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TETRAHEDRON

Synthesis of [2.2]Paracyclophane Annelated Cycloproparenes

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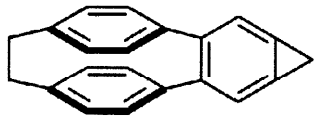
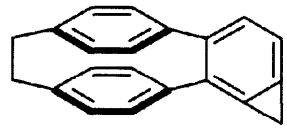
Abstract: The [2.2]paracyclophane annelated cycloproparenes **2** and **3** were synthesized by dehydrohalogenation of the adducts prepared by reacting 1-bromo-2-chlorocyclopropene with 1-vinyl[2.2]paracyclophane-1-ene and 1,2-dimethylene[2.2]paracyclophane, respectively.

Although Cram and Steinberg introduced the name cyclophane to describe compound **1** in which two benzene rings are tethered face to face by methylene bridges,[1] more recently this definition has been broadened to include the family of aromatic compounds bridged by at least one aliphatic *n*-membered bridge.[2] Indeed, cyclophane chemistry has played a central role in the development of important new areas including host-guest complexation.[3] In this paper we describe the synthesis of the new cyclophanes **2** and **3** in which a benzocyclopropene unit[4] replaces the ethano bridge in **1**.

1



2



3

The synthesis of **2** is illustrated in Scheme 1. A key step involves the use of 1-bromo-2-chlorocyclopropene **4**[5] as the cycloproparene synthon.[4] Thus, addition of **4** to 1,2-dimethylene[2.2]paracyclophane **5**[6] yields the adduct **6**. Due to the low thermal stability of **4**, the Diels-Alder reaction was carried out at -20° C. At this temperature the reactivity of the cyclopropene is low, and the adduct **6** could only be isolated in 23% yield (colorless crystals, m.p. 185° C). Dehydrohalogenation of **6** using a fivefold excess of potassium *t*-butoxide in tetrahydrofuran provides the desired cycloproparene **2** in 67% yield.[4]

The ^{1}H NMR spectrum of **2** exhibits characteristic signals at δ = 3.10 (s, 4H), 3.42 (s, 2H), 6.54 (s, 8H), and 7.51 (s, 2H). The ^{13}C NMR signal at δ = 113.5 is in agreement with the one for benzocyclopropene which appears at δ = 114.7. This high-field shift is typical of carbon atoms ortho to the cyclopropyl ring.[4]

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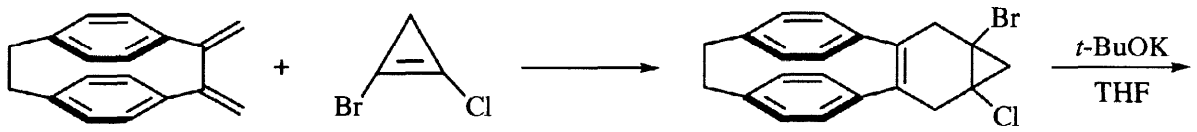
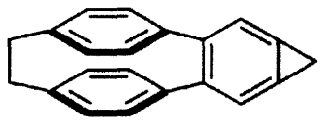
The cycloproparene is a colorless, crystalline substance that decomposes upon heating. Due to its low volatility, the foul odor characteristic of cycloproparenes is somewhat subdued.

Scheme 1



5 **4** **6**

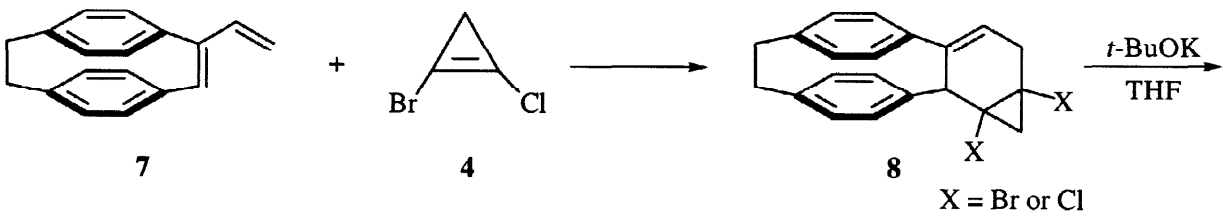


2

The synthesis of **3** (Scheme 2) requires 1-vinyl[2.2]paracyclophane-1-ene **7** as one of the starting materials. The diene was prepared in four steps from [2.2]paracyclophane as described previously.[7] When **7** was added to a freshly prepared solution of **4** in THF and kept at -20° C for five days, none of the desired addition product **8** could be detected (TLC). However, when a twenty-fold excess of the cyclopropene was used and the reaction mixture was warmed slowly to room temperature over the course of several days, **8** could be isolated in 9% yield (colorless crystals, m.p. 196-200° C). The adduct **8** could be converted to the cycloproparene **3** in 50% yield.

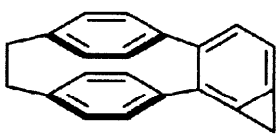
Attempts to improve the yield of **8** by using a forty-fold excess of **4** led instead to the formation of a mixture of polymeric byproducts resulting from the cyclopropene. We were unable to catalyze the reaction using $BF_3{\cdot}Et_2O$ or $ZnCl_2$ as described previously for another system.[8]

Scheme 2



7 **4** **8**

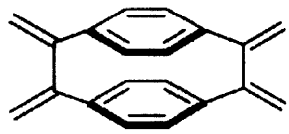
X = Br or Cl



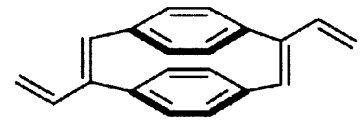
3

The tetraenes **9** and **10** were also synthesized and reacted under ambient pressure with **4** to yield **11** and

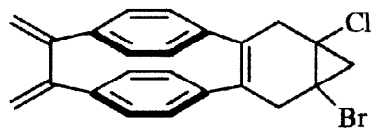
12 in 8% and 24% yield, respectively. The formation of *bis* adducts was not observed under these conditions. This may be attributed to the additional strain that would be imposed by fusion of a second cyclohexenyl ring to the cyclophane. Similarly, the addition of a Lewis acid catalyst ($BF_3{\cdot}Et_2O$ or $ZnCl_2$) does not affect the yield of the Diels-Alder reactions.



9

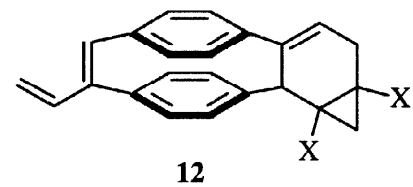


10



11

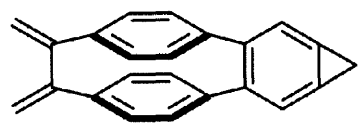
X = Br or Cl



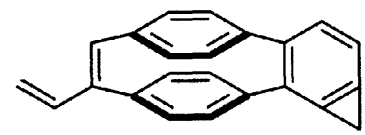
12

X = Br or Cl

Conversion to the respective cycloproparenes (**13** and **14**) could be achieved readily using the reaction conditions described above for the synthesis of **2**. Compound **13** could be isolated in 61% yield and **14** in 57% yield.



13



14

Studies on the dimerization of these cycloproparenes by silver ion to yield new dimeric paracyclophanes[9] will be carried out when larger samples become available.

EXPERIMENTAL SECTION

General. ^1H and ^{13}C NMR spectra were recorded in deuteriochloroform using a Bruker 250 MHz (^1H: 250 MHz, ^{13}C: 62.9 MHz) spectrometer. Chemical shifts (δ) are expressed downfield from tetramethylsilane using the residual chloroform as internal standard. Coupling constants are expressed in Hertz. Infrared spectra of new compounds were recorded using a Nicolet 205 FT-IR spectrophotometer. High resolution mass spectra were recorded using a Finnigan Mat 95 (70 eV) spectrometer. UV spectra were recorded using a Hewlett Packard HP8452A spectrometer. Column chromatography was performed using Spectrum silica gel grade 60. Whatman silica gel plates 60 K6F were used for analytical thin layer chromatography.

Paracyclophane **5**. 1,2-Dimethylene[2.2]paracyclophane **5** was prepared as described by König and de Meijere.[6]

Paracyclophanes 7 and 10. 1-Vinyl[2.2]paracyclophane-1-ene **7** and 1,9-divinyl[2.2]paracyclo-phane-1,9-diene **10** were prepared by the method of Psiorz.[7]

Paracyclophane 9. 1,2,9,10-Tetra(bromomethyl)[2.2]paracyclophane-1,2-diene was prepared using the method of König and de Meijere[6] and treated with NaI in acetone as described below. Thus tetra(bromomethyl)[2.2]paracyclophane-1,2-diene (265 mg, 0.44 mmol) was added to a solution of sodium iodide (2.650 g, 0.0177 mol) in acetone (20 mL). The mixture was then sonicated at room temperature for 3 hrs. The solvent was removed *in vacuo* and CH_2Cl_2 (50 mL) was added to the residue. The insoluble salts were removed by filtration and the filtrate was washed with saturated $Na_2S_2O_3$ (20 mL) followed by water (20 mL). After drying over anhydrous magnesium sulfate, the solvent was removed in vacuo. The brown residue was chromatographed on silica gel with hexanes, yielding 59 mg (52 %) of **9**. The spectroscopic data are consistent with the literature.[6]

1-Bromo-2-chlorocyclopropene 4. 1-Bromo-1-trimethylsilyl-2,2-dichlorcyclopropane[5] (1 equiv) was added to a solution of tetra-*n*-butylammonium fluoride (1.5 equiv) in THF (ca 2 mL/g Bu_4NF) and then cooled to -40° C. The mixture was stirred at -25° C for 1 h. The THF and the cyclopropene were then vacuum distilled (0.1 Torr) into a trap cooled with liquid nitrogen. The reaction flask was then warmed slowly to room temperature to ensure complete distillation of the cyclopropene. After the distillation was completed, the distillate was warmed to -78° C in an acetone/dry-ice bath under argon. The trap was then removed quickly from the distillation apparatus and capped with a rubber septum.

General Procedure for the Diels-Alder Addition Dienes 5 and 7 and Tetraenes 9 and 10 to Cyclopropene 4. A solution of the diene or tetraene in THF (1 mL) was added via a syringe to a stirred solution of **4** (twenty-fold excess) in THF at -78° C. The solution was warmed slowly to -20° C and kept in the freezer at this temperature for two days. The mixture was then warmed to 0° C and stored at 0° C for 2 days. The mixture was then immersed in an ice bath and warmed to room temperature. After removal of the solvent *in vacuo,* the residue was chromatographed on a silica gel column (18 x 1.5 cm) with chloroform/hexanes 1:3: Unreacted starting material elutes first followed by the Diels-Alder product.

Compound 6. Reaction of **5** (95 mg; 0.41 mmol) with a twenty-fold excess of **4** yields 47 mg (30 %) of **6**. Colorless crystals, m.p. 185° C; IR: ν = 3060 cm^{-1} (w), 3000 (w), 2920 (m), 2840 (w), 1575 (m), 1480 (m), 1425 (m), 1400 (m), 1075 (s), 1025 (s), 930 (m), 800 (s), 725 (s), 625 (s). - ^{1}H-NMR: δ = 1.65 (d, ^{2}J=7.5 Hz, 1 H, cyclopropane CH_2), 1.95 (d, ^{2}J=7.5 Hz, 1 H, cyclopropane CH_2), 3.01 (s, 4 H, -CH_2-CH_2-), 3.45-3.67 (m, 4 H, allyl CH_2), 6.22-6.48 (m, 8 H, ArH). - ^{13}C-NMR: δ = 25.9 (cyclopropane CH_2), 34.6 (-CH_2-CH_2), 39.6, 38.1, 41.9, 46.1, 130.6, 131.5, 132.2, 132.3, 137.7, 137.9, 139.1, 139.8, 139.9. - MS: m/z (%) = 388 (26) [M$^+$], 386 (100) [M$^+$], 384 (74) [M$^+$], 270 (14), 239 (13), 202 (18), 165 (10), 127 (7), 115 (12), 91 (6), 65 (5). - $C_{21}H_{18}{}^{81}Br^{35}Cl$: calcd. 386.0261; found 386.0263 (MS).

Compound 8. Diene **7** (57 mg; 0.25 mmol) gave 7 mg (9%) of **8** as colorless crystals, m.p. 196-200° C. - IR (KBr): ν = 3050 cm^{-1} (w), 2950 (m), 2925 (m), 2850 (w), 1620 (m), 1525 (m), 1430 (s), 1110 (m), 980 (s). - ^{1}H-NMR: δ = 1.70 (d, ^{2}J=7.5 Hz, 1 H, cyclopropane CH_2), 2.30 (d, ^{2}J=7.5 Hz, 1H, cyclopropane CH_2), 3.03 -3.15 (m, 6 H, -CH_2-CH_2-, allyl CH_2), 4.33 (m, 1 H, CH), 5.78 (m, 1 H, C=CH), 6.35-6.72 (m, 8 H, ArH). - ^{13}C-NMR: δ = 24.35 (cyclopropane CH_2), 24.42 (cyclopropane CH_2), 34.80 (-CH_2-CH_2-), 34.83 (-CH_2-CH_2-), 34.97, 37.03,37.35, 43.83, 45.28, 50.62, 55.25, 56.92, 119.25, 119.45, 131.47, 131.79, 131.81, 131.97, 132.09, 132.46, 132.55, 132.57, 133.62, 133.72, 133.77,

133.79, 134.67, 139.28, 139.33, 139.34, 139.98, 140.12, 140.17, 140.79, 144.32, 144.68. - MS: m/z (%) = 388 (9) [M+], 386 (41) [M+], 384 (31) [M+], 271 (17), 270 (14), 256 (10), 239 (14), 235 (60), 233 (57), 189 (100), 115 (44), 89 (8). - $C_{21}H_{18}{}^{79}Br^{35}Cl$: calcd. 384.0280; found 384.0279 (MS).

Compound 11. Reaction of **9** (85 mg; 0.33 mmol) with **4** gave 33 mg (24 %) of colorless crystals, m.p. 175 °C.- IR: ν = 3080 cm^{-1} (w), 3020 (w), 2900 (w), 2825 (w), 1725 (w), 1655 (w), 1580 (w), 1430 (m), 1405 (s), 1075 (s), 1025 (s), 910 (s), 830 (s), 730 (s), 615 (s). - ^{1}H-NMR: δ = 1.65 (d, ^{2}J=7.5 Hz, 1 H), 1.93 (d, ^{2}J=7.5 Hz, 1 H, cyclopropane CH_2), 3.45-3.70 (m , 2 H, allyl CH_2), 5.32 (d, ^{2}J=1.7 Hz, 2 H, C=CH_2), 5.67 (d, ^{2}J=1.7 Hz, 2 H, C=CH_2), 6.30-6.61 (m, 8 H, ArH). - ^{13}C-NMR: δ = 25.8 (cyclopropane CH_2), 37.8, 39.2, 41.4, 45.9, 109.9 (*C*=CH_2), 130.22, 130.26, 131.0, 132.29, 132.31, 137.2, 137.3, 138.8, 139.0, 140.6, 152.4.- MS: m/z (%) = 412 (29) [M+], 410 (100) [M+], 408 (72) [M+], 375 (5), 373 (5), 329 (28), 278 (22), 252 (12), 189 (10), 165 (18), 139 (16), 115 (11). - $C_{23}H_{18}{}^{81}Br^{35}Cl$: calcd. 410.0260; found: 410.0264 (MS).

Compound 12. Tetraene **10** (57 mg; 0.22 mmol) gave 7 mg (8%) of **12** as colorless crystals, m.p. 172-173° C. - IR: ν = 3100 cm^{-1} (w), 3010 (w), 2925 (w), 2875 (w), 2840 (w), 1610 (m), 1590 (m), 1490 (m), 1400 (m), 1060 (s), 1000 (s), 925 (s), 850 (s), 700 (s), 650 (s). - ^{1}H-NMR: δ = 1.70 (d, ^{2}J=7.5 Hz, 1 H, cyclopropane CH_2), 2.27 (d, ^{2}J=7.5 Hz, 1 H, cyclopropane CH_2), 3.23 (m, 2 H, allyl CH_2), 4.28 (m, 1 H, CH) 5.41 (m, 2 H, H_2C=CH-), 5.82 (m, 1 H, C=C*H*-CH_2-), 6.31 (m, 3 H, ArH), 6.52-6.67 (m, 4 H, ArH), 6.79 (dd, $^3J_{cis}$=12.5 Hz, $^3J_{trans}$=17.5 Hz, 1 H, HC=C-C*H*=CH_2), 6.88 (m, 1 H, ArH), 7.12 (s, 1 H, *H*C=C-CH=CH_2) - ^{13}C-NMR: δ = 24.29 (cyclopropane *C*H_2), 24.37 (cyclopropane *C*H_2), 34.86, 37.02, 37.24, 43.82, 45.26, 50.71, 54.69, 56.34, 118.97, 119.73, 129.22, 129.25, 130.67, 130.69, 131.11, 131.21, 132.75, 132.77, 132.84, 133.82, 133.85, 134.13, 137.18, 137.23, 138.60, 139.37, 139.57, 140.40, 141.00, 143.31, 143.66, 150.84. - MS: m/z (%) = 412 (29) [M+], 410 (100) [M+], 408 (80) [M+], 329 (59), 294 (20), 289 (12), 277 (25), 265 (25), 239 (22), 202 (16), 189 (13), 139 (23), 115 (30). - $C_{23}H_{18}{}^{81}Br^{35}Cl$: calcd. 410.0260; found 410.0260

General Procedure for the Preparation of the Cyclopropparenes. A solution of the starting dihalide in dry THF (1 mL) was added rapidly to a stirred suspension of potassium *t* -butoxide in THF (2 mL) under an atmosphere of argon at - 50° C. The mixture was then warmed to - 20° C and stirred for one hour. The solvent was removed *in vacuo* and the residue extracted with pentane. The pentane extract was filtered over a florisil-plug. Removal of the solvent i*n vacuo* yields nearly pure cyclopropparene.

Cyclopropparene 2. Treatment of **6** (20 mg; 0.05 mmol) with 56 mg (0.50 mmol) of *t*-BuOK gives 9 mg (67 %) of **2** as fine colorless crystals, dec. > 200° C. - IR: ν = 2940 cm^{-1} (m), 2850 (w), 1660 (m), 1410 (m), 960 (m), 725 (s), 625 (s). - UV (hexane): λ_{max} (lg ε) = 200 nm (4.46), 224 (4.33), 280 (3.66). - ^{1}H-NMR: δ = 3.10 (s, 4 H, -CH_2-CH_2-), 3.42 (s, 2 H, CH_2), 6.54 (s, 8 H, p-ArH), 7.51 (s, 2 H, o-ArH). - ^{13}C-NMR: δ = 20.1 (-CH_2-), 34.8 (-CH_2-CH_2-), 113.5, 124.8, 132.2, 132.8, 139.2, 140.7, 139.2, 140.7, 146.9. - MS: m/z (%) = 268 (100) [M+], 267 (9), 265 (9), 253 (7), 252 (21), 239 (7), 126 (5). - $C_{21}H_{16}$: calcd. 268.1252; found: 268.1249 (MS).

Cyclopropparene 3. Reaction of **8** (11 mg; 0.03 mmol) with *t*-BuOK (28 mg; 0.25 mmol) yields 4 mg (50 %) of **3** as fine colorless powder, dec. > 200° C. - IR: ν = 2925 cm^{-1} (s), 2850 (s), 1740 (m), 1450 (m), 1400 (m), 1260 (m), 825 (s), 730 (s). - UV (hexane): λ_{max} (lg ε) = 200 nm (4.52), 222 (4.46), 276 (3.27) - ^{1}H-NMR: δ = 3.13 (s, 4 H, -CH_2-CH_2-), 3.42 (s, 2 H, CH_2), 6.56 (s, 4 H, p-ArH), 7.28 (d, ^{3}J=7.5 Hz, 1 H,

o-ArH), 7.49 (d, ^{3}J=7.5 Hz, 1 H, o-ArH).- ^{13}C-NMR: δ = 19.7, 34.8, 34.9, 113.3, 121.3, 124.9, 126.8,, 132.30, 132.34, 132.49, 132.53, 137.8, 139.3, 139.6, 140.6, 147.5. - MS: m/z (%) = 292 (100) [M$^+$], 291 (8), 289 (12), 276 (13), 263 (11), 146 (5) - $C_{21}H_{16}$: calcd. 268.1252; found: 268.1250 (MS).

Cycloproparene ***13***. Dehydrohalogenation of **11** (24 mg, 0.06 mmol) using *t*-BuOK (67 mg, 0.60 mmol) gives 10 mg (57 %) of **13** as fine, colorless powder, dec. > 150°C. - IR: ν = 2950 cm^{-1} (m), 2850 (w), 1660 (m), 1590 (m), 1500 (w), 1450 (m), 905 (s), 840 (s), 740 (s), 625 (s) - UV (hexane): λ_{max} (lg ε) = 202 nm (4.58), 226 (4.31), 280 (3.85) - ^{1}H-NMR: δ = 3.42 (s, 2 H, cyclopropene CH_2), 5.39 (d, ^{2}J=1.5 Hz, 2 H, C=CH_2), 5.72 (d, ^{2}J=1.5 Hz, 2 H, C=CH_2), 6.63 (m, 8 H, p-ArH), 7.55 (s, 2 H, o-ArH).^{13}C-NMR: δ = 19.9 (-CH_2-), 109.8, 113.5, 125.0, 132.27, 132.27, 139.6, 140.6, 145.9, 152.8. - MS: m/z (%) = 292 (100) [M$^+$], 289 (13), 276 (13), 263 (11), 146 (5). - $C_{23}H_{16}$: calcd. 292.1252; found: 292.1251 (MS).

Cycloproparene ***14***. Reaction of **12** (15 mg, 0.04 mmol) with *t*-BuOK (45 mg, 0.4 mmol) yields 7 mg (61 %) of **14** as fluffy, colorless powder, dec. > 170° C. - IR: ν = 2990 cm^{-1} (w), 2950 (w), 1675 (w), 1600 (w), 1550 (w), 1490 (w), 1440 (w), 1000 (m), 925 (m), 840 (s), 730 (s), 650 (s). - UV (hexane): λ_{max} (lg ε) = 202 nm (4.45), 220 (4.47), 276 (3.24) - ^{1}H-NMR: δ = 3.42 (s, 2 H, cyclopropene CH_2), 5.44 (m, 2 H, H_2C=CH-), 6.53-6.71 (m, 8 H, p-ArH), 6.82 (dd, $^3J_{cis}$=10 Hz, $^3J_{trans}$=17 Hz, 1 H, HC=C-C*H*=CH_2), 7.15 (s,1 H, *H*C=C-CH=CH_2), 7.30 (d,^{3}J=7.5 Hz, 1 H, o-ArH), 7.51 (d,^{3}J=7.5 Hz, 1 H, o-ArH). - ^{13}C-NMR: δ = 19.7 (-CH_2-),, 113.4, 118.8, 121.3, 125.0, 126.6, 130.5, 131.0, 131.65, 131.67, 131.8, 134.2, 137.4, 137.7, 139.0, 140.3, 146.5, 150.6. - MS: m/z (%) = 292 (100) [M$^+$], 289 (24), 276 (23), 263 (17), 138 (8), 132 (7). - $C_{23}H_{16}$: calcd. 292.1252; found: 292.1250 (MS).

Acknowledgments

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