that the mixture was slowly warmed from 60 to 120 °C. After 3 h the reaction was worked up as before. Development of preparative layer plates with 1:9 methanol–dichloromethane gave a trace of starting **6** and 0.129 g (0.568 mmol, 56.8%) of **9**, which was recrystallized from 10 mL of Skellysolve C to give white scales of **9**: mp 93–95 °C; ^{13}C NMR, see Table I; ^{1}H NMR, see Table II; UV, see Table III; mass spectrum, *m/z* 228 (^{81}BrM$^+$), 226 (^{79}BrM$^+$), 199, 197, 147, 119, 92, 65.

Anal. Calcd for $C_7H_7N_4Br$: C, 37.0; H, 3.1; N, 24.7. Found: C, 37.4; H, 3.2; N, 24.6.

6-Iodo-9-ethylpurine (10). A mixture of 0.163 g (1.0 mmol) of **6** and 2.7 mL (20 mmol) of *n*-pentyl nitrite was treated with 5 mL of diiodomethane as in **5b** and warmed to 80 °C. After 10 h, the reaction was worked up and treated to remove iodine color as before. Preparative layer chromatography on silica gel (1:9 methanol–methylene chloride for development) gave at R_f 0.49 0.0964 g (0.345 mmol, 34.5%) of **10**, which was recrystallized from Skellysolve C to give a dense pale yellow powder: mp 141–143 °C; ^{13}C NMR, see Table I; ^{1}H NMR, see Table II; UV, see Table III; mass spectrum, *m/z* 274 (M$^+$), 147, 119, 92, 65.

Anal. Calcd for $C_7H_7N_4I$: C, 30.7; H, 2.6; N, 20.5. Found: C, 31.5; H, 2.7; N, 20.0.

6-Chloro-9β-(2′,3′,5′-tri-*O*-acetyl)-D-ribofuranosylpurine (3b). Under a nitrogen atmosphere, 0.393 g (1.0 mmol) of dry **2b** was added to a solution of 0.3 mL (2.24 mmol) of *n*-pentyl nitrite in 40 mL of carbon tetrachloride. The suspension was stirred and illuminated as for **1b** and warmed to 80 °C. Reaction was discontinued after 23 h and the red-brown mixture, worked up as for **1b**, gave, after development of preparative layer plates with 1:9 methanol-methylene chloride, 0.270 g of **3b** (0.656 mmol, 65.5%) as a yellow oil (R_f 0.58). Recovery of 0.093 g (0.236 mmol, 23.6%) of **2b** was made. Similar reaction using 2.7 mL (20 mmol) of *n*-pentyl nitrite gave a trace of starting compound **2b** (R_f 0.27) and 0.296 g (0.718 mmol, 71.8%) of **3b**: ^{13}C NMR, see Table I; ^{1}H NMR, see Table II; UV, see Table III.

Anal. Calcd for $C_{16}H_{17}N_4O_7Cl{\cdot}H_2O$: C, 44.6; H, 4.4; N, 13.0. Found: C, 43.9; H, 4.2; N, 11.9.

6-Bromo-9β-(2′,3′,5′-tri-*O*-acetyl)-D-ribofuranosylpurine (4b). A mixture of 0.393 g (1.0 mmol) of **2b**, 2.7 mL (20 mmol) of *n*-pentyl nitrite, and 15 mL of bromoform was reacted as for **1b**, with the solution maintained at 80 °C. The reaction mixture turned a golden color; gas evolution ceased and reaction was stopped after 3.5 h. After workup using 1:9 methanol-dichloromethane as developing solvent for silica gel preparative layer plates, 0.030 g (0.077 mmol, 7.7%) of **2b** was recovered (R_f 0.30) and 0.332 g (0.727 mmol, 72.7%) of **4b** was isolated as a pale yellow oil (R_f 0.59): ^{13}C NMR, see Table I; ^{1}H NMR, see Table II; UV, see Table III.

Anal. Calcd for $C_{16}H_{17}N_4O_7Br{\cdot}H_2O$: C, 40.4; H, 3.6; N, 11.8. Found: C, 40.6; H, 3.8; N, 11.6.

6-Iodo-9β-(2′,3′,5′-tri-*O*-acetyl)-D-ribofuranosylpurine (5b). A mixture of 0.393 g (1.0 mmol) of **2b** and 2.7 mL (20 mmol) of *n*-pentyl nitrite was stirred at 60 °C under nitrogen. Diiodomethane (5 mL) was added at once, under illumination as for **1b**, with stirring. After 2 h the red reaction mixture was cooled and worked up as before except that the methylene chloride solution of the residue was treated with saturated aqueous sodium sulfite solution to remove the free iodine before drying. Development with 1:9 methanol-methylene chloride gave a 0.056-g (0.143 mmol, 14.3%) recovery of **2b** (R_f 0.30) and 0.346 g (0.686 mmol, 68.6%) of **5b**, as a yellow oil which darkens upon standing (R_f 0.61): ^{13}C NMR, see Table I; ^{1}H NMR, see Table II; UV, see Table III; mass spectrum, *m/z* 504 (M$^+$).

Anal. Calcd for $C_{16}H_{17}N_4O_7I$: C, 38.1; H, 3.4; N, 11.1. Found: C, 38.3; H, 3.5; N, 11.0.

Registry No. 1a, 550-33-4; **1b**, 15981-63-2; **2b**, 7387-57-7; **3b**, 5987-73-5; **4b**, 74465-47-7; **5b**, 5987-74-6; **6**, 2715-68-6; **7**, 5427-23-6; **8**, 5462-86-2; **9**, 74465-48-8; **10**, 74465-49-9; adenine, 73-24-5; sodium adeninide, 40428-86-2; purine, 120-73-0; 6-chloropurine, 87-42-3.

Macro Rings. 49. Use of Transannular Reactions to Add Bridges to [2.2]Paracyclophane[1,2]

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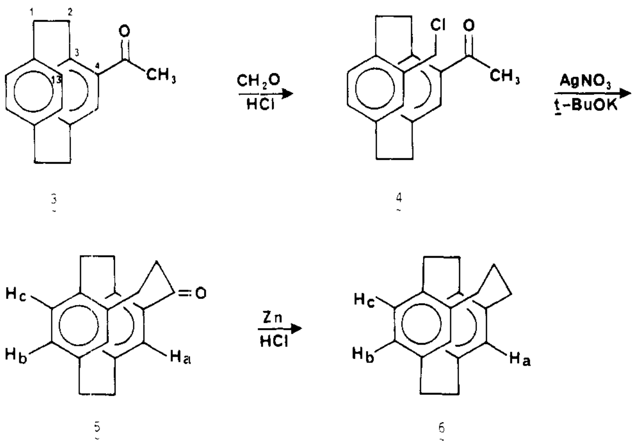
New transannular reactions were used to introduce additional bridges into [2.2]paracyclophane (**1**). With CH_2O–HCl, 4-acetyl[2.2]paracyclophane (**3**) gave (55%) 4-acetyl-13-(chloromethyl)[2.2]paracyclophane (**4**), whose substituents are pseudogem to one another. With $AgNO_3$-*t*-BuOK, **4** gave (84%) 1-keto[3.2.2](1,2,5)cyclophane (**5**), reduction of which produced (78%) [3.2.2](1,2,5)cyclophane (**6**). Treatment of **4** with NaOBr gave a mixture (90%) of *pseudogem*-carboxy(hydroxymethyl)[2.2]paracyclophane (**7**) and *pseudogem*-aldehydocarboxy[2.2]paracyclophane (**8**), each of which was isolated and characterized. Oxidation of the mixture with $KMnO_4$ gave (70%) *pseudogem*-dicarboxy[2.2]paracyclophane (**9**), whereas reduction with $LiAlH_4$ produced (72%) *pseudogem*-bis(hydroxymethyl)[2.2]paracyclophane (**10**). With PBr_3, **10** gave (81%) *pseudogem*-bis(bromomethyl)-[2.2]paracyclophane (**11**), which with Na_2S gave (39%) 2-thia[3.2.2](1,2,5)cyclophane (**12**). With Ag_2O, **11** produced 26% each of *pseudogem*-aldehydomethyl[2.2]paracyclophane (**13**) and 2-oxa[3.2.2](1,2,5)cyclophane (**14**). With TsOH-AcOH, diol **10** gave 82% of aldehyde **13** and 13% of ether **14**. With $BF_3{\cdot}O(Et)_2$, **14** rearranged to **13** (89%). Butyllithium mixed with dibromide **11** gave (65%) [2.2.2](1,3,5)cyclophane (**2**). The tosylhydrazone of aldehyde **13** (compound **17**), when heated with $NaOCH_3$ or irradiated, also gave **2** (71 and 85%, respectively). Comparisons of the ^{1}H NMR and UV spectra of hydrocarbons **1**, **2**, and **6** suggest that **2** is more rigid and strained than the other two. When heated with dimethyl acetylenedicarboxylate, **2** formed a 1:1 Diels–Alder adduct (**19**, 68%) involving the 5,8-positions of **2**, whereas with **1** or **6**, no such reaction occurred. That **2** is aromatic is illustrated by the fact that with AcCl-$AlCl_3$ it acetylated to give (79%) 6-acetyl[2.2.2](1,3,5)cyclophane (**20**). When heated with thiophenol, a good H· donor, **1** gave *p*,*p*′-dimethylbibenzyl (71%). When similarly treated, **2** gave (88%) 5,14-dimethyl[2.2](1,2)cyclophane (**22**). When heated at 220 °C with diethyl fumarate or maleate, **2** cycloadded across the benzyl-benzyl bond remote from the other two bridges to give (51 and 42%, respectively) a diastereomeric mixture of 2,3-bis(carboethoxy)[4.2.2](1,3,4)cyclophanes (**23**). The unusual reactions of the pseudogem-disubstituted [2.2]paracyclophanes are discussed in terms of proximity effects. The unusual spectral and reactivity effects of [2.2.2](1,2,5)cyclophane are interpreted in terms of compression and bent benzene effects.

Diparaxylylene was first obtained in 1949 by the extraction of polymer prepared by pyrolysis of *p*-xylene.[4] It was identified and characterized solely by its X-ray structure (later corrected),[5] melting point, and insolubility.[4]

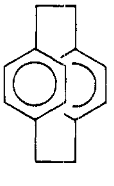
0022-3263/80/1945-3974$01.00/0

Scheme I

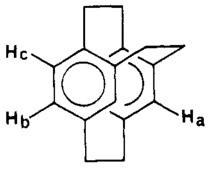


In 1951 we introduced the term *paracyclophane* to link the structures with the unusual properties of the lower homologous [*m.n*]paracyclophanes, whose designed syntheses were first reported.[6] We had accomplished but not communicated the synthesis of [2.2]paracyclophane at the time its extraction from polymer was communicated. Since that time, many beautiful cyclophanes have been prepared for a variety of interesting studies centering on transannular π interactions and bent benzene effects on physical properties and reactivity.[7] The recently reported "superphane" represents the ultimate in introducing more and more stress into [2.2]paracyclophane by appending the maximum number of two-carbon methylene bridges between two benzene rings.[8]

This paper reports reactions useful for introducing a variety of additional bridges into [2.2]paracyclophane (1), which is now a commercial material. When we first reported [2.2.2](1,2,4)cyclophane (2),[2a] [2.2.2](1,3,5)-cyclophane was the only cyclophane synthesized with three two-atom bridges.[9] Subsequently, three other groups using other methods reported [2.2.2](1,2,4)cyclophane, which exhibited physical properties identical with those of ours.[10]

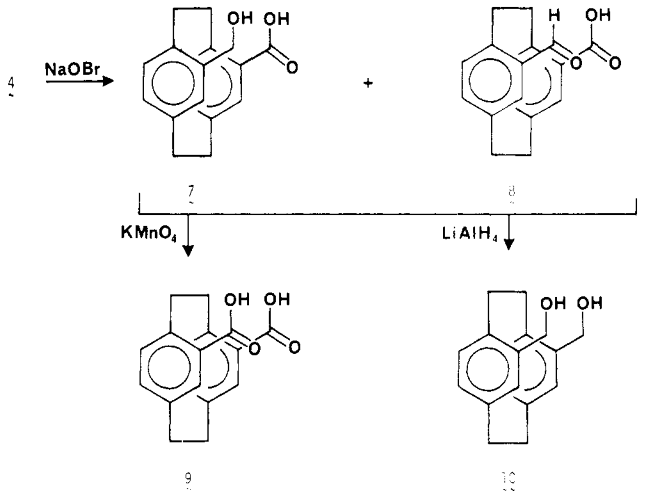


1

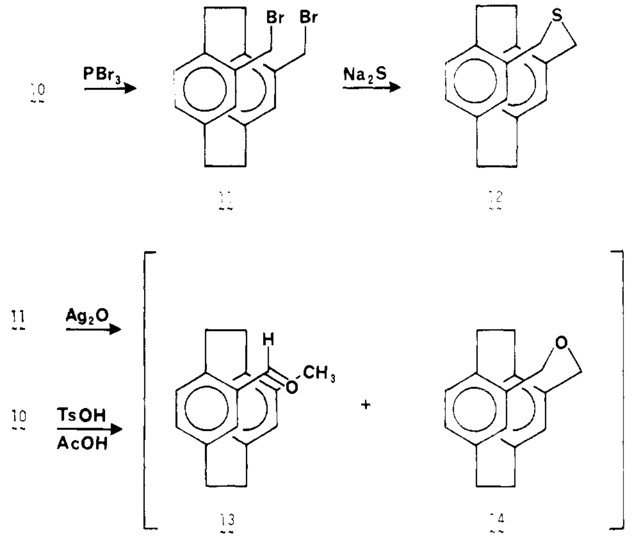


2

Scheme II



Scheme III



Results and Discussion

Syntheses. The key reaction in our syntheses of tribridged cyclophanes utilized the unusual ability of 4-acetyl[2.2]paracyclophanes (2)[11] to direct entry of an electrophile into the transannular ring at the position (pseudogem) closest to the acetyl group. Earlier work demonstrated that acetyl, carboxyl, carbomethoxyl, and nitro groups in the 4-position of [2.2]paracyclophane directed bromine substitution to occur nearly exclusively in the 13-position to give the pseudogem-disubstituted derivative.[12] Isotope- and medium-effect studies indicated that this directing effect involved a mechanism in which proton transfer from the σ complex to the oxygen of the transannularly located group was rate determining and product controlling.[12] It seemed possible that other electrophiles such as $(CH_2OH)^+$ could be similarly directed.[13]

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(1) This work was supported in part by a grant from the National Science Foundation (GP 4395).

(2) Protions of this work have been communicated: (a) Truesdale, E. A.; Cram, D. J. *J. Am. Chem. Soc.* **1973**, *95*, 5825; (b) Cram, D. J.; Hornby, R. B.; Truesdale, E. A.; Reich, H. J.; Delton, M. H.; Cram, J. M. *Tetrahedron* **1974**, *30*, 1757.

(3) National Science Foundation Trainee, 1969–1973.

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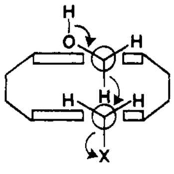
Addition of finely divided **3** to a solution of paraformaldehyde in concentrated hydrochloride acid (Scheme I) gave (55%) 4-acetyl-13-(chloromethyl)[2.2]paracyclophane (**4**). Apparently, even in this medium the product-controlling and rate-limiting step involved an intramolecular proton transfer from the σ complex to the oxygen of the acetyl group. Compound **4** is the first example of a cyclophane bearing dissimilar carbon side chains in a pseudogem relationship. The following reactions demonstrate the remarkable proximity effects of two functional groups supported by a rigid backbone.

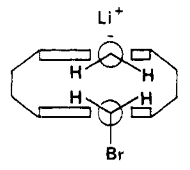
When treated with a mixture of silver nitrate and potassium *tert*-butoxide, **4** ring closed to give **5** (84%). Reduction of **5** with zinc and acid gave a mixture of **6** and an alkene, which when reduced with hydrogen and palladium gave (78% overall) [3.2.2](1,2,5)cyclophane (**6**). Treatment of **4** with bromine–potassium hydroxide gave a mixture (~90%) of hydroxy acid **7** and aldehyde acid **8**, each of which was characterized (Scheme II). The mixture was oxidized with potassium permanganate to diacid **9** on the one hand (~70%) and reduced with lithium aluminum hydride to diol **10** on the other (72%).

Diol **10** served as starting material for a number of unusual transannular reactions growing out of the proximity of the two side chains. With phosphorus tribromide, diol **10** gave dibromide **11** (81%), which when treated with sodium sulfide produced cyclic sulfide **12** (39%), as expected (Scheme III). However, with silver oxide, **11** in tetrahydrofuran (THF) gave equal quantities (~26% each) of rearranged product **13** and the expected cyclic ether **14**. When the reaction was carried out in cyclohexane, 80% of aldehyde **13** was produced along with only traces of **14**. The transannular hydride shift also occurred when diol **10** was heated with *p*-toluenesulfonic acid in acetic acid. At 120 °C for 5 min a solution of **10** in this medium produced a transient purple color. From the solution was isolated 82% of aldehyde **13** and 13% of ether **14**. At 50 °C for 12 h, 67% ether and 29% aldehyde were produced. Ether **14** at 25 °C in benzene–boron trifluoride etherate rearranged (89%) to aldehyde **13**. This rearrangement formally resembles that of epoxides which undergo 1,2 hydride shifts when treated with boron trifluoride.[14]

The transannular hydride shift in medium-sized carbocycles has been recognized for over 20 years.[15] Its occurrence has been attributed to the proximity and steric interference of nonadjacent carbon atoms in 8–11-membered rings. The rearrangement of diol **10**, dibromide **11**, and ether **14** to aldehyde **13** also appears to involve hydride migrations growing out of proximity effects. No prior rearrangements to our knowledge are known to involve primary benzyl reaction centers. The acid-catalyzed rearrangements probably involve as a transient reaction intermediate a benzyl carbonium ion whose nearest neighbor is a transannularly located C–H bond. Such an intermediate is compatible with the transient colors observed in the reactions when they are rapid and with the reaction conditions used. The base-catalyzed rearrangement involving silver oxide may be driven by formation of an alkoxide, whose negative charge pushes a hydride from one pseudogem methylene group to the other. Molecular models (CPK, with shaved benzene rings) of the systems involved indicate the starting materials for the rearrangements possess the enforced conformations shown in **15**. In **15**, the C–H bond of one methylene sits between the two C–H bonds of the other in an arrangement ideal for rearrangement.

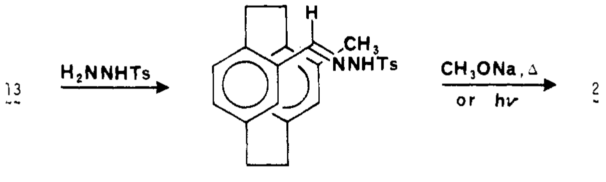


15, X = $\overset{+}{O}H_2$ or Br



16

Syntheses of [2.2.2](1,2,5)cyclophane (**2**) were completed, again making use of transannular proximity effects. In the first synthesis, treatment of dibromide **11** with butyllithium at -80 °C gave **2** in 65% yield. The first step of this reaction probably involved monolithiation of **11** to give intermediate **16**. In a second stage, the negative charge on one benzyl position displaced bromide from the second benzyl position to form the third bridge. In the second synthesis, the tosylhydrazone of aldehyde **13** (compound **17**) was heated in diethylene glycol dimethyl ether with sodium methoxide. Cycle **2** was formed in 71% yield, presumably by a transannular carbene insertion reaction. In a third synthesis, **17** was irradiated to give an 85% yield of **2**, again by a carbene insertion reaction. Similar nontransannular insertion reactions of these types are known.[16]



17

Spectral Properties of (1,2,4)Cyclophanes. Comparisons of the ^1H NMR spectra of **1**, **2**, and **6** provide clues as to the direction of structural perturbation due to the extra ethylene bridge in **2**. In **6**, the eight ethylene bridge protons appear as a singlet at about the same chemical shift as those of [2.2]paracyclophane,[17] whereas the trimethylene bridge appears as a multiplet at δ 2.60–3.65. The aromatic protons of **6** are shifted slightly upfield from unsubstituted **1**, probably due to the presence of the propylene bridge possessing an effect similar to that of alkyl substituents. The assignments of H_a, H_b, and H_c were made on the basis of their coupling constants. Thus H_a is farthest downfield (δ 6.435, $J_{a,b} = 1.9$ Hz), and H_b and H_c produce an AB quartet (δ 6.15 and 6.35, respectively, $J_{b,c} = 8.1$ Hz). Proton H_b was assigned on the basis of meta coupling.[17] In **2**, the bridge protons produce a complicated multiplet (δ 2.50–3.45). This suggests the system is much more rigid than **1**, which oscillates between two noneclipsed conformations in the crystalline state[5] and probably in solution as well. The same is probably true for **6**.

The most interesting features of the ^1H NMR spectrum of **2** are the chemical shifts of H_a and H_b. Their relative positions have been reversed compared to those of the corresponding protons in **6**. For **2**, H_a appeared at δ 6.05 ($J_{a,b} = 1.9$ Hz), and H_b and H_c gave an AB quartet at δ 6.37 and 6.18, respectively ($J_{b,c} = 8.2$ Hz). Molecular models of **2** indicate the benzene rings are tilted so that their H_a protons and attached carbons are close to one another,

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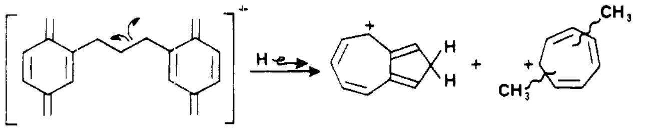
while the H_b and H_c protons and their attached carbon pairs are correspondingly further apart. In the model of **6**, the relative positions of the aromatic rings and their protons are more similar to those of **1**.

Differences in the shapes of **2** and **6** are also reflected in their UV spectra. The shape of the curve and the extinction coefficients of **6** are nearly identical with those of **1** with λ_{max} at 227 nm (ϵ 18 000), 291 (200), and 301 (160, sh).[18] The spectrum of **2** with λ_{max} at 223 nm (ϵ 12 000), 291 (440), and 305 (220, sh) more resembles that of [2.3]paracyclophane[6] in which the major planes of the aromatic rings are no longer parallel, as has been postulated for **2**.[19]

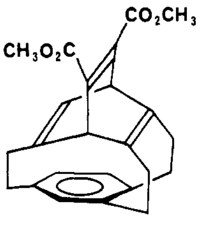
The mass spectrum of **6** was relatively simple: *m/e* (relative intensity) 289 (9), 130 (12), 129 (11), 119 (40), 118 (10), 115 (13), 91 (10). Paracyclophanes undergo efficient cycloreversion on electron impact, affording *p*-xylylene fragments.[17] Such cleavage with **6** should yield bridged fragments such as **18**, which might fragment further as indicated. The mass spectrum of **2** gave the following: *m/e* (relative intensity) 234 (M^+, 100), 219 (31), 207 (12), 206 (37), 205 (16), 204 (12), 203 (12), 202 (12), 144 (13), 143 (27), 141 (13), 129 (12), 128 (20), 127 (12), 117 (18), 116 (17), 115 (42), 91 (27). Loss of methyl (P − 15) and ethylene (P − 28) are the major fragmentation pathways. The most prominent fragment (*m/e* 115) is characteristic of cyclophane mass spectra, as is tropilium (*m/e* 91). The complexity of the spectrum relative to that of **6** is indicative of deep-seated rearrangements on electron impact.



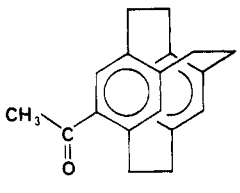
18 (mass 248) mass 129 mass 119

Reactions of Cyclophanes. The spectral data suggest that the addition of a third dimethylene bridge to [2.2]paracyclophane increases the strain of the cycle, while addition of a trimethylene bridge perturbs the system no more than is expected with simple alkyl substitution. Two useful probes for determining the chemical consequences of strain in cyclophane compounds have been the measurement of π basicity[20] and thermal generation of benzyl radicals.[21]

When a 1:1 mixture of **6** and tetracyanoethylene (TCNE) was prepared in dichloromethane, a charge-transfer band at λ_{max} 563 nm (ϵ 75) was observed. A similar band for the π salt of **2** and TCNE was observed at λ_{max} 541 nm (ϵ 56). At room temperature within 25 min the red-purple color of the latter complex faded to a pale pink (ϵ 25). The likelihood that this reduction in extinction coefficient was indicative of a cycloaddition reaction between **2** and TCNE prompted the following experiment. A sample of **2** was heated in a solution of dimethyl acetylenedicarboxylate at 120–170 °C. The cyclophane underwent a Diels–Alder reaction to give (68%) the bridge barrelene adduct **19**. Prolonged heating of the reaction mixture did not result in formation of the bis adduct. Attempts to run similar reactions with **1** and **6** were unsuccessful, although **1** undergoes cycloaddition with the stronger dienophiles dicyanoacetylene and benzyne.[22] Of the three possible isomers of **19**, only formation of the 5,8-adduct would result in a substantial relief of strain energy. The ^1H NMR spectrum of the adduct confirms that it has structure **19**. The spectrum contains one olefinic proton (δ 5.36), two barrelene bridgehead protons[23] (δ 4.18 and 4.04), and three aromatic protons (δ 6.52–6.85).



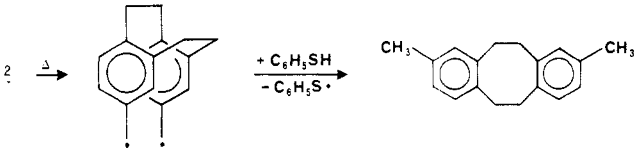
19



20

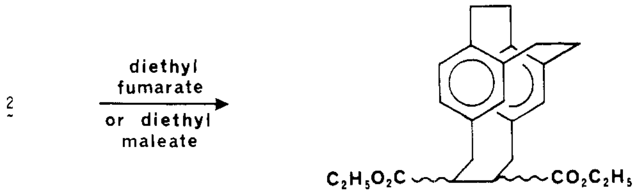
In spite of the facility with which one aromatic ring of **2** undergoes cycloaddition, the compound maintains its aromatic character in the sense that it acetylated with acetyl chloride–aluminum chloride to give **20** (79%). Formation of **20** brings up the possibility of adding more ethylene bridges to **2** via reactions that led from **1** to **2**.

Earlier work established that when [2.2]paracyclophane (**1**) was heated to 200 °C, the benzyl–benzyl bond cleaved to give a diradical intermediate whose fate depended on the medium.[21] In the hydrogen-atom-donating solvent thiophenol at 220 °C, **1** gave *p,p'*-dimethylbibenzyl (71%). Diethyl fumarate and maleate as solvents for **1** at similar temperatures cycloadded across the benzyl–benzyl bond of **1**.[21] When **2** was heated for 3 days in thiophenol, **22** was formed (88%), undoubtedly via diradical **21**. Cleavage of the other bridges of **2** would lead to diradicals held close to one another, which would favor ring closure to give starting material. Obviously, cleavage of **2** to **21** would release more strain energy than cleavage of the two alternative CH_2–CH_2 bonds.



21 22

When **2** was heated in diethyl fumarate or maleate at 220 °C for 3 days, a 1:1 adduct of cyclophane to olefin was formed (51 and 42%, respectively). The UV spectrum of this material is similar to derivatives of [2.4]paracyclophane.[21] Two different kinds of ethyl groups were visible in its ^1H NMR spectrum. The facts coupled with the intermediacy of **21** in producing **22** suggest that the adduct possesses structure **23** and is a mixture of cis and trans isomers.



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Cyclophane **6** when similarly heated in thiophenol, diethyl fumarate, or diethyl maleate failed to react in other than minor amounts. Although a diradical was probably formed in these attempts, it appeared to ring close again faster than it underwent radical capture. Thus diradical **21** derived from **2** underwent hydrogen atom and alkene capture while that derived from **6** did not. Ring closure to regenerate starting material competes with diradical capture. The greater strain of **2** compared to that of **6** probably depresses the rate of ring closure leading to **2** compared to that leading to **6**. Thus the diradical from **2** appears to last long enough to undergo bimolecular reactions, whereas that from **6** does not.

Conclusions

Coupling the side chains of pseudogem-disubstituted [2.2]paracyclophanes has proven to be an efficient means of preparing multibridged cyclophanes. Indeed, modifications of the chloromethylation, debromination, and carbene-insertion reactions reported earlier[2] and detailed here have been employed in the preparation of the three isomeric cycles containing four ethylene bridges.[24] The proximity effect of pseudogem substituents has been further demonstrated by the transannular hydride shift which is either acid or base catalyzed.

Comparison of the thermal reactions of **2** and **6** indicates the former to be the more strained, a conclusion supported by the differences in their UV spectra. Recent π-SCF force field calculations[25] predict a shallow twist-boat conformation for the aromatic rings of **2** and an increase in strain energy over that of [2.2]paracyclophane of ~6 kcal/mol.

Experimental Section

General Comments. Commercial [2.2]paracyclophane was recrystallized from chloroform before use. All solvents were reagent grade unless otherwise specified, except pentane (technical) which was distilled prior to use. Dry ether or tetrahydrofuran refers to solvents distilled from lithium aluminum hydride. Dry benzene refers to solvent distilled from calcium hydride. Melting points were taken on a Thomas-Hoover Uni-Melt apparatus and are uncorrected. Merck chromatographic grade silica gel (30–60 mesh) was consistently used for column chromatography, and Baker-Flex commercial plates were used for thin-layer chromatography. Ether–pentane mixtures were used exclusively as developers in thin-layer chromatograms and as eluants for column chromatograms. Granular, anhydrous sodium sulfate was uniformly used as a drying agent. Routine mass spectra (70 eV) were taken on an MS-21 spectrometer, and high-resolution spectra were taken on an AEI Model MS-9 instrument. Infrared spectra were taken of potassium bromide pellets on a Beckman IR-5 spectrophotometer. Ultraviolet spectra were taken in ethanol or dichloromethane on a Cary Model 14 M spectrophotometer in 1-cm quartz cells. Proton nuclear magnetic resonance spectra were taken in deuteriochloroform with tetramethylsilane as internal standard on a Varian A60-D spectrophotometer except as indicated. The 100-MHz spectra were taken on a Varian HA-100 spectrophotometer.

4-Acetyl[2.2]paracyclophane (3). To 190 g of [2.2]paracyclophane (1) in 800 mL of dichloromethane at −50 °C was added a solution of 136 mL of acetyl chloride, 214 g of aluminum chloride, and 200 mL of dichloromethane. The solution was stirred for 15 min while it slowly warmed to −20 °C. The solution was filtered through a glass-wool plug to remove unreacted starting material and treated with ice and 6 N hydrochloric acid. The mixture was stirred until it was colorless, and sufficient ether was added to make the organic phase less dense than water. The organic layer was washed twice with saturated sodium bicarbonate and saturated sodium chloride. The solution was dried and the solvent evaporated. The product was recrystallized from ether–pentane to give 166 g of **3** (74%), mp 109–110 °C (lit.[26] mp 109–110 °C).

***pseudogem*-Acetyl(chloromethyl)[2.2]paracyclophane (4).** A mixture of 90 g of paraformaldehyde and 1.2 L of concentrated hydrochloric acid was stirred until clear at room temperature. Finely divided 4-acetyl[2.2]paracyclophane (**3**, 12.5 g) was added in one portion, and the mixture was heated slowly to 55 °C where it was maintained for an additional 3.75 h with vigorous stirring. The reaction was quenched by pouring the mixture over 1 kg of ice and extracting twice with 400-mL portions of dichloromethane. Ether (1 L) was added to the combined extracts, and the solution was washed twice each with water, saturated sodium bicarbonate, and saturated sodium chloride aqueous solutions. The organic solution was dried and evaporated at reduced pressure. The residue was recrystallized from dichloromethane–acetone, affording 7.7 g of **4** (average of three experiments, 55%), mp 213–215 °C. Anal. Calcd for $C_{19}H_{19}OCl$: C, 76.37; H, 6.41. Found: C, 76.21; H, 6.49. The ^1H NMR spectrum exhibited a doublet at δ 6.95 (1 H), a multiplet between δ 6.7 and 6.4 (5 H), an AB quartet at δ 4.65 and 4.15 (2 H, J = 12 Hz, CH_2Cl), a multiplet between δ 4.3 and 2.95 (8 H, CH_2CH_2), and a singlet at δ 2.4 (3 H, $COCH_3$). The IR spectrum exhibited bands at 3.35 (w), 5.95 (s), 6.2 (w), 6.4 (w), 6.7 (w), 6.9 (w), 7.3 (m), 7.85 (m), 10.44 (w), 10.80 (w), 11.20 (w), 11.78 (w), 13.64 (m), 14.47 (m), and 15.33 μm (m). The mass spectrum exhibited the following: m/e (relative intensity) 300 (23), 299 (10), 298 (59, M^+, Cl^{35}), 263 (10), 154 (11), 152 (28), 147 (11), 146 (100), 145 (68), 144 (14), 131 (14), 119 (12), 118 (11), 117 (25), 115 (20), 104 (16), 103 (13), 91 (12), 71 (10).

***pseudogem*-Aldehydocarboxy[2.2]paracyclophane (8).** A solution of 75 g of potassium hydroxide and 280 mL of water was cooled to 0–5 °C. Bromine (19 mL) was added dropwise with vigorous stirring. A solution of 21.1 g of **4** in 500 mL of freshly distilled dioxane was prepared by warming the solvent and adding the compound dropwise to the reagent over 30 min. The reaction mixture was stirred at room temperature for 17 h, heated briefly to reflux, and quenched by the addition of 16 g of solid sodium bisulfite. The reaction mixture was acidified with 6 N hydrochloric acid to precipitate the product, which was collected and washed with acetone (16.2 g of acids, about 80%). The sample was 70% acid aldehyde **8** and 30% acid alcohol **7** by ^1H NMR integration. For the purification of a sample for analysis, a column was prepared by washing 50 g of silica gel with 1:1 (v/v) acetic acid–pentane, decanting the solvent, and rinsing the silica gel with pentane. The silica gel was packed in pentane, and a slurry of 1 g of the mixed acids (**7** and **8**) in 50 mL of pentane was passed through the column. Elution with 1% ether–pentane containing 0.1% acetic acid afforded a solid beginning with fraction 3 (150-mL fractions). Fraction 4 contained material which crystallized from acetic acid: 10 mg of **8**; mp 277–278 °C dec; high-resolution mass spectrum, calcd for $C_{18}H_{16}O_3$ m/e 280.1099, found m/e 280.1101 ± 0.0006. Anal. Calcd for $C_{18}H_{16}O_3$: C, 77.12; H, 5.75. Found: C, 77.14; H, 5.73. The ^1H NMR spectrum (60 MHz, Me_2SO-d_6) exhibited a singlet at δ 9.8 (1 H, CHO), a broad signal at δ 7.9 (2 H, aromatic), a broad signal at δ 6.65 (4 H, aromatic), and complex signals at δ 4.1–3.7 and 3.1–2.7 (8 H, CH_2CH_2). The IR spectrum exhibited the following bands: 5.90 (s), 5.95 (s), 6.07 (s), and broad bands at 3.43, 7.72, 7.95, 8.38, and 9.34 μm. The mass spectrum exhibited the following: m/e (relative intensity) 296 (2), 280 (83, M^+), 148 (91), 133 (100), 132 (49), 131 (37), 105 (65), 104 (58), 103 (23), 91 (23), 78 (17), 77 (20).

***pseudogem*-Carboxy(hydroxymethyl)[2.2]paracyclophane (7).** A solution of 74 g of potassium hydroxide and 254 mL of water was cooled to 0–5 °C. Bromine (19 mL) was added dropwise with vigorous stirring. A solution of 21.9 g of **4** in 345 mL of freshly distilled dioxane was prepared by warming the solvent. This solution was added dropwise to the reagent over 30 min. The reaction mixture was stirred at room temperature for 15 min and then heated slowly (1 °C/min) to 80 °C. The mixture was allowed to cool for 15 min before being quenched with 16 g of solid sodium bisulfite. The mixture was extracted with 70% ether–chloroform (v/v). The aqueous phase was acidified with 6 N hydrochloric acid, and the crude product was collected by vacuum filtration,

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washed with water, and dried under vacuum at room temperature (20 g of crude acids, 92%). The ^{1}H NMR spectrum of this product indicated that it was a mixture of 60% **7** and 40% **8**. For the preparation of a sample of pure acid alcohol **7**, a sample of the mixture (150 mg) was treated with excess sodium borohydride in 15 mL of ethanol and stirred at 40 °C for 3.5 h. The reaction was quenched with water and dilute hydrochloric acid and the product collected. The solid was washed with acetone and dried under vacuum, affording 126 mg of **7** (83%): mp 245–246 °C (gas evolution); high-resolution mass measurement, calcd for $C_{18}H_{18}O_3$ *m/e* 282.1256, found *m/e* 282.1256 ± 0.0004. The ^{1}H NMR spectrum exhibited a doublet at δ 7.05 (1 H, aromatic), a multiplet between δ 6.60 and 6.20 (5 H, aromatic), an AB quartet at δ 4.5 and 4.05 (2 H, J = 12, CH_2OH), and a broad signal at δ 3.0 (8 H, CH_2CH_2). The IR spectrum exhibited the following bands: 3.41 (br, ms), 5.8 (sh), 5.96 (s), 6.27 (w), 6.43 (w), 7.70 (s), 7.85 (s), 8.34 (m), 9.30 μm (w). The mass spectrum exhibited the following: *m/e* (relative intensity) 296 (1), 282 (25, M^+), 265 (11), 264 (57), 252 (16), 236 (10), 149 (14), 148 (23), 146 (14), 137 (14), 134 (33), 133 (16), 131 (14), 125 (28), 123 (19), 119 (21), 118 (50), 117 (63), 115 (21), 113 (14), 111 (41), 110 (14), 109 (19), 105 (100), 104 (60), 103 (13), 97 (63), 95 (41), 91 (50).

***pseudogem*-Dicarboxy[2.2]paracyclophane (9).** In 200 mL of hot 20% potassium hydroxide solution was dissolved 5.7 g of a mixture of acid alcohol **7** and acid aldehyde **8**. The solution was cooled to 0 °C, and 15 g of solid potassium permanganate was added all at once. The solution was stirred at room temperature until it had turned from dark purple to bright green and was then allowed to stand overnight. The resulting brown precipitate was separated from the dark orange solution by filtration and was washed twice with hot 20% potassium hydroxide solution. The combined filtrates were acidified with 6 N hydrochloric acid and filtered again to yield 4.48 g (~70%) of the diacid **9**: mp 335–340 °C; high-resolution mass measurement, calcd for $C_{18}H_{16}O_4$ *m/e* 296.1048, found *m/e* 296.1047 ± 0.0003. The ^{1}H NMR spectrum (60 MHz, Me_2SO-d_6) exhibited a broad signal at δ 6.95 (2 H, aromatic), a broad signal at δ 6.55 (4 H, aromatic), and a complex multiplet between δ 4.2 and 3.9 and between δ 3.15 and 2.80 (8 H, CH_2CH_2). The IR spectrum exhibited the following bands: 3.42 and 3.68 (br, s), 5.92 (doublet, s), 6.28 (m), 6.42 (m), 6.70 (m), 6.86 (m), 6.95 (m), 7.04 (m), 7.13 (m), 7.65 (s), 7.81 (s), 8.24 (m), 9.25 (m), 10.70 (m), 11.00 (m), 11.54 (m), 13.15 (m), 14.12 (m). The mass spectrum exhibited the following: *m/e* (relative intensity) 296 (2, M^+), 278 (100), 149 (40), 148 (88), 133 (5), 132 (5), 131 (60), 117 (8), 105 (25), 104 (20), 103 (12), 91 (40), 77 (20).

***pseudogem*-Bis(hydroxymethyl)[2.2]paracyclophane (10).** To 500 mL of dry tetrahydrofuran was added 31 g of a mixture of acid alcohol **7** and acid aldehyde **8**. An excess of lithium aluminum hydride was then added, and the mixture was stirred and refluxed for 4 days. The reaction was quenched with water and dilute hydrochloric acid. The mixture was extracted twice with ether–dichloromethane, and the combined extracts were washed with saturated aqueous sodium bicarbonate and saturated sodium chloride solutions. The organic solution was dried over sodium sulfate and the solvent evaporated at reduced pressure. The residue was chromatographed on 200 g of silica gel. The column was eluted with 5 L of 10% ether–pentane (v/v) and 3 L of 25% ether–pentane (v/v) which yielded only trace materials. Elution with ether gave 22.2 g of **10** (72%), mp 208–210 °C. Anal. Calcd for $C_{18}H_{20}O_2$: C, 80.56; H, 7.51. Found: C, 80.70; H, 7.61. The ^{1}H NMR spectrum exhibited a doublet at δ 6.48 (2 H, aromatic), a singlet at δ 6.29 (4 H, aromatic), an AB quartet at δ 4.64 and 4.32 (2 H, J = 12 Hz, CH_2OH), a complex group of signals between δ 3.55 and 2.85 (8 H, CH_2CH_2), and a broad signal at δ 2.68 (2 H, OH). The mass spectrum exhibited the following: *m/e* (relative intensity) 268 (17, M^+), 251 (13), 250 (82), 207 (10), 144 (12), 135 (12), 134 (91), 133 (17), 132 (31), 131 (26), 121 (42), 119 (58), 118 (82), 117 (10), 115 (11), 106 (18), 105 (100), 104 (16), 103 (14), 91 (66).

***pseudogem*-Bis(bromomethyl)[2.2]paracyclophane (11).** A solution of 865 mg of diol **10** in 80 mL of dry dichloromethane was cooled to −20 °C. An excess of phosphorus tribromide was added and the mixture stirred for 30 min. Ice and water were added to quench the excess reagent, and the mixture was extracted with ether. The resulting solution was washed with water, saturated sodium bicarbonate, and saturated sodium chloride solutions and then dried. The solvent was removed at reduced pressure and the residue recrystallized from dichloromethane–pentane at −15 °C, affording 700 mg of dibromide **11**, mp 133–135 °C. The mother liquor was reworked to give an additional 329 mg of **11** (81%), high-resolution mass measurement, calcd for $C_{18}H_{18}Br_2$ *m/e* 391.9776, found *m/e* 391.9779 ± 0.0008. Anal. Calcd for $C_{18}H_{18}Br_2$: C, 54.84; H, 4.60. Found: C, 54.81; H, 4.80. The ^{1}H NMR spectrum exhibited a doublet at δ 6.45 (4 H, aromatic), a singlet at δ 6.40 (2 H, aromatic), an AB quartet at δ 4.57 and at 4.08 (4 H, J = 10 Hz, CH_2Br), and a complex multiplet from δ 3.55 to 2.85 (8 H, CH_2CH_2). The mass spectrum exhibited the following: *m/e* (relative intensity) 394 (13, M^+), 315 (10), 313 (11), 252 (10), 251 (42), 132 (10), 131 (9), 123 (9), 119 (20), 118 (100), 117 (23), 115 (15), 109 (19), 103 (9), 91 (14).

Reaction of *pseudogem*-Bis(bromomethyl)[2.2]paracyclophane (11) with Silver Oxide. Method A. In 5 mL of dry tetrahydrofuran was dissolved 150 mg of dibromide **11**, and to this solution was added 90 mg of silver oxide. The reaction was stirred in the dark for 4 days and filtered. The solid salts were washed repeatedly with ether. The ether filtrates were combined and dried, and the solvent was removed at reduced pressure. The residue was chromatographed on 70 g of silica gel, and product was eluted with 2 L of 0.5% ether–pentane and 1% ether–pentane, taking 100-mL fractions. Fractions 23–27 were combined to give 17 mg of bridged ether **14**, mp 203–204 °C. Anal. Calcd for $C_{18}H_{18}O$: C, 86.36; H, 7.25. Found: C, 86.41; H, 7.43. The ^{1}H NMR spectrum exhibited a doublet at δ 6.45 (2 H), a broad singlet at δ 6.30 (4 H), an AB quartet at δ 4.90 and at 4.34 (4 H, J = 12 Hz), and a complex group of signals from δ 3.30 to 2.85 (8 H). The mass spectrum exhibited the following: *m/e* (relative intensity) 250 (100, M^+), 205 (10), 144 (15), 133 (15), 132 (25), 131 (23), 119 (50), 118 (95), 117 (26), 115 (24), 105 (20), 104 (10), 103 (10), 91 (18).

Fraction 28–31 contained 31 mg of a mixture of bridged ether **14** and aldehyde **13**. Fractions 32–39 contained 23 mg of aldehyde **13**, mp 199–200 °C. Anal. Calcd for $C_{18}H_{18}O$: C, 86.36; H, 7.25. Found: C, 86.34; H, 7.29. The ^{1}H NMR spectrum exhibited a singlet at δ 10.1 (1 H, CHO), a doublet at δ 6.95 (1 H, aromatic), a multiplet between δ 6.70 and 6.30 (4 H, aromatic), a broad signal at δ 6.05 (1 H, aromatic), a multiplet between δ 3.95 and 2.80 (8 H, CH_2CH_2), and a singlet at δ 1.95 (3 H, CH_3). The mass spectrum gave the following: *m/e* (relative intensity) 250 (50, M^+), 132 (12), 119 (22), 118 (100), 117 (16), 115 (9), 103 (11), 91 (8).

Method B. A solution of 300 mg of dibromide **11** in cyclohexane was stirred in the dark for 5 days at room temperature with excess silver oxide (400 mg). The solution was filtered and the solid washed with ether. The solution was dried and evaporated at reduced pressure to give 153 mg (80%) of white solid which by ^{1}H NMR contained methyl aldehyde **13** and a trace of ether **14** (less than 5%).

Dehydration of *pseudogem*-Bis(hydroxymethyl)[2.2]paracyclophane (10). Method A. A sample of diol **10** (0.998 g) in 10 mL of acetic acid containing 1% acetic anhydride and a trace of *p*-toluenesulfonic acid was heated to reflux. Immediately on dissolution (5–10 min at 120 °C) the mixture was poured over ice and extracted with ether. The organic layer was washed with saturated sodium bicarbonate and saturated sodium chloride and dried. The solvent was removed at reduced pressure, and the residue was chromatographed on 10 g of silica gel with 2% ether–pentane as the eluting agent. All of the eluted material was combined to give 884 mg of white solid which by ^{1}H NMR integration contained 86% methyl aldehyde **13** and 14% ether **14** (95% total yield)

Method B. A solution of 10 g of diol **10** in 300 mL of acetic acid was heated to 50 °C for 12 h. The product was chromatographed on 100 g of silica gel as before, affording 8.9 g (95%) of a mixture of 70% ether **14** and 30% methyl aldehyde **13** by ^{1}H NMR integration.

Reaction of 18-Oxa-[3.2.2](1,2,5)cyclophane (14) with Boron Trifluoride. A sample weighing 216 mg which was 90% bridged ether **14** and 10% aldehyde **13** was dissolved in a minimum of dry benzene at room temperature, and an excess of boron trifluoride etherate was added in one portion. The flask was covered and allowed to stand at room temperature for 30 min. The mixture was poured over ice and extracted with ether. The ether layer was washed with hydrochloric acid, saturated sodium bicarbonate, and saturated sodium chloride and evaporated at reduced pressure. The residue was chromatographed on 10 g of silica gel and product eluted with 2% ether-pentane. All of the eluted material was combined to give 194 mg of methyl aldehyde **13** (89%), identified by its ^{1}H NMR spectrum and a mixture melting point (199–201 °C) with an authentic sample. No trace of ether **14** was detected in the sample by ^{1}H NMR.

Reaction of *pseudogem*-Bis(bromomethyl)[2.2]paracyclophane (11) with Sodium Sulfide. A solution of 150 mg of dibromide **11** and 10 mL of absolute ethanol was warmed to dissolve the substrate and then cooled to room temperature. Sodium sulfide (anhydrous, 24 mg) which had been dried under high vacuum at 110 °C for 2 days was added, and the mixture was stirred at room temperature for 8 h. The reaction mixture was extracted with ether and washed with water. The organic phase was dried and evaporated at reduced pressure, and the residue was chromatographed on 10 g of silica gel. The product was eluted with 0.5% ether-pentane in 75-mL fractions. Fractions 3–5 afforded 40 mg of sulfide **12** (39%), mp 242–244 °C. Anal. Calcd for $C_{18}H_{18}S$: C, 81.17; H, 6.81. Found: C, 81.15; H, 6.80. The ^{1}H NMR spectrum exhibited a singlet at δ 6.9 (2 H, aromatic), a broad signal at δ 6.3 (4 H, aromatic), an AB quartet at δ 4.2 and at 3.45 (4 H, J = 15 Hz, CH_2S), and a multiplet from δ 3.6 to 2.8 (8 H, CH_2CH_2). The mass spectrum exhibited the following: *m/e* (relative intensity) 266 (71, M^+), 149 (38), 148 (52), 147 (100), 134 (19), 119 (50), 117 (10), 115 (19), 91 (10).

1-Keto[3.2.2](1,2,5)cyclophane (5). To 50 mL of dry tetrahydrofuran was added 400 mg of **4** and 200 mg of potassium *tert*-butoxide. The solution was stirred briefly before the addition of 450 mg of solid silver nitrate. The mixture was stirred for 4 h at room temperature in the dark, and dilute hydrochloric acid was added to precipitate any remaining silver ion. Aqueous ammonia was added to dissolve most of the silver chloride. Ether and dichloromethane were added, and the organic phase was washed with water, dried over sodium sulfate, and evaporated. The residue was chromatographed on silica gel, and the product eluted with 10% ether-pentane (v/v). All of the eluted material was collected and recrystallized from acetone to yield 276 mg of **5** (84%), mp 193–194 °C. Anal. Calcd for $C_{19}H_{18}O$: C, 86.98; H, 6.91. Found: C, 86.77; H, 6.93. The ^{1}H NMR spectrum exhibited a multiplet from δ 6.5 to 6.2 (6 H, aromatic) and a multiplet from δ 3.5 to 2.5 (12 H, CH_2). The IR spectrum gave a strong carbonyl absorption at 5.95 μm. The mass spectrum contained the following: *m/e* (relative intensity) 262 (64, M^+), 145 (15), 144 (100), 131 (14), 115 (18), 91 (10).

[3.2.2](1,2,5)Cyclophane (6). Mossy zinc (3.6 g), 1.6 g of mercuric chloride, 8 mL of water, and 0.5 mL of concentrated hydrochloric acid were agitated for 10 min, and the liquid was decanted. To the zinc amalgam was added 50 mL of water, 100 mL of concentrated hydrochloric acid, and 1.98 g of ketone **5** dissolved in 50 mL of toluene. The mixture was heated to reflux and held there for 30 h. Ether was added, and the organic phase was washed with sodium bicarbonate and saturated sodium chloride, treated with activated charcoal, filtered, and evaporated at reduced pressure. For the reduction of the alkene produced as a byproduct, the solid was dissolved in 50 mL of ethanol and the mixture stirred for 5 h with 150 mg of 10% palladium on charcoal under 2 atm of hydrogen. The reaction mixture was filtered and the filtrate evaporated at reduced pressure to give 1.62 g of **6** (78%), mp 135–137 °C. A sample was sublimed for analysis: high-resolution mass measurement, calcd for $C_{19}H_{20}$ *m/e* 248.1565, found *m/e* 248.1568 ± 0.0005. Anal. Calcd for $C_{19}H_{20}$: C, 91.88; H, 8.12. Found: C, 91.80; H, 8.18. The ^{1}H NMR spectrum exhibited a doublet at δ 6.48 (2 H, J = 1.8 Hz), an AB quartet at δ 6.36 and at 6.16 (4 H, J = 8.1 Hz, the upfield doublet further split, J = 1.8 Hz), and a multiplet between δ 3.6 and 2.48 (14 H) (see text for assignments). The UV spectrum (ethanol) exhibited the following: λ_{max} 227 nm (ϵ 18000), 291 (200), 302 (160, sh). The mass spectrum exhibited the following: *m/e* (relative intensity) 248 (9, M^+), 130 (12), 129 (100), 128 (11), 119 (40), 118 (10), 115 (13), 91 (10).

[2.2.2](1,2,4)Cyclophane (2). Method A. A solution of 201 mg of dibromide **11** in 50 mL of dry tetrahydrofuran was cooled to −60 °C. A solution of 2 mL of *n*-butyllithium (1.6 M in hexane) in 10 mL of dry tetrahydrofuran was added dropwise over 20 min. The reaction was stirred an additional 10 min before ice and water were added. The mixture was extracted with ether, and the organic phase was washed with water and dried. The solution was evaporated at reduced pressure, and the residue was chromatographed on 10 g of silica gel. Product was eluted with 1% ether-pentane to give 81 mg of **2** (68%). An analytical sample was prepared by recrystallization from ether-cyclohexane; mp 168–169 °C. Anal. Calcd for $C_{18}H_{18}$: C, 92.26; H, 7.74. Found: C, 92.04; H, 8.04. The ^{1}H NMR spectrum exhibited an AB quartet at δ 6.37 and at 6.17 (4 H, J = 8.2 Hz, the downfield doublet is further split, J = 1.9 Hz), a doublet at δ 6.05 (2 H, J = 1.9 Hz), and a complex multiplet between δ 3.3 and 2.48 (12 H) (see text for assignments). The UV spectrum (ethanol) exhibited the following: λ_{max} 223 nm (ϵ 12000), 291 (44), 305 (220, sh). The mass spectrum exhibited the following: *m/e* (relative intensity) 234 (100, M^+), 219 (31), 207 (12), 206 (37), 205 (16), 204 (12), 203 (12), 202 (12), 144 (13), 143 (27), 141 (13), 129 (12), 128 (20), 127 (12), 117 (18), 116 (17), 115 (42), 91 (27).

Method B. A mixture of 200 mg of aldehyde **13**, 200 mg of tosylhydrazine, 50 mL of dry benzene, and a trace of sulfuric acid was refluxed 15 min, and then 40 mL of benzene was distilled. The remaining solvent was removed at reduced pressure to give a viscous oil. The oil was dissolved in 30 mL of diethylene glycol dimethyl ether and treated with 90 mg of sodium methoxide. The reaction mixture was heated to reflux for 2 h. The mixture was extracted with ether and the ether layer was washed with water, dried, and evaporated at reduced pressure to give 134 mg of **2** (71%), which was identical with an authentic sample by ^{1}H NMR and mixture melting point (168–169 °C).

Method C. A solution of 200 mg of aldehyde **13**, 200 mg of tosylhydrazine, 50 mL of dry benzene, and a trace of sulfuric acid was refluxed for 15 min, 40 mL of benzene was distilled, and the remaining solvent was removed at reduced pressure. The resulting oil was dissolved in 210 mL of dry tetrahydrofuran and treated with 80 mg of sodium methoxide. The solution was placed in an immersion well and irradiated with a Hanovia 450-W medium-pressure lamp at 20 °C for 70 min. The solvent was removed at reduced pressure, the residue was dissolved in ether, and the mixture was washed with water, dried over sodium sulfate, and evaporated at reduced pressure to give 159 mg of **2** (85%), which was identical with an authentic sample by ^{1}H NMR and mixture melting point (168–169 °C).

Acetylation of [2.2.2](1,2,4)Cyclophane (2). A solution of 510 mg of **2** in 200 mL of dichloromethane was cooled to −70 °C. A solution of 1.0 mL of acetyl chloride and 1 g of aluminum chloride in 10 mL of dichloromethane was added in one portion. The dark red reaction mixture was stirred for 20 min and then poured into ice and dilute hydrochloric acid. The mixture was agitated until colorless, extracted with ether, and washed with saturated sodium bicarbonate and saturated sodium chloride. The organic layer was dried and evaporated at reduced pressure. The residue was chromatographed on 10 g of silica gel with 10% ether-pentane as the eluting medium. All of the solid obtained was combined and recrystallized from ether-pentane, yielding 473 mg of **20** (79%), mp 144–145 °C. Anal. Calcd for $C_{20}H_{20}O$: C, 86.92; H, 7.29. Found: C, 86.79; H, 7.34. The ^{1}H NMR spectrum exhibited a singlet at δ 6.65 (1 H, aromatic), an AB quartet at δ 6.38 and at 6.17 (2 H, J = 9, aromatic, the downfield proton is further split, J = 2), a singlet at δ 6.15 (1 H, aromatic), a multiplet between δ 4.2 and 2.55 (12 H, CH_2CH_2), and a singlet at δ 2.43 (3 H, $COCH_3$). The IR spectrum (KBr) exhibited a carbonyl stretch at 5.98 μm. The mass spectrum exhibited the following: *m/e* (relative intensity) 276 (100, M^+), 261 (14), 233 (8), 115 (8), and 91 (6).

Reaction of [2.2.2](1,2,4)Cyclophane (2) with Dimethyl Acetylene Dicarboxylic Acid (DMADC). A mixture of 100 mg of **2**, 10 mg of *p*-dihydroquinone, and 5 mL of DMADC was prepared in a heavy-walled glass tube. The solution was degassed and the tube sealed at 0.03 mm and heated at 120 °C for 3.5 h. The tube was cooled to room temperature and opened, and the contents were emptied directly onto a column of silica gel (70 g) packed in pentane. The column was washed with pentane (11 fractions, 50 mL each) and 5% ether-pentane (37 fractions, 50 mL each). Fractions 12–19 contained DMADC. Fractions 21–32 contained 110 mg of **19** (68%), mp 148–148.5 °C, high-resolution mass measurement, calcd for $C_{24}H_{24}O_4$, *m/e* 376.1674, found *m/e*

376.1679 ± 0.0008. Anal. Calcd for $C_{24}H_{24}O_4$: C, 76.57; H, 6.43. Found: C, 76.66; H, 6.39. The ^{1}H NMR spectrum of **19** exhibited a multiplet from δ 6.86 to 6.45 (3 H, aromatic, see text), a multiplet from δ 5.4 to 5.36 (1 H, vinyl), a doublet at δ 4.18 (1 H, J = 10 Hz, CH), a doublet at δ 4.04 (1 H, J = 2 Hz, CH), a singlet at δ 3.68 (6 H, CH_3), and a multiplet from δ 3.4 to 2.2 (12 H, CH_2CH_2). The UV spectrum (ethanol) exhibited the following: λ_{max} 220 nm (ϵ 20 000), 284 (1200), 291 (1130), 323 (730). The mass spectrum exhibited the following: m/e (relative intensity) 376 (100, M$^+$), 348 (14), 344 (24), 329 (10), 318 (23), 317 (78), 316 (35), 285 (20), 258 (24), 257 (39), 276 (61), 269 (50), 167 (23), 155 (21), 154 (19), 153 (21), 141 (39), 129 (33), 128 (39), 117 (23), 116 (19), 115 (73), 91 (58).

Reaction of [2.2]Paracyclophane (1) with Thiophenol. To a tared, heavy-walled glass tube were added 96 mg of **1** and 1 mL of thiophenol. The tube was degassed, sealed at 0.03 mm, and heated at 220 ± 0.5 °C for 73 h. The tube was allowed to cool to room temperature, was frozen in liquid nitrogen, and was then opened. The contents were dissolved in ether and extracted three times with aqueous potassium carbonate. The organic phase was dried, and the solvent was removed at reduced pressure. The residue was chromatographed on 15 g of silica gel, with pentane as the eluting agent. Fractions 3–5 (35 mL each) contained only diphenyl disulfide. Fraction 6 contained 102 mg of diphenyl disulfide and 17 mg of p,p'-dimethylbibenzyl (by ^{1}H NMR integration). Fractions 7–15 contained an additional 56 mg of p,p'-dimethylbibenzyl (71% total), 80.5–82 °C (lit.[6] mp 81–82 °C). No starting material was detected.

Reaction of [2.2.2](1,2,4)Cyclophane (2) with Thiophenol. To a tared, heavy-walled glass tube were added 73 mg of **2** and 1 mL of thiophenol. The tube was degassed, sealed at 0.03 mm, and heated at 220 ± 0.5 °C for 73 h. The tube was cooled to room temperature, frozen in liquid nitrogen, and opened. The contents were dissolved in ether and extracted three times with aqueous potassium carbonate. The organic phase was dried and evaporated at reduced pressure, and the residue chromatographed on 15 g of silica gel. The column was eluted with pentane in 35-mL fractions. Fractions 8–21 contained 64 mg of **22** (88%), mp 135–135.5 °C. Anal. Calcd for $C_{18}H_{20}$: C, 90.47; H, 8.53. Found: C, 90.57; H, 8.46. The ^{1}H NMR spectrum indicates a doublet at δ 6.23 (6 H, aromatic), a singlet at δ 3.02 (8 H, CH_2CH_2), and a singlet at δ 2.73 (6 H, CH_3). The UV spectrum exhibited the following: λ_{max} 201 nm (ϵ 31 000), 203 (31 800), 204 (31 700), 262 (560, sh), 268 (92), 272 (740), 277 (1060). The mass spectrum exhibited the following: m/e (relative intensity) 236 (71, M$^+$), 221 (100), 207 (12), 206 (23), 193 (12), 131 (15), 130 (16), 119 (30), 118 (20), 116 (14), 91 (12).

Reaction of [3.2.2](1,2,5)Cyclophane (6) with Thiophenol. To a tared heavy-walled glass tube was added 95 mg of **6** and 1 mL of thiophenol. The tube was degassed, sealed at 0.03 mm, and heated at 220 ± 0.5 °C for 73 h. The tube was allowed to cool at room temperature, was frozen in liquid nitrogen, and was then opened. The contents were chromatographed directly on 15 g of silica gel, with pentane as the eluting agent. Fractions 2–7 (35 mL each) contained diphenyl disulfide. Fractions 13–24 were combined and sublimed (80 °C, 0.06 mm) to give 81 mg of solid. The ^{1}H NMR spectrum of this solid exhibited the same spectrum observed for **6** and three additional singlets: δ 6.96 (6 H, aromatic), 2.85 (10 H, $CH_2CH_2CH_2$, CH_2CH_2), 2.33 (6 H, CH_3). The composition of the mixture was 78% **6** by ^{1}H NMR integration: high-resolution mass measurement, calcd for $C_{19}H_{22}$ m/e 250.1721, found m/e 250.1719 ± 0.0005.

Reaction of [2.2.2](1,2,4)Cyclophane (2) with Diethyl Fumarate. To a dry, tared, heavy-walled glass tube was added 105 mg of **2**, 1 mL of diethyl fumarate, and 2 mg of p-dihydroquinone. The tube was degassed, sealed at 0.03 mm, and heated to 220 °C for 72 h. The tube was cooled at room temperature and opened. The contents were chromatographed on 12 g of silica gel with 1 L of 1% ether–pentane, 1 L of 5% ether–pentane, and 1 L of 10% ether–pentane (v/v) as the eluting agents. Fractions of 100 mL were collected. Fraction 2 contained 36 mg of **2**. Fractions 15–26 contained diethyl fumarate. Fractions 27–29 contained 60 mg of **23** (51%, based on recovered **2**), mp 129–132 °C. Anal. Calcd for $C_{26}H_{30}O_4$: C, 76.82; H, 7.44. Found: C, 76.65; H, 7.28. The ^{1}H NMR spectrum exhibited a complex multiplet from δ 6.60 to 6.12 (6 H, aromatic), two quartets at δ 4.15 and 4.12 (4 H, J = 6 Hz, CH_2CH_3), a complex multiplet from δ 3.4 to 2.4 (10 H, CH_2CH_2), and two triplets at δ 1.39 and 1.38 (6 H, J = 6 Hz, CH_2CH_3). The UV spectrum exhibited the following: λ_{max} 215 nm (ϵ 1100), 273 (690), 287 (580). The mass spectrum exhibited the following: m/e (relative intensity) 406 (64, M$^+$), 361 (33), 360 (25), 333 (25), 332 (100), 314 (52), 234 (93), 219 (20), 149 (35), 143 (28), 129 (34), 128 (26), 127 (41), 115 (32), 112 (24), 91 (32).

Reaction of [2.2.2](1,2,4)Cyclophane (2) with Diethyl Maleate. To 1.5 mL of diethyl maleate was added 105 mg of **2** and 5 mg of p-dihydroquinone. The solution was flushed with nitrogen for 15 min and heated at 220 °C for 43 h. The reaction mixture was chromatographed on 70 g of silica gel with 1 L of 1% ether–pentane, 2 L of 5% ether–pentane, and 2 L of 10% ether–pentane (v/v) as the eluting agents. Fractions of 100 mL were collected. Fractions 5–7 afforded 61 mg of **2**. Fractions 10–21 contained only diethyl maleate, and fractions 24–29 contained 29 mg of **23** (42%, based on **2** consumed), mp (with **23** obtained above) 128.5–132.5 °C. The ^{1}H NMR spectrum of this material was identical with that prepared above from dimethyl fumarate.

Registry No. **1**, 1633-22-3; **2**, 58002-98-5; **3**, 10029-00-2; **4**, 43044-95-7; **5**, 43044-96-8; **6**, 43044-97-9; **7**, 74498-48-9; **8**, 74498-49-0; **9**, 74524-22-4; **10**, 43044-98-0; **11**, 43045-00-7; **12**, 74498-50-3; **13**, 74498-51-4; **14**, 43044-99-1; **19**, 43045-02-9; **20**, 42053-17-8; **22**, 69978-57-0; **23**, 74498-52-5; phosphorus tribromide, 7789-60-8; sodium sulfide, 1313-82-2; DMADC, 762-42-5; thiophenol, 108-98-5; p,p'-dimethylbibenzyl, 538-39-6; diethyl fumarate, 623-91-6; diethyl maleate, 141-05-9.