for 15 h, and hydrolyzed by adding ice and 6 *N* hydrochloric acid. Additional ether was required to extract the mixture. The ether layer was separated, dried ($MgSO_4$), and evaporated *in vacuo* to give a light yellow solid. Recrystallization from 95% ethanol, followed by two recrystallizations from Skelly B, with charcoal, gave 3 g (61.3%) of product, m.p. 141–145°. Sublimation at 140° (0.05 Torr) gave pure material, m.p. 141.5–143°.

Anal. Calcd. for $C_{18}H_{14}F_8$: C, 56.55; H, 3.69. Found: C, 56.60; H, 3.74.

2,3,4,5,6-Pentafluorobenzyltriphenylphosphonium Bromide

A mixture of 26.2 g (0.1 mol) of triphenylphosphine and 26.1 g (0.1 mol) of pentafluorobenzyl bromide in 180 ml of *p*-xylene was heated under reflux for 20 h. A white solid began to separate within ½ h. The white solid was collected and washed with 100 ml of *p*-xylene. Recrystallization from a 95:5 mixture of ether–methanol gave 51 g (97.5%) of the phosphonium salt: m.p. 240–241°; n.m.r. ($CDCl_3$) δ 8.15–7.60 (m, 15, aromatic) and two multiplets separated by 14 Hz, centered at 5.58 (2, C_6F_5—CH_2—P—).

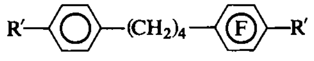
Anal. Calcd. for $C_{25}H_{17}F_5BrP$: C, 57.38; H, 3.27. Found: C, 57.27; H, 3.11.

1-Pentafluorophenyl-4-phenylbutane

In a 1-l three-necked flask, equipped with a magnetic strirrer, a reflux condenser, a pressure equalizing dropping funnel connected to a nitrogen supply, and a 125 ml Erlenmeyer flask connected to the reaction flask with Gooch tubing for solid addition, was placed 0.12 mol of *n*-butyllithium (75.36 ml of 15% *n*-butyllithium in hexane, Foote Mineral Co.) in 400 ml of dry benzene. To this solution, cooled to 15° by a water bath, was added 62.76 g (0.21 mol) of 2,3,4,5,6-pentafluorobenzyltriphenylphosphonium bromide in an Erlenmeyer flask disposed in a dive position, over a period of 10 min. The resulting orange-yellow solution was stirred for 1 h at room temperature and then brought to reflux. To the hot phosphorane solution, was added slowly 0.132 mol of hydrocinnamaldehyde or *trans*-cinnamaldehyde. The red color disappeared and the resulting mixture was heated under reflux for 14 h and filtered. The filter cake was washed with additional benzene, with water, 50 ml of ether, and then dried to give 30 g (90%) of triphenylphosphine oxide.

The filtrate (benzene layer) was evaporated *in vacuo* to give a mixture of *cis* and *trans* isomers of 1-pentafluorophenyl-4-phenyl-1-butene (70.9%) (b.p. 104–108° (0.05 Torr)), or *trans,trans*-1-pentafluorophenyl-4-phenyl-1,3-butadiene (73%), respectively. The butadiene: m.p. 145–147°; i.r. ($CHCl_3$) 1515, 1494, 1000, and 965 cm^{-1}; n.m.r. ($CDCl_3$) δ 7.6–6.3 (m, ArH and vinyl). The *trans,trans* configuration was supported by the presence of λ_{max} (EtOH) 327 and a shoulder at 314 nm (5) and by the ab-

TABLE 1. Physical and analytical data for substituted 1-pentafluorophenyl-4-phenylbutanes



R′	R″	Recrystallization solvent	% yield	Melting or boiling point °C (Torr)	Analysis (%) Calculated C	Calculated H	Found C	Found H
H	H		90	124–125.5 (1.3)*	68.08	5.00	68.60	4.18
H	CHO	Et_2O	75.3	70.5–72	65.81	4.55	66.11	4.62
H	CH_2OH	Hexane	76.0	43.5–45	65.38	5.16	65.59	5.32
H	CH_2Br	CH_3OH	71.4	70–71	54.42	4.03	54.37	4.42
CH_2Br	CH_2Br	Skelly B – sublimation at 120° (1 Torr)	48	118.5–120	48.18	3.46	48.20	3.51

*n_D^{25} 1.5033.

sence of out-of-plane rocking of H atoms attached to a *cis* double bonded carbon (976 cm^{-1}) in its i.r. spectrum (6).

Anal. Calcd. for $C_{16}H_9F_5$: C, 64.87; H, 3.06. Found: C, 64.91; H, 3.54.

Hydrogenation of this butene or butadiene over 5% palladium-on-charcoal afforded 95% of 1-pentafluorophenyl-4-phenylbutane: b.p. 115–118° (1 Torr), m.p. 17–20°; $n_D^{26.5}$ 1.4982.

Anal. Calcd. for $C_{16}H_{13}F_5$: C, 64.00; H, 4.36. Found: 64.28; H, 4.35.

1-(4′-Bromomethyl-2′,3′,5′,6′-tetrafluorophenyl)-4-phenylbutane

This compound was prepared via the same series of reactions and procedures described earlier in the synthesis of octafluoro[4.2]paracyclophane. Pertinent data are collected in Table 1.

1-(4′-Bromomethyl-2′,3′,5′,6′-tetrafluorophenyl)-4-(4″-bromomethylphenyl)butane

This compound was prepared from its precursor above by a bromomethylation procedure described previously (7). The relevant data are found in Table 1.

6,7,9,10-Tetrafluoro[4.2]paracyclophane (2)

The mono Grignard reagent, prepared by reaction of 6.02 g (0.015 mol) of 1-(4′-bromomethyl-2′,3′,5′,6′-tetrafluorophenyl)-4-(4″-bromomethylphenyl)butane in 60 ml of tetrahydrofuran and 0.40 g (0.0165 g-atom) of magnesium turnings, was stirred for 48 h under a nitrogen atmosphere. The resulting mixture was acidified with 100 ml of water and 40 ml of dilute hydrochloric acid, filtered, and washed with water. Sublimation of the white solid at 150° (0.1 Torr) gave 0.28 g of sublimate whose p.m.r. spectrum revealed that this substance was about a 50:50 mixture of the intramolecularly cyclized product, **2** (δ's similar to those for compound **1**), and its open-chain analog, p-$CH_3C_6F_4CH_2CH_2CH_2CH_2C_6H_4CH_3$-$p$, (—$C_6F_4$-$CH_3$), δ 2.27 (t), $^4J_{HF}$ = 2.25 Hz. Efforts to separate the two components by column chromatography on alumina, followed by fractional crystallizations from various solvents, *e.g.*, acetone, hexane, methylcyclohexane, acetic acid, and ethanol, were unsuccessful.

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