Thermolysis and Transannular Reactions of 8,8-Dichloro-2,3:5,6-dibenzobicyclo[5.1.0]octane Derivatives

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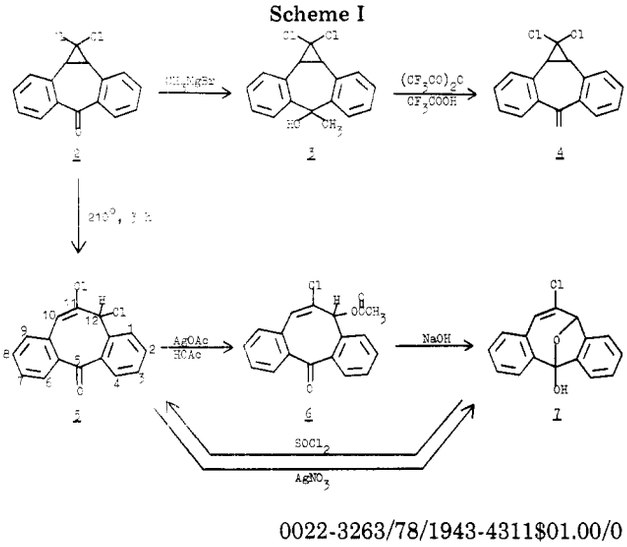
Several 8,8-dichloro-2,3:5,6-dibenzobicyclo[5.1.0]octane derivatives have been prepared and their propensity to thermolyze to functionally substituted, ring-expanded, dibenzo[*a,d*]cyclooctene derivatives has been investigated. 8,8-Dichloro-2,3:5,6-dibenzobicyclo[5.1.0]octan-4-one (**2**) undergoes a facile dichlorocyclopropane ring opening to give **5** in 93% yield, but the corresponding 4-methylene (**4**), 4-hydro (**13**), cis-4 alcohol (**8**), *cis*-4-methyl ether (**14**), and *cis*-4-methylamine (**16**) derivatives fail to undergo similar dichlorocyclopropane ring-opening reactions on heating. Thermolysis of trans alcohol **9** and *trans*-methyl ether **15**, however, leads to the ring-expanded, bridged ring ether **12**, and thermolysis of *trans*-methylamine **17** affords the bridged ring imine **18**. A possible explanation of these transformations in terms of anchimerically assisted dichlorocyclopropane ring-opening reactions is proposed.

Many molecules containing the dibenzo[*a,d*]cycloheptene ring system as a principle structural entity are richly endowed with a spectrum of biological activities.[1a-e] Consequently, the chemistry of derivatives of this type has been studied extensively, including the synthesis of carbon,[2,3] nitrogen,[4a-e] and oxygen[1c,5] bridged analogues. Surprisingly, the use of 5*H*-dibenzo[*a,d*]cycloheptenes as templates for the construction of derivatives of the next higher homologue, dibenzo[*a,d*]-cyclooctene, has not been reported. The availability of 8,8-dichloro-2,3:5,6-dibenzobicyclo[5.1.0]octan-4-one (**2**),[6,7] derived from dichlorocarbene addition to 5*H*-dibenzo[*a,d*]cyclohepten-5-one, suggested that entry into the homologous ring system via the well-documeted thermal-ring expansion of bicyclic 1,1-dihalocyclopropane compounds[8-10] would be feasible. Furthermore, the possibility that analogues of **2** containing appropriate oxygen and nitrogen substituents at C-4 (see Figure 1) might be converted directly to heteroatom bridged structures through transannular participation in the ring-opening process was attractive. Reported here is the experimental verification that both the ring expansion and heteroatom bridging processes occur and that they are related and dependent on the nature of the functionality at C-4 in 8,8-dichloro-2,3:5,6-dibenzobicyclo[5.1.0]octane derivatives.

Reactants, Synthesis, and Stereochemistry

Although 8,8-dichloro-2,3:5,6-dibenzobicyclo[5.1.0]-octan-4-one (**2**) was recovered unchanged after prolonged heating with an aqueous ethanolic solution of silver nitrate,[9] it undergoes a facile ring opening reaction when heated for 3 h in refluxing nitrobenzene to afford a 93% yield of the dichlorocyclopropyl ring-opened ketone **5**. Reaction of **5** with silver acetate in glacial acetic acid at reflux gave acetoxy ketone **6** in 98% yield. Saponification of the ester moiety of **6** led to the transannular hemiketal **7** (99% yield). The same product was obtained by treatment of **5** with aqueous ethanolic silver nitrate solution. Treatment of the hemiketal **7** with refluxing thionyl chloride proceeded smoothly to give crystalline **5** as the sole product.

Scheme I



The addition of methylmagnesium bromide to **2** gave alcohol **3** which was dehydrated to the olefin, **4**, by trifluoroacetic anhydride in trifluoroacetic acid. Attempts to effect thermolysis of the dichlorocyclopropane ring moiety of **4** in refluxing nitrobenzene (bp 210 °C), *o*-bromochlorobenzene (bp 204 °C), or in a neat melt at 200–210 °C were not successful. Starting material was substantially recovered after heating for 2 h. Prolonged heating at this temperature resulted in extensive decomposition.

Potassium borohydride reduction of **2** gave alcohol **8** that was obtained as a single stereoisomer as determined by GLC and ^{1}H NMR analysis. This alcohol has been assigned a *cis* configuration by analogy with Winstein's observation[11,12] that sodium borohydride reduction of 8,8-dibromo-2,3:5,6-dibenzobicyclo[5.1.0]octan-4-one gave the single stereoisomer **1** (X = Br, R_{ax} = H, R_{eq} = OH) that has the hydroxyl group cis with respect to the cyclopropyl ring. In this study of 2,3:5,6-dibenzobicyclo[5.1.0]octane derivatives, Winstein[12] also showed that not only do the cyclopropane rings in these compounds occupy a pseudoequatorial position, but that in C-4 epimeric alcohols, acetates, and methoxy ethers, the resonance of the pseudoaxial C-4 proton (R_{ax}) occurs further downfield in the NMR spectrum than that of the pseudoequatorial C-4 proton (R_{eq}). Equilibration of **8** in acidified aqueous dioxane for 48 h gave a mixture of the epimeric alcohols **8** and **9**. Analysis of this mixture by GLC showed an equilibrium composition in an 85/15 ratio with the more abundant isomer being the starting alcohol **8**. The trans alcohol **9** was separated from this mixture of epimers by chromatography. The ^{1}H NMR spectrum of *trans*-**9** is similar to the NMR spectrum of *cis*-**8** except for the chemical shift of the carbinyl proton (C-4). The pseudoaxial C-4 proton of the cis alcohol **8** has a chemical shift at δ 6.35 while the pseudoequatorial C-4 proton of the trans alcohol **9** has a chemical shift at δ 5.31.

The cis alcohol **8** (mp 170.5–172 °C) when heated at 190 °C melted and then crystallized cleanly to a new product that was identified as the bisether **10**. The same product was formed on heating **8** for 1 h in refluxing nitrobenzene. In this case, however, there appeared to be some decomposition as evi-

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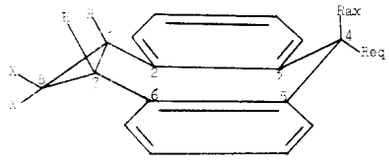


Figure 1.

denced by a slight evolution of HCl gas and rapid darkening of the solution.

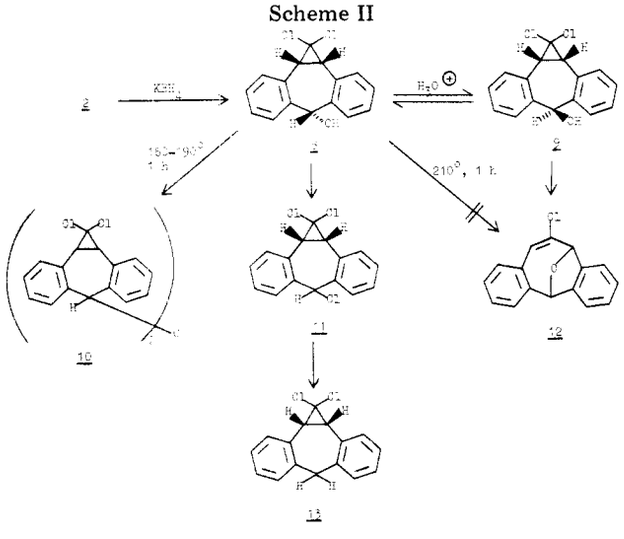
The trans alcohol **9**, when heated for 2 h in refluxing nitrobenzene, gave a new, bridged ring ether **12**. This ether, isolated in crystalline form by chromatography, results from a dichlorocyclopropane ring opening with an intramolecular, transannular participation of the C-4 pseudoaxial hydroxyl group.

Reaction of **8** with thionyl chloride gave a trichloro compound **11** that was solvolyzed in aqueous dimethoxyethane in the presence of sodium borohydride according to the procedure of Bell and Brown.[13] The crystalline chlorohydrocarbon **13** was stable at 150–160 °C for 1 h in a neat melt but underwent rapid decomposition in refluxing nitrobenzene.

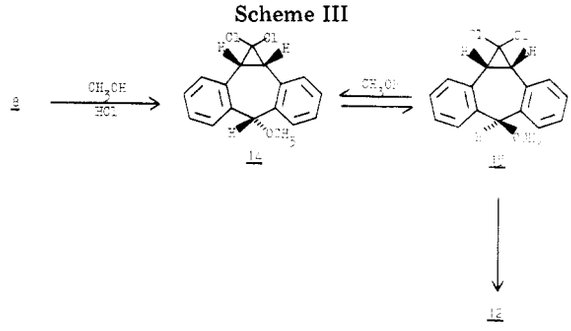
Treatment of the cis alcohol **8** with acidic methanol under reflux for 144 h gave a mixture of the methoxy ethers **14** and **15**. Analysis of this mixture by GLC showed an equilibrium composition in a 21 to 79 ratio. The more abundant isomer was isolated by direct crystallization while the less abundant isomer was isolated by chromatography. As with the epimeric alcohols **8** and **9**, the ^{1}H NMR spectra of methoxy ethers **14** and **15** were similar except for the resonances attributed to the protons α to the methoxy groups. The less abundant epimer was assigned the cis configuration **14** based on the low-field position of its pseudoaxial proton (δ 5.87) relative to the position of the pseudoequatorial proton (δ 4.82) in the more abundant trans isomer **15**. Thermolysis of trans ether **15** at 190–195 °C for 30 min in a neat melt gave the same bridged ring ether **12** as was obtained by thermolysis of trans alcohol **9**. Under the same conditions, cis ether **14** was recovered unchanged.

Titanium tetrachloride promoted addition of methylamine to ketone **2** followed by in situ reduction of the resulting imine with sodium cyanoborohydride gave a mixture of the methylamines **16** and **17**.[14] These amines were readily separated by fractional crystallization of their hydrochloride salts. The ^{1}H NMR spectra of these amines, as bases or as salts, were quite similar except for the chemical shifts of the C-4 protons. By analogy with the alcohols **8** and **9** and the ethers **14** and **15**, the epimeric amine having the low-field C-4 singlet proton resonance (δ 5.36) was assigned the cis configuration **16** while

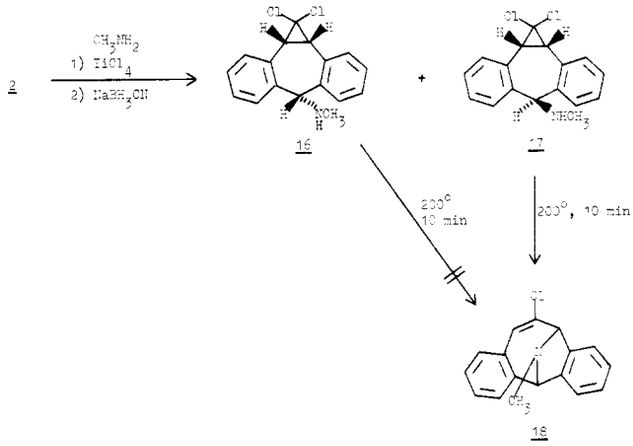
Scheme II



Scheme III



Scheme IV



the amine having the upfield resonance (δ 4.33) was assigned the trans configuration **17**. Additional confirmation of the stereochemical assignments of **16** and **17** was obtained by a comparison of the ^{1}H NMR spectra of the hydrochloride salts *vs.* the free amines. Examination of a Dreiding model of the trans isomer **17** indicates that the nitrogen atom is in close proximity to the bridgehead protons of the cyclopropane ring (see Figure 1, C_1C_7–H). For *trans*-**17**, these bridgehead protons have a signal at δ 3.49 ($CDCl_3$) in the base and at δ 3.74 (Me_2SO-d_6) in the hydrochloride salt. In cis isomer **16**, the bridgehead protons have a resonance at δ 3.55 ($CDCl_3$) in the base and at δ 3.62 (Me_2SO-d_6) in the hydrochloride salt. Thus, in *trans*-**17** the resonance of these protons is displaced 0.18 ppm further downfield on salt formation than for *cis*-**16**. The selective deshielding of the bridgehead protons of **17** that occurs by salt formation thus agrees with the assigned trans configuration.

When **17** was thermolyzed without solvent at 200 °C (10 min), heated for 10 min at 200 °C in hexamethylphosphoramide, or heated in refluxing tetramethylurea (bp 177 °C) for 2 h, it was smoothly converted to the nitrogen bridged compound **18**. Under the same conditions, *cis*-**16** was recovered unchanged.

Discussion

The observation that the dichlorocyclopropyl ketone **2** undergoes a facile thermolysis to give **5** appears to be another example of the well-known thermal rearrangement of a dichlorocyclopropane ring to an allyl cation resulting in a ring-expanded product.[8–10] It was surprising, therefore, that when thermolysis reactions were carried out on the closely related methylene compound **4** or on the dichlorohydrocarbon **13** no apparent ring-opening reactions occurred. The failure of these compounds to undergo the thermolysis reaction suggests a role for the carbonyl oxygen atom of **2** in the ring-opening process leading to **5**. Participation of an oxygen atom in transannular reactions in dibenzo[*a*,*d*]cycloheptene nuclei is well known.[5] Indeed, if neighboring group participation is required during thermolysis for the dichlorocyclopropane ring of 8,8-di-

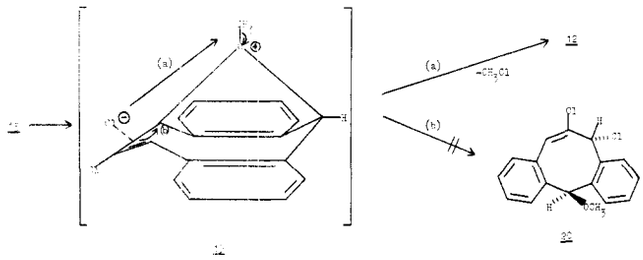


Figure 2.

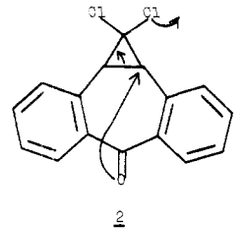


Figure 3.

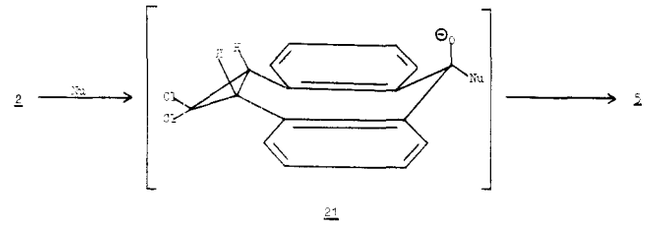


Figure 4.

chloro-2,3:5,6-dibenzobicyclo[5.1.0]octane derivatives to open to product at a temperature lower than that which induces decomposition, then the trans alcohol 9, having an oxygen atom in the pseudoaxial position and hence in close proximity to the C_1C_7 bond, should undergo thermolysis with a concomitant transannular ring formation while cis alcohol 8, with its hydroxyl group positioned in an unfavorable pseudoequatorial orientation, should not undergo a facile thermolysis of the dichlorocyclopropane ring. In fact, this conclusion was borne out by the experimental results described above. The thermolysis experiments of the epimeric amines **16** and **17** and ethers **14** and **15** provide further support for the idea that nucleophilic assistance from a heteroatom is needed to lower the activation energy for ring opening below that required for general decomposition. Thus, with the chlorohydrocarbons **4** and **13,** prolonged heating led to gross decomposition whereas compounds **2, 9, 15,** and **17** gave clean thermolysis products. In one of the latter cases, the smooth conversion of **15** to **12,** rather than to **20,** with methyl chloride evolution, suggested that the reaction passes through an intermediate such as **19** in which the oxygen bears a positive charge.

The degree and nature of oxygen participation in the conversion of ketone **2** to **5,** of course, remains open to question. The limiting intermediate oxonium ion structure arising from **2** would appear to be of high energy. The conversion of **7** to **5** on treatment with thionyl chloride, however, suggests that bridged oxygen structures of this type may also tolerate a significant degree of positive charge on C-4. One possibility might involve reversible attack of adventitious nucleophiles (Nu), either in solution or on the surfaces of the reaction vessel, to produce the intermediate **21** in which the participating nucleophile is the negatively charged oxygen atom. However, with the available data, a precise formulation is not possible.[15]

In general, we conclude that the formation of a resonance-stabilized allylic, benzylic carbonium ion and the attendant relief of the strain energy of the cyclopropane ring does not appear to be sufficient to account for any of these ring openings. Rather, the above observations suggest a requirement of participation by a group in the C-4 position capable of efficiently stabilizing or accepting the developing positive charge arising from cleavage of the C_1C_7 bond. For compounds **9, 15,** and **17,** such participation is clearly evident from the configurational dependence of the process, though for ketone **2** such participation is a matter of surmise.

Experimental Section

Melting points were determined on a Thomas-Hoover Unimelt capillary melting point apparatus and are uncorrected. Nuclear magnetic resonance (NMR) spectra were determined on Varian A-60A, T-60, EM-90, and HA-100 spectrometers. Except for the hydrochloride salts of **16** and **17,** which were recorded in deuterated dimethyl sulfoxide, all NMR spectra were recorded using deuteriochloroform as solvent and all chemical shifts are relative to tetramethylsilane as an internal standard. Gas-liquid chromatographic analyses were carried out on a Hewlett-Packard Model 5700A/3370B gas chromatograph using a column (6 ft × 2 mm) packed with 1% OV-17 on 100/120 Gas-Chromosorb Q. Infrared spectra were recorded on a Perkin-Elmer Model 21 spectrophotometer. Analytical TLC was carried out on 250 μm, 5 × 20 cm, Silica Gel GF plates (Analtech, Inc.) using ultraviolet light and iodine vapor for visualization.

5,6-Dichloro-5,12-dihydrodibenzo[*a,d*]cycloocten-12-one (5). A solution of 12.0 g (0.0415 mol) of ketone **2** dissolved in 125 mL of nitrobenzene was stirred and heated at reflux for 3 h. The nitrobenzene was steam distilled from the reaction mixture as rapidly as possible. The dark reaction mixture was extracted with benzene which was washed with water, dried, and evaporated. The residue was chromatographed on a silica gel column using benzene as an eluant to give 9.25 g (93%) of ketone **5.** An analytical sample was prepared by recrystallization from methanol: mp 120–122 °C; NMR δ 6.43 (s, 1 H, allylic C**H**), 6.92 (s, 1 H, vinyl C**H**), 7.2–8.3 (m, 8 H, ArH). The material gave an immediate positive test with alcoholic silver nitrate.

Anal. Calcd for $C_{16}H_{10}Cl_2O$: C, 66.45; H, 3.49; C, 24.52. Found: C, 66.67; H, 3.35; Cl, 24.44.

5-Acetoxy-6-chloro-5,12-chloro-5,12-dihydrodibenzo[*a,d*]cycloocten-12-one (6). A mixture of 7.06 g (0.0245 mol) of ketone **5,** 4.18 g (0.025 mol) of silver acetate, and 140 mL of glacial acetic acid was heated at reflux for 3 h. The cooled mixture was filtered and the solvent was removed. The residue was recrystallized from benzene to give 7.53 g (98%) of the acetoxy ketone **6:** mp 117–118 °C; NMR δ 2.14 (s, 3 H, CH_3CO), 6.72 (s, 1 H, C_5H), 6.94 (s, 1 H, C_7H), 7.3–7.7 (m, 7 H, ArH), and 8.1–8.3 (m, 1 H, ArH).

Anal. Calcd for $C_{18}H_{13}ClO_3$: C, 69.13; H, 4.19; Cl, 11.34. Found: C, 69.20; H, 4.07; Cl, 11.45.

6-Chloro-5,12-dihydro-5,12-epoxydibenzo[*a,d*]cycloocten-12-ol (7). A solution of 1.0 g (0.0031 mol) of the acetoxy ketone **6,** 10 mL of 5 N sodium hydroxide, and 10 mL of ethanol was heated on the steam bath for 5 min. The cooled solution was filtered and concentrated. The oil that precipitated was extracted into benzene, washed with water, and dried over magnesium sulfate. After evaporation of the benzene, 0.83 g (99%) of hemiketal **7** was obtained. The product was recrystallized from benzene: mp 167–168 °C; NMR δ 4.1 (s, 1 H, O**H**), 5.40 (s, 1 H, C_5H), 6.32 (s, 1 H, C_7H), 7.0–7.5 and 7.8–8.0 (m, 8 H, ArH); IR (Nujol) 3450 cm^{-1} (OH), no C=O.

Anal. Calcd for $C_{16}H_{11}ClO_2$: C, 70.99; H, 4.10; Cl, 13.09. Found: C, 70.94; H, 4.20; Cl, 12.89.

A solution of 5.37 g (0.0186 mol) of ketone **5** in 100 mL of aqueous acetone (1:3) was treated with a solution of 3.46 g (0.0204 mol) of silver nitrate dissolved in 6.5 mL of water. The mixture was stirred and refluxed for 3 h. The silver chloride was removed by filtration, and the solution was concentrated. The oil that precipitated was extracted into ether and the ether layer was washed with water, dried ($MgSO_4$), and then concentrated. The solid obtained (2.62 g) was recrystallized from benzene to give the hemiketal **7,** mp 167–169 °C; an infrared spectrum of this material was identical to the spectrum of material obtained by saponification of the acetoxy ketone **6.**

Reaction of 6-Chloro-5,12-dihydro-5,12-epoxydibenzo[*a,d*]cycloocten-12-ol (7) with Thionyl Chloride. A solution of 3.43 g (0.0127 mol) of the hemiketal **7** in 75 mL of thionyl chloride was stirred and refluxed for 4 h. The solvent was removed under reduced pressure and the residue was coevaporated with two 100-mL portions of toluene. Examination of the crystalline residue by TLC (fluorescent silica

gel/toluene) showed essentially a single spot. Recrystallization of the material from methanol gave 2.30 g (63%) of **5** as white needles, mp 117–120 °C, mixture melting point with authentic **5** 116–120 °C; TLC homogeneous both alone and when admixed with authentic **5**. An infrared spectrum of the material was identical to an infrared spectrum of authentic ketone **5**.

4-Methylene-8,8-dichloro-2,3:5,6-dibenzobicyclo[5.1.0]octane (4). To an ice-cooled solution of 15.0 g (0.0519 mol) of ketone **2** dissolved in 200 mL of dry THF was added dropwise over 30 min 28.6 mL of a 1.92 M solution of methylmagnesium bromide in THF–benzene. After the addition was complete, the solvent was removed on a rotary evaporator. The remaining red oily residue was dissolved in ether and water was added dropwise until a clear ether supernatant and a semisolid aqueous residue were obtained. The ether phase was decanted and the residue was extracted twice more with ether. The combined ether phases were dried ($MgSO_4$) and filtered and the filtrate was concentrated to afford 14.1 g (89%) of the crystalline alcohol **3**, mp 141–148 °C.

A solution of 6.0 g (0.020 mol) of the above alcohol dissolved in 50 mL of trifluoroacetic anhydride and 50 mL of trifluoroacetic acid was stirred and refluxed for 3 h. The solid that precipitated on cooling was removed by filtration. Recrystallization from acetonitrile gave 4.9 g (87%) of **4**: mp 187–189 °C; NMR δ 3.30 (s, 2 H, bridge H), 5.36 (s, 2 H, vinyl C**H**), 7.1–7.4 (m, 8 H, ArH).

Anal. Calcd for $C_{17}H_{12}Cl_2$: C, 71.09; H, 4.21; Cl, 24.70. Found: C, 70.72; H, 4.39; Cl, 24.63.

The olefin **4** was held as a neat melt in an oil bath at 200–210 °C for 2.5 h. On cooling, the material crystallized, mp 184–187 °C. An NMR spectrum was identical to that of the starting material, **4**. Olefin **4** was heated in refluxing nitrobenzene and also in refluxing 2-bromochlorobenzene (bp 204 °C). Employing the same procedure used in the isolation of **5**, olefin **4** was recovered after 1 h of heating, but then decomposition began to occur.

8,8-Dichloro-*cis*-4-hydroxy-2,3:5,6-dibenzobicyclo[5.1.0]octane (8). To a solution of 2.0 g (0.0069 mol) of ketone **2** dissolved in 40 mL of refluxing methanol was added dropwise over 15 min a solution of 0.941 g (0.0175 mol) of potassium borohydride dissolved in 10 mL of water. After the addition had been completed, the solution was refluxed for 1.5 h. Evaporation of the methanol gave a crystalline product that was collected by filtration, washed with water, and then collected and dried. The colorless material was recrystallized from aqueous methanol to give 1.51 g (75%) of cis-alcohol **8**: mp 170.5–172.5 °C; NMR δ 2.38 (d, 1 H, J = 2 Hz, D_2O exchangeable, HCO**H**), 3.26 (s, 2 H, bridge C**H**), 6.35 (d, 1 H, J = 2 Hz, **H**-COH), 7.1–7.6 (m, 8 H, Ar**H**).

Anal. Calcd for $C_{16}H_{12}Cl_2O$: C, 66.00; H, 4.14; Cl, 24.36. Found: C, 65.85; H, 4.22; Cl, 24.44.

Bis(8,8-dichloro-2,3:5,6-dibenzobicyclo[5.1.0]oct-4-yl) Ether (10) from the Attempted Thermolysis of cis-Alcohol 8. A sample of the cis-alcohol **8** (2.0 g, mp 170.5–172.5 °C) in a round-bottom flask was placed in an oil bath at 190 °C for 30 min. The compound quickly melted and then crystallized. Examination of this solid by TLC (fluorescent silica gel/toluene) showed none of the cis-alcohol **8** (R_f 0.39), but only a new product at R_f 0.92. Recrystallization from toluene gave 1.0 g of the bisether **10**: mp 250–252 °C; NMR δ 3.10 (s, 2 H, bridge H), 3.42 (s, 2 H, bridge H), 5.10 (s, 1 H, C_4**H**), 6.02 (s, 1 H, C_4**H**), 7.0–7.6 (m, 16 H, Ar**H**).

Anal. Calcd for $C_{32}H_{22}Cl_4O$: C, 68.10; H, 3.93; Cl, 25.13. Found: C, 67.94; H, 3.87; Cl, 24.79.

A solution of 0.75 g of the cis-alcohol **8** in 2 mL of nitrobenzene was heated under reflux for 1 h. The nitrobenzene was removed by coevaporation with water on a rotary evaporator. Examination of the black residue by TLC (fluorescent silica gel/toluene) showed no alcohol **8**, but rather a spot at R_f 0.93 indicative of the ether **10**. There was black decomposition material at the origin.

Equilibration of 8,8-Dichloro-*cis*-4-hydroxy-2,3:5,6-dibenzobicyclo[5.1.0]octane (8) to a Mixture of *cis*-8 and *trans*-9 Alcohols. A solution of 4.54 g of cis-alcohol **8** in 200 mL of peroxide free dioxane and 50 mL of water containing 0.5 mL of 72% perchloric acid was stirred and heated at 80–85 °C under a nitrogen atmosphere for 48 h. The bulk of the dioxane was removed under reduced pressure and 500 mL of water and 100 mL of a saturated sodium bicarbonate solution were added. The oil that precipitated was extracted into two 200-mL portions of ether. The ether phase was washed with water and dried over $MgSO_4$. Evaporation of the ether under reduced pressure gave 4.4 g of a mixture of the alcohols **8** and **9**. Analysis of this mixture by GLC showed 85% cis-alcohol **8** and 15% trans-alcohol **9** at equilibrium. The epimeric alcohols are readily distinguished by TLC (fluorescent silica gel/toluene): cis-alcohol **8**, R_f 0.39; trans-alcohol **9**, R_f 0.16.

8,8-Dichloro-*trans*-4-hydroxy-2,3:5,6-dibenzobicyclo[5.1.0]octane (9). The mixture of epimeric alcohols **8** and **9**, obtained from the previous equilibration experiment, (4.4 g), was separated into its constituent epimers by chromatography on 12 preparative, fluorescent, silica gel plates (2000 μm, 8 in. × 8 in.) using toluene as a developing solvent. The band centered at R_f 0.16 was removed from each plate and the product was eluted by washing the silica gel with warm methanol. The methanol extracts were filtered and the methanol was removed on a rotary evaporator. The residue was recrystallized from acetonitrile to give 0.41 g of TLC homogeneous trans-alcohol **9**: mp 115.5–117.5 °C; NMR δ 2.81 (d, 1 H, $J \sim 1$ Hz, D_2O exchangeable, H-C-O**H**), 3.40 (s, 2 H, bridge CH), 5.31 (d, 1 H, $J \sim 1$ Hz, **H**-C-OH), 7.1–7.8 (m, 8 H, ArH).

Anal. Calcd for $C_{16}H_{12}Cl_2O$: C, 66.00; H, 4.14; Cl, 24.36. Found: C, 66.14; H, 4.05; Cl, 24.28.

6-Chloro-5,12-epoxy-5,12-dihydrodibenzo[*a,d*]cyclooctene (12). A solution of 0.25 g of trans-alcohol **9** in 2.5 mL of nitrobenzene was stirred at reflux for 2 h. The nitrobenzene was removed by coevaporation with water on a rotary evaporator. The remaining dark residue was chromatographed on two preparative silica gel plates (2000 μm, 8 in. × 8 in.) using toluene as a developing solvent. Apart from some black decomposition byproduct at the origin, the only UV absorbing material was located in bands centered at R_f 0.79. These bands were removed from each plate and the product was eluted by washing the silica gel with warm methanol. The extracts were filtered and the methanol was removed on a rotary evaporator to give 0.077 g (35%) of an oil that crystallized on standing. The product was purified by sublimation at 100 °C (0.1 mm) followed by recrystallization from methanol to give **12** as colorless prisms: mp 112.5–114 °C; NMR δ 5.6 (s, 1 H, C_5H), 6.0 (s, 1 H, C_{12}H), 6.25 (s, 1 H, C_7H), 6.8–8.0 (m, 8 H, Ar**H**).

Anal. Calcd for $C_{16}H_{11}ClO$: C, 75.44; H, 4.35; Cl, 13.92. Found: C, 75.48; H, 4.47; Cl, 13.79.

8,8-Dichloro-2,3:5,6-dibenzobicyclo[5.1.0]octane (13). A solution of 10.0 g of the alcohol **8** dissolved in 100 mL of thionyl chloride was stirred and refluxed for 18 h. Removal of the thionyl chloride on a rotary evaporator afforded a crystalline solid **11**. A solution of 7.0 g (0.023 mol) of this solid and 6.0 g of sodium borohydride in 87.5 mL of 80% aqueous dimethoxyethane containing 10 mL of 10% aqueous sodium hydroxide was stirred at 45 °C for 4 h and then was allowed to stand overnight at room temperature. The solution was diluted with 200 mL of water and the oil that precipitated was extracted into ether. The ether layer was washed with three 100-mL portions of water and dried ($MgSO_4$), and the ether was removed to give crude **13**. This material was chromatographed on Alumina using petroleum ether as an eluant to give **13** as TLC homogeneous, colorless crystals. An analytical sample was prepared by recrystallization from ethanol: mp 109–110 °C; NMR δ 3.22 (s, 2 H, bridge **H**), 3.22 and 4.48 (d of d, 2 H, J = 6.5 Hz, ArCH_2Ar), 7.0–7.4 (m, 8 H, ArH).

Anal. Calcd for $C_{16}H_{12}Cl_2$: C, 69.83; H, 4.40; Cl, 25.77. Found: C, 69.81; H, 4.58; Cl, 25.58.

The chlorohydrocarbon **13** was recovered unchanged after being held in a neat melt at 150–160 °C for 1 h. When **13** was heated for 2 h in refluxing nitrobenzene, extensive decomposition occurred.

8,8-Dichloro-*trans*-4-methoxy-2,3:5,6-dibenzobicyclo[5.1.0]octane (15). A solution of 6.0 g of **8** in 250 mL of methanol containing 0.5 mL of concentrated hydrochloric acid was stirred and refluxed for 65 h. The bulk of the methanol was removed on a rotary evaporator. The residue was dissolved in ether and this ethereal solution was washed with a saturated sodium carbonate solution and water and then dried ($MgSO_4$). After filtration, the ether was removed under reduced pressure. The white crystalline residue was recrystallized from methanol to afford 3.27 g of trans-ether **15** that was TLC homogeneous (fluorescent silica gel, toluene, R_f 0.53): mp 118–120 °C; NMR δ 3.30 (s, 3 H, OCH_3), 3.40 (s, 2 H, bridge CH), 4.82 (s, 1 H, C_4H), 7.1–7.4 (m, 8 H, ArH).

Anal. Calcd for $C_{17}H_{14}Cl_2O$: C, 66.90; H, 4.62; Cl, 23.24. Found: C, 67.13; H, 4.52; Cl, 23.18.

6-Chloro-5,12-epoxy-5,12-dihydrodibenzo[*a,d*]cyclooctane (12) from Thermolysis of *trans*-Methyl Ether 15. A 1.0-g sample of *trans*-methyl ether **15** in a round-bottom flask was placed in an oil bath at 190–195 °C for 30 min. The compound quickly melted and gas evolution was observed. The clear, light tan residue was chromatographed on two preparative silica gel plates (2000 μm, 8 in. × 8 in.) using toluene as a developing solvent. The only fluorescent band, at R_f 0.65 to 0.80, was removed from each plate and the product was eluted by washing the silica gel with warm methanol. The extracts were filtered and the methanol was removed on a rotary evaporator. The residue was dissolved in chloroform and filtered, and the chloroform was removed under reduced pressure. The residue was rec-

rystallized from methanol to afford 0.50 g (60%) of colorless prisms, **12**, mp 112–114 °C (mmp with **12**, 112–114 °C). The material was homogeneous by TLC (fluorescent silica gel/toluene), R_f 0.75, when assayed alone or when admixed with authentic **12**.

8,8-Dichloro-*cis*-4-methoxy-2,3:5,6-dibenzobicyclo[5.1.0]octane (14). A solution of 6.32 g of cis-alcohol **8** in 250 mL of methanol containing 2 mL of concentrated hydrochloric acid was refluxed for 144 h. The cooled solution was poured into an excess of sodium carbonate solution and was extracted with ether. The ether phase was washed with water and dried ($MgSO_4$), and the ether was removed on a rotary evaporator to give a mixture of the methyl ethers **14** and **15**. Analysis of this mixture by GLC showed 21% cis-ether **14** and 79% trans-ether **15**. The bulk of the trans-ether **15** was removed by crystallization and the mother liquor, containing the desired cis-ether **14**, was concentrated on a rotary evaporator. The residue, 2.04 g, was chromatographed on four preparative silica gel plates (2000 μm, 8 in. × 8 in.) using toluene as a developing solvent. The band at R_f 0.70 to 0.80 was removed from each plate and the product was eluted by washing the silica gel with warm methanol. After filtration, the methanol was removed under reduced pressure. The residue was recrystallized from methanol to give 0.51 g of TLC homogeneous (silica gel/toluene, R_f 0.74) cis-ether **14**: mp 136–138 °C; NMR δ 3.25 (s, 2 H, bridge CH), 3.50 (s, 3 H, OCH_3), 5.87 (s, 1 H, C_4H), 7.1–7.5 (m, 8 H, ArH).

Anal. Calcd for $C_{17}H_{14}Cl_2O$: C, 66.90; H, 4.62; Cl, 23.24. Found: C, 66.69; H, 4.67; Cl, 23.37.

Cis-ether **14** was recovered unchanged after heating in a neat melt at 190–195 °C for 30 min.

***N*-Methyl-8,8-dichloro-*trans*-2,3:5,6-dibenzobicyclo[5.1.0]octan-4-amine (17).** To a solution of 3.1 g (0.10 mol) of anhydrous methylamine in 150 mL of benzene was added 7.5 g (0.026 mol) of ketone **2**. A solution of 2.47 g (0.013 mol) of titanium tetrachloride in 20 mL of benzene was added and the mixture was stirred overnight at room temperature. The mixture was filtered. Evaporation of the solvent under reduced pressure gave an oil that was dissolved in 75 mL of acetonitrile and then 2.36 g (0.037 mol) of sodium cyanoborohydride was added. The solution was stirred overnight at room temperature. The solution was diluted with 150 mL of water and 100 mL of 1 N sodium hydroxide. The mixture was extracted with three 100-mL portions of ether and the combined ethereal layers were washed with water and dried over anhydrous sodium sulfate. Removal of the solvent gave 8.9 g of a pale orange oil that was dissolved in 50 mL of methanol and was acidified with 8 N ethanolic HCl. On standing, a white crystalline solid separated. Recrystallization of this solid from methanol (250 mL)–ethanol (150 mL) afforded 2.53 g (29%) of the hydrochloride salt of the trans-amine **17**, mp 280–285 °C. An NMR spectrum was taken on the free base **17**: NMR ($CDCl_3$) δ 1.80 (s, 1 H, NH), 2.23 (s, 3 H, CH_3), 3.49 (s, 2 H, bridge CH), 4.33 (s, 1 H, C_4H), 7.0–7.4 (m, 8 H, ArH).

Anal. Calcd for $C_{17}H_{15}Cl_2N$·HCl: C, 59.93; H, 4.73; Cl, 31.22; N, 4.11. Found: C, 59.92; H, 4.88; Cl, 31.14; N, 4.23.

***N*-Methyl-8,8-dichloro-*cis*-2,3:5,6-dibenzobicyclo[5.1.0]octan-4-amine (16).** All of the mother liquors from the preceding experiment were combined and concentrated by boiling to a volume of 150 mL. On standing, 2.2 g (25%) of the hydrochloride salt of the cis-amine **16** crystallized, mp >340 °C. An NMR spectrum was taken on the free base **16** that was generated from the crystalline hydrochloride salt: NMR ($CDCl_3$) δ 1.70 (s, 1 H, NH), 2.52 (s, 3 H, CH_3), 3.55 (s, 2 H, bridge H), 5.36 (s, 1 H, C_4H), 7.0–7.5 (m, 8 H, ArH).

Anal. Calcd for $C_{17}H_{15}Cl_2N$·HCl: C, 59.93; H, 4.73; Cl, 31.22; N, 4.11. Found: C, 59.60; H, 4.87; Cl, 31.23; N, 4.29.

The amine **16** was recovered unchanged after being held in a neat melt at 200 °C for 10 min, being heated in HMPA at 200 °C for 10 min, or being heated in refluxing tetramethylurea for 2 h.

***N*-Methyl-6-chloro-5,12-dihydrodibenzo[*a,d*]cyclooctene-5,12-imine (18).** A solution of 2.0 g (0.0059 mol) of the free base **17** in 25 mL of HMPA was heated at 200 °C for 10 min. The solvent was removed under reduced pressure, and the residue was slurried with 100 mL of 1 N sodium hydroxide solution. The mixture was extracted with three 100-mL portions of chloroform, and the combined chloroform extracts were dried (Na_2SO_4) and filtered. Removal of the chloroform gave an oil that was dissolved in 100 mL of 1 N methanolic HCl. Evaporation of the solvent gave 1.5 g of a crystalline solid that was recrystallized from acetonitrile–acetone (1:1) to afford 1.3 g (73%) of the hydrochloride salt of **18**, mp 225–228 °C. An NMR spectrum was taken on the free base **18** that was generated from the hydrochloride salt: NMR ($CDCl_3$) δ 2.32 (s, 3 H, NCH_3), 4.7 (s, 1 H, allylic **CH**), 5.03 (s, 1 H, benzhydryl **CH**), 6.42 (s, 1 H, vinyl **CH**), 7.0–7.4 (m, 8 H, ArH).

Anal. Calcd for $C_{17}H_{14}ClN$·HCl: C, 67.11; H, 4.97; N, 4.60. Found: C, 66.81; H, 5.06; N, 4.50.

The same product, **18**, was obtained when **17** was held in a neat melt at 200 °C for 10 min, and also when **17** was heated in refluxing tetramethylurea (bp 177 °C) for 2 h.

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(14) This reaction may be viewed as a modification of the Borsch reaction in which methylamine hydrochloride, a byproduct of imine formation, acts as an in situ proton source thus allowing reduction of the protonated imine by sodium cyanoborohydride. This method avoids isolation of potentially unstable imines.
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