

# Formation of Homologous Bird-Cage Molecules. Strain and Transannular Effects<sup>1</sup>

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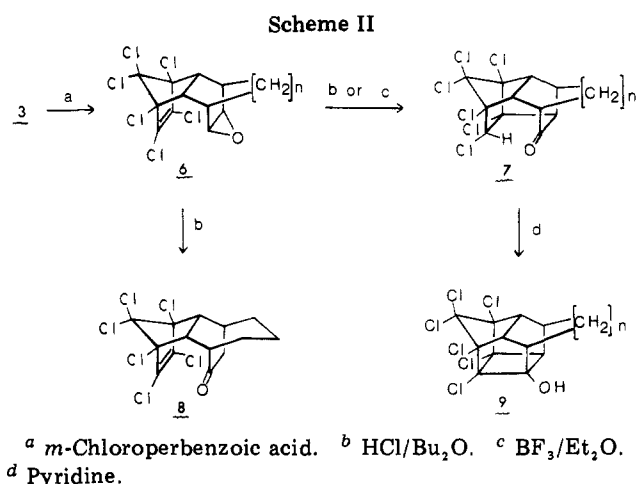
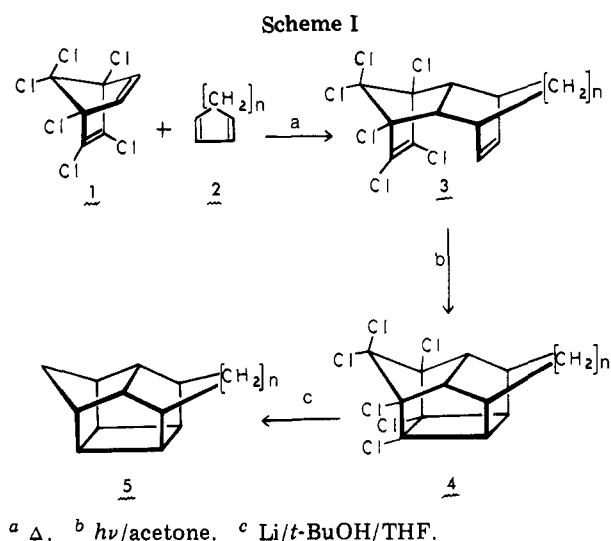
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The three endo-endo dienes **3** ( $n = 1-3$ ) were prepared by Diels-Alder reaction of 1,2,3,4,7,7-hexachloro-norborna-1,5-diene with the cyclic dienes **2** ( $n = 1-3$ ). The reactivity of the dienes **3** in forming the cage compounds **4** under the influence of bromine or UV light decreased with  $n$  from 1 to 3. The same effect of  $n$  on reactivity was shown in formation of the half-cage ketones **7** ( $n = 1-3$ ) from the epoxides **6** ( $n = 1-3$ ) and of the cage alcohols **9** ( $n = 1-3$ ) from the ketones **7** ( $n = 1-3$ ). An explanation based on the effect of  $n$  on the difference in strain energy of products and reactants is advanced.

Although reactions leading to the "bird-cage" hydrocarbon **5** ( $n = 1$ ) have been much investigated,<sup>2-16</sup> there is only one report<sup>17</sup> of a derivative (dibromo) of the homologue **5**,  $n = 2$ , and none of the higher homologue **5**,  $n = 3$ . In the present paper we report syntheses of the two homologues **5**,  $n = 2$  and 3, by essentially the same route (Scheme I) used for **5**,  $n = 1$ ,<sup>2-6</sup> and some other reactions of dienes **3** ( $n = 1-3$ ), epoxides **6** ( $n = 1-3$ ), and ketones **7** ( $n = 1-3$ ) derived from them (Scheme II). The reactivities of these homologues showed a marked variation with  $n$  which we discuss and attempt to explain in the sequel.

## Results

**Synthesis of Cage Compounds 4 and 5.** The insecticide "Isodrin" (**3**,  $n = 1$ ) is made by the Diels-Alder reaction of cyclopentadiene (**2**,  $n = 1$ ) with hexachloro-norbornadiene (**1**);<sup>2b</sup> homoisodrin (**3**,  $n = 2$ ) and bishomoisodrin (**3**,  $n = 3$ ) were prepared in good yields by similar reactions of 1,3-cyclohexadiene (**2**,  $n = 2$ ) and 1,3-cycloheptadiene (**2**,  $n = 3$ ). Ultraviolet irradiation of the Isodrin homologues in acetone<sup>3,6</sup> gave the hexachloro cage



(1) Work supported by the Natural Sciences and Engineering Research Council of Canada.

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compounds **4** ( $n = 2$  and 3), which were dechlorinated by lithium in *tert*-butyl alcohol-tetrahydrofuran<sup>5</sup> to "homo bird cage" (**5**,  $n = 2$ ) and "bishomo bird cage" (**5**,  $n = 3$ ). The cage structures of the compounds follow from their empirical formulas and from the absence of olefinic linkages, as indicated by IR,<sup>4-6</sup> <sup>1</sup>H NMR, and <sup>13</sup>C NMR spectra (the last to be discussed in a subsequent paper).

As expected for compounds having rigid and nearly spherical molecules,<sup>18</sup> compounds **5** have high melting

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Table I. Effect of Reaction<sup>a</sup> Time on Yields of Epoxides 6 ( $n = 1-3$ )

$n$	time, h								
	15	17.5	39	51	72	88	112	160	240
1	100								
2	86	89	100						
3	45	55	72	82	83	87	90	94	100

<sup>a</sup> 20% excess *m*-chloroperbenzoic acid in  $\text{CDCl}_3$  used; yield monitored by NMR examination of solution.

points, decreasing in the order: 5 ( $n = 1$ , mp 165–167 °C) > 5 ( $n = 2$ ) > 5 ( $n = 3$ ).

Cyclization of Isodrin (3,  $n = 1$ ) to the cage molecule 4 ( $n = 1$ ) has also been accomplished by treatment with sulfuric acid and refluxing acetic acid,<sup>5</sup> hydrogen bromide,<sup>4,6</sup> or bromine.<sup>4,6</sup> Our preliminary studies showed that treatment of the homologue 3 ( $n = 2$ ) with sulfuric acid in acetic acid gave a complex mixture, but treatment with hydrobromic acid gave a high yield of the cage molecule 4 ( $n = 2$ ).<sup>19</sup> This is probably a radical reaction involving atomic bromine, because it is inhibited by hydroquinone, and because hydrochloric and hydriodic acids under similar conditions were completely ineffective.<sup>20</sup> Furthermore, NMR studies showed that bromine in carbon tetrachloride in the presence of diffused light was also effective in inducing the conversion of all three compounds 3 ( $n = 1-3$ ) to their cage isomers 4 ( $n = 1-3$ ), bromine atoms again presumably being the effective agent, since the reaction did not take place in the dark.<sup>21</sup> The products were not isolated from these experiments, but the NMR spectra indicated that the cage molecules 4 ( $n = 1-3$ ) make up about 99% of the product from 3 ( $n = 1$  and 2) and about 40% of the product from 3 ( $n = 3$ ).

In a study of the relative reactivities of 3 ( $n = 1-3$ ), a 20:1 mol ratio of diene to bromine was illuminated with a neon lamp under standard conditions. The relative rates of formation of 4 ( $n = 1-3$ ), monitored by NMR, were as follows:  $n = 1$  (complete in less than 30 min) >  $n = 2$  (50% complete in 30 min) >  $n = 3$  (1% complete after 240 min, 40% complete after 120 h). Again, the NMR spectra showed the cage compounds 4 ( $n = 1$  and 2) as virtually the only products from 3 ( $n = 1$  and 2). The diene 3 ( $n = 3$ ) yielded three other compounds (as revealed by thin-layer chromatography) in addition to 4 ( $n = 3$ ). One of these compounds was isolated by chromatography, and turned out to be the ketone 7 ( $n = 3$ ). Various routes from 3 ( $n = 3$ ) to 7 ( $n = 3$ ) can be envisaged, depending on oxidation by molecular oxygen or hypobromous acid (from bromine and adventitious water), but further experimental data are required to distinguish between them.

The relative reactivities of the dienes 3 ( $n = 1-3$ ) to photocyclization in acetone were less clearly differentiated, being  $n = 1 \approx n = 2$  (about 90% cage 4 isolated after 60–70 min of irradiation under standard conditions) >  $n = 3$  (57% of 4 ( $n = 3$ ) isolated after 300 min).

**Formation and Reactions of Epoxides 6 ( $n = 1-3$ ).** Treatment of the epoxide 6 ( $n = 1$ ) (the insecticide Endrin) with boron trifluoride<sup>3b</sup> or hydrochloric acid<sup>4</sup> produced the "half-cage" ketone 7 ( $n = 1$ ). It became of interest to investigate this reaction with the homologous epoxides 6 ( $n = 1-3$ ).

These epoxides were obtained by oxidation of dienes 3 ( $n = 1-3$ ) with *m*-chloroperbenzoic acid at 23 °C. The

reaction required many hours, as shown in Table I; by contrast, cyclohexene, cyclohexadiene, norbornene, and norbornadiene under the same conditions were shown by NMR to be epoxidized in less than 5 min. The three epoxides 6 ( $n = 1-3$ ) were treated for 24 h with a refluxing mixture of *n*-butyl ether and concentrated hydrochloric acid. The epoxides 6 ( $n = 1$  and 2) furnished the homologous half-cage ketones 7 ( $n = 1$  and 2) in 78% and 73% yield, respectively. By contrast, epoxide 6 ( $n = 3$ ) was very sluggish, the normal ketone 8 being isolated in 5% yield and none of the transannular product 7 ( $n = 3$ ); most of the starting material was recovered unchanged. The transannular compound 7 ( $n = 3$ ) could, however, be obtained in 44% yield by treatment of epoxide 6 ( $n = 3$ ) with boron trifluoride etherate in refluxing carbon tetrachloride. The transannular products 7 ( $n = 1-3$ ) are easily distinguished from normal rearrangement products such as 8 by the absence of an IR band at about 1600  $\text{cm}^{-1}$ , characteristic of the  $\text{ClC}=\text{CCl}$  group.<sup>3-6</sup>

On being heated in a sealed test tube to 200 °C for 2 h, 6 ( $n = 1$ ) gave only 7 ( $n = 1$ ), but 6 ( $n = 3$ ) gave mostly starting material, with small amounts of 7 ( $n = 3$ ) and 8 (in a mol ratio of 8:1:1 by NMR).

The results above indicate that the ease of the transannular reaction 6 → 7 decreases in the order:  $n = 1 > n = 2 \gg n = 3$ .

#### Homoenolization of Half-Cage Ketones 7 ( $n = 1-3$ ).

The half-cage ketone 7 ( $n = 1$ ) is known to homoenolize under basic conditions to alcohol 9 ( $n = 1$ ).<sup>4,9</sup> We have followed the homoenolization of the homologous ketones 7 ( $n = 1-3$ ) in refluxing pyridine-*d*<sub>5</sub> by NMR. Formation of the bird-cage alcohol 9 ( $n = 1$ ) from 7 ( $n = 1$ ) was completed within 1 day. Under the same conditions, only 40–45% of homo bird-cage alcohol 9 ( $n = 2$ ) from 7 ( $n = 2$ ) was detected, complete reaction requiring 5 days. None of the bishomo bird-cage alcohol 9 ( $n = 3$ ) was detected after 5 days or more.

The ease of reaction 7 → 9 evidently decreases in the order:  $n = 1 > n = 2 \gg n = 3$ .

#### Discussion

The results above indicate that the ease of formation of both cage (4, 9) and half-cage compounds (7) decreases with the increase of  $n$  from 1 to 3, although the reactions follow a variety of mechanisms (ionic, radical, photochemical).

A possible explanation comes from a consideration of the variation with  $n$  of  $\Delta_{\text{strain}}$ , the increase in strain in going from reactant to product. Osawa et al.<sup>22</sup> calculated  $\Delta_{\text{strain}}$  by the methods of molecular mechanics for a number of photosensitized [ $2_{\pi} + 2_{\pi}$ ] cycloaddition reactions of dienes to give cage cyclobutanes and showed that yields become negligible when  $\Delta_{\text{strain}}$  exceeds about 70  $\text{kcal}\cdot\text{mol}^{-1}$ . There would seem to be no reason why  $\Delta_{\text{strain}}$  should not affect the ease of ground-state as well as photochemical reactions. We can estimate the change in  $\Delta_{\text{strain}}$  with  $n$  by measurements on Dreiding models along with considerations of nonbonded interactions.<sup>23,24</sup> Strain in a molecule causes bond angles, torsional angles, and distances between nonbonded atoms to depart from their ideal values; it also causes slight stretching or compression of bond lengths, but these changes are very small. Consequently, Hendrickson<sup>25</sup> in his calculations of the energies of molecules

(19) NMR studies showed that hydrobromic acid also gave a good yield of 4 ( $n = 3$ ), but the product was not isolated.

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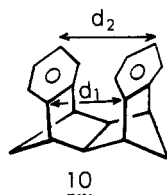
(24) Bondi, A. J. *Phys. Chem.* 1964, 68, 441.

(25) Hendrickson, J. B. *J. Am. Chem. Soc.* 1964, 86, 4854.

chose to keep bond lengths constant and to vary bond angles, torsional angles, and distances between nonbonded atoms in order to discover the geometry of minimum energy. We assume that the conformation of a molecule shown by Dreiding or Fieser models (fixed bond lengths) is that in which Baeyer strain due to distortion of bond angles is minimized. Measurements on Dreiding models show the distance  $d$  between the double bonds of **3** to vary with  $n$  as follows:

$n$	1	2	3
$d$ , Å	1.98	2.23	2.58

Dreiding models take no account either of torsional strain, which, however, is not likely to contribute much to  $\Delta_{\text{strain}}$  for **3**  $\rightarrow$  **4** and which we shall ignore, or of nonbonded repulsions. These latter will be important. The van der Waals radius (1.8 Å) for trigonal carbon<sup>24</sup> indicates that when  $d$  becomes less than 3.6 Å, the compressive energy due to nonbonded repulsive forces rises steeply. Consequently  $d$  must be greater than the values given above by Dreiding models; the final shapes of the molecules **3** ( $n = 1-3$ ) will represent the best compromise between decreasing compressive energy and increasing Baeyer strain as  $d$  is increased. The molecular-mechanics calculations of Osawa et al.<sup>22</sup> indicate  $d = 2.94$  Å for the parent diene (lacking the six chlorine atoms) of **3** ( $n = 1$ ), and X-ray crystallographic studies of Prinzbach et al.<sup>16</sup> show  $d_1 = 3.04$  Å and  $d_2 = 3.82$  Å in the dibenzo derivative **10** of this



parent diene. Consequently, we may expect  $d \approx 3.0$  Å in **3** ( $n = 1$ ) and a very slightly larger value in **3** ( $n = 2$  and  $3$ ). Thus, the increase in  $d$  from the values indicated by the Dreiding models, and hence the increase in total strain of **3** ( $n = 1-3$ ), will be in the order:  $n = 3 < n = 2 < n = 1$ .

The strain in the products **4** ( $n = 1-3$ ) will follow the opposite order ( $n = 1 < n = 2 < n = 3$ ), since now the formerly separate olefinic carbon atoms have been joined by C-C bonds about 1.54 Å long. This requires increasing distortion from the shapes indicated by the Dreiding models as  $n$  increases from 1 to 3.

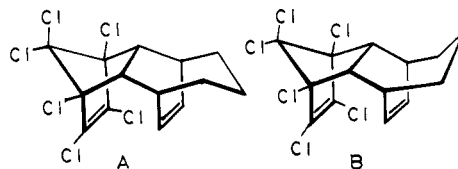
These considerations indicate that  $\Delta_{\text{strain}}$  for the reaction **3**  $\rightarrow$  **4** increases in the order  $n = 1 < n = 2 < n = 3$ , which is the order of increasing difficulty found experimentally. The conversions of **3**  $\rightarrow$  **4** by bromine or hydrogen bromide are both presumably ground-state processes involving bromine atoms. These induce equilibration between **3** and **4** which is thermodynamically controlled. The acetone-sensitized photoreaction, on the other hand, is more likely to be controlled by factors which affect the decay of the initially formed triplet of **3** to the ground-state surface connecting **3** and **4**.<sup>26</sup> The treatment of Dougherty<sup>27</sup> predicts that the photochemical reaction occurs more easily when its thermal counterpart is more difficult. However, our present results indicate about the same order of reactivities in photochemical and free-radical reactions, although the differences are much diminished in the photochemical reactions.

Our results closely parallel those of Miller and co-workers,<sup>28</sup> who report the ease of photocyclization of other dienes to cage compounds.

Similar considerations of  $\Delta_{\text{strain}}$  would explain the differing ease of formation of the half-cage ketones **7** from the epoxides **6** and of the cage alcohols **9** from the half-cage ketones **7**. In Dreiding models the distance in **7** between the carbonyl carbon and the atom to which it becomes linked in **9** increases from 2.23 to 2.33 to 2.38 Å as  $n$  increases from 1 to 3.

In oxidation of the dienes **3** ( $n = 1-3$ ) to the epoxides **6** ( $n = 1-3$ ), the hydrogen atoms attached to  $sp^2$  carbon atoms in **3** are pushed toward transannular chlorine atoms as these carbon atoms become  $sp^3$  hybridized in **6**. This must result in  $\Delta_{\text{strain}}$  increasing in the order  $n = 3 < n = 2 < n = 1$ .<sup>29</sup> In fact, as shown in Table I, the order of reactivities is the reverse of that predicted on this basis.

It seems likely that in the other reactions discussed above the steric demands of the reagent (bromine atoms, acid, base) are of minor importance but that this is not true of the more bulky *m*-chloroperbenzoic acid. The greater hindrance offered by the ethylene bridge of **3** ( $n = 2$ ), as compared with the methylene bridge of **3** ( $n = 1$ ), to the approach of the peracid to the double bond accords with the observations of Brown et al.<sup>30</sup> The still greater hindrance of the trimethylene bridge would be expected if **3** ( $n = 3$ ) has conformation A and not B.<sup>31</sup> This seems likely



on the basis of minimizing nonbonded interactions. The generally sluggish epoxidation of all the dienes **3** ( $n = 1-3$ ) is probably due to the field effect of the six chlorine atoms, since this reaction is known to be sensitive to substituent effects of this type ( $\rho = -1.2$  for epoxidation of substituted stilbenes<sup>32</sup>).

The dienes **3** ( $n = 1-3$ ) are now readily available, and studies of their reactivities with other reagents (cf. ref 30) would be interesting in attempting to disentangle the relative importance of steric and transannular effects.

### Experimental Section

Melting points were taken in capillary tubes using a Gallenkamp melting-point apparatus and are uncorrected. NMR spectra were recorded on a Varian T-60A spectrometer in  $CDCl_3$  containing tetramethylsilane as internal standard. IR spectra were recorded on a Perkin-Elmer 297 spectrophotometer. Mass spectra were recorded at 70 eV on an LKB 9000 or a Hewlett-Packard mass spectrometer. <sup>13</sup>C NMR spectra were recorded on a Bruker 90 spectrometer. Irradiations were carried out under a nitrogen atmosphere with a Hanovia medium-pressure mercury-vapor lamp contained in a water-cooled quartz immersion well. Petroleum ether refers to the fraction with bp 30–60 °C. *tert*-Butyl alcohol was used without purification (Fisher spectrograde). Tetrahydrofuran was redistilled and dried over 4-Å molecular sieve.

**5,6,7,8,9,9-Hexachloro-1,4,4a,5,8,8a-hexahydro-endo,endo-1,4-ethano-5,8-methanonaphthalene (3,  $n = 2$ ).** A mixture of hexachloronorborene (1; 36 g, 0.12 mol), 1,3-cyclohexadiene (20 g, 0.25 mol), and hydroquinone (0.1 g) in a pressure bottle

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(31) Models indicate that A and B are not, like chair and boat cyclohexanes or the *cis*-decalin conformations, easily interconvertible.

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(27) Dougherty, R. C. *J. Am. Chem. Soc.* **1971**, *93*, 7187.

was heated at 120–135 °C for 39 h. Excess 1,3-cyclohexadiene was removed by distillation, and the yellow oily residue was crystallized from ethyl ether as colorless needles (39.6 g, 87%), mp 183–185.5 °C, raised by recrystallization to mp 188–189 °C; NMR  $\delta$  6.07 (m, 2 H, olefinic protons), 2.87 (s, 2 H), 2.80 (br s, 2 H,  $W_{1/2}$  = 8 Hz, partially overlapped with s at 2.87), 1.44 (m, 4 H); IR (KBr) 3050 (m), 1608 (s)  $\text{cm}^{-1}$ ; mass  $m/e$  376, 378, 380, 382 (molecular ion, with an intensity profile characteristic of the  $\text{Cl}_6$  multiplet),<sup>33</sup> 278 (3), 276 (7), 274 (8), 272 (4), 269 (8), 267 (25), 265 (38), 263 (24), 79 (100).

Anal. Calcd for  $\text{C}_{13}\text{H}_{10}\text{Cl}_6$ : C, 41.20; H, 2.66; Cl, 56.14. Found: C, 41.26; H, 3.12; Cl, 55.90.

**5,6,7,8,9,9-Hexachloro-1,4,4a,5,8,8a-hexahydro-endo,endo-1,4-propano-5,8-methanonaphthalene (3,  $n = 3$ ).** A mixture of hexachloronorborene (3.0 g, 10 mmol), 1,3-cycloheptadiene (9.4 g, 100 mmol), and hydroquinone (0.1 g) was heated at 175 °C for 72 h in a pressure bottle. Excess 1,3-cycloheptadiene was removed by distillation and the dark residue was dissolved in chloroform and percolated quickly through a column of neutral alumina (100 g) with petroleum ether as eluant. The oily brown residue from concentration of the eluate was chromatographed again on neutral alumina (100 g). Elution with petroleum ether gave a colorless oil which crystallized on standing overnight in the refrigerator as colorless plates (2.21 g, 56%): mp 103–104 °C; NMR  $\delta$  5.92 (m, 2 H, olefin), 3.2 (s, 2 H), 2.5–2.8 (unresolved m, 2 H), 1.5–1.9 (unresolved m, 6 H, methylene protons); IR (KBr) 3040 (m), 1608 (s)  $\text{cm}^{-1}$ ; mass spectrum,  $m/e$  390, 392, 394, 396 (molecular ion, with an intensity profile characteristic of the  $\text{Cl}_6$  multiplet),<sup>33</sup> 120 (8), 119 (11), 108 (9), 107 (100), 91 (37).

Anal. Calcd for  $\text{C}_{14}\text{H}_{12}\text{Cl}_6$ : C, 42.79; H, 3.08; Cl, 54.13. Found: C, 42.93; H, 3.21; Cl, 54.02.

**1,8,9,12,13,13-Hexachlorohexacyclo[6.4.1.0<sup>2,7</sup>.0<sup>3,11</sup>.0<sup>6,10</sup>.0<sup>9,12</sup>]-tridecane (4,  $n = 2$ ).** (a) **By UV Irradiation.** Homoisodrin (3,  $n = 2$ ) (7.0 g, 18.5 mmol) in acetone (300 mL) was irradiated for 1 h. Evaporation of acetone solution in vacuo gave a colorless solid (6.4 g, 91%), mp 172–174 °C. An analytical sample was obtained by recrystallization from ethyl ether: mp 181–182.5 °C; NMR  $\delta$  2.94 (t, 4 H), 2.60 (br s,  $W_{1/2}$  = 9 Hz, 2 H), 1.68 (m, 4 H); IR (KBr) no absorption in olefinic region; mass spectrum,  $m/e$  376, 378, 380, 382 (molecular ion, with an intensity profile characteristic of the  $\text{Cl}_6$  multiplet),<sup>33</sup> 347 (22), 345 (66), 343 (100), 341 (63), 307 (22).

Anal. Calcd for  $\text{C}_{13}\text{H}_{10}\text{Cl}_6$ : C, 41.20; H, 2.66; Cl, 56.14. Found: C, 41.47; H, 2.88; Cl, 55.79.

In a separate experiment, it was shown (NMR) that no detectable reversion of product to starting material took place under the conditions of this reaction.

(b) **By Treatment of 3 ( $n = 2$ ) with Hydrobromic Acid.** A mixture of homoisodrin (3,  $n = 2$ ) (0.379 g, 1.0 mmol), 48% hydrobromic acid (1.2 mL), and butyl ether (1.8 mL) was refluxed for 3 h. The solution was diluted with water (20 mL) and extracted with ethyl ether (3  $\times$  50 mL). The ether extract was washed successively with water, bicarbonate solution, and water and dried ( $\text{Na}_2\text{SO}_4$ ). Evaporation of solvent gave 0.330 g of 4 ( $n = 2$ ) (87%), mp 181–182 °C, identical with the material obtained above. When the reaction was repeated with the addition of hydroquinone (1.0 g), only starting material was recovered. The same was true when concentrated hydrochloric acid (1.2 mL) or 57% hydriodic acid (1.2 mL) was used in place of hydrobromic acid.

(c) **By Treatment of 3 ( $n = 2$ ) with Bromine.** One drop of bromine was added to a solution of homoisodrin (3,  $n = 2$ ) (0.379 g, 1.0 mmol) in carbon tetrachloride (10 mL) at room temperature. The solution was stirred at ambient temperature in daylight for 22 h, and the solvent was then removed. The crude residue crystallized from ethyl ether to give 0.33 g (87%) of 4 ( $n = 2$ ), mp 180–181 °C, identical (NMR, IR) with material obtained above.

**1, 9, 10, 13, 14, 14-Hexachlorohexacyclo[7.4.1.0<sup>2,8</sup>.0<sup>3,12</sup>.0<sup>7,11</sup>.0<sup>10,13</sup>]-tetradecane (4,  $n = 3$ ).** (a) **By UV Irradiation.** Bishomoisodrin (3,  $n = 3$ ) (2.0 g, 5.09 mmol) in acetone (300 mL) was irradiated for 5 h. The yellow solution was concentrated in vacuo and chromatographed on neutral alumina (50 g). Elution with petroleum ether (200 mL) gave recovered

3 ( $n = 3$ ) (0.20 g, 10%). Elution with petroleum ether–diethyl ether (4:1) gave the crude product 4 ( $n = 3$ ) (1.30 g, 65%), mp 139–141 °C. An analytical sample was obtained by recrystallization from ethyl ether–pentane as colorless needles: mp 146–147 °C; NMR  $\delta$  3.00 (unresolved m, 4 H), 2.6–2.9 (unresolved m, 2 H), 1.6–2.0 (m, 6 H, methylene protons); IR (KBr) no absorption in olefinic stretching region; mass spectrum,  $m/e$  390, 392, 394, 396 (molecular ion with an intensity profile characteristic of the  $\text{Cl}_6$  multiplet),<sup>33</sup> 355 (15), 319 (4), 247 (11), 149 (24), 107 (100).

Anal. Calcd for  $\text{C}_{14}\text{H}_{12}\text{Cl}_6$ : C, 42.75; H, 3.08; Cl, 54.13. Found: C, 42.67; H, 3.45; Cl, 53.82.

In a separate experiment, it was shown that no reversion of product to starting material took place under the conditions of this reaction.

(b) **By Treatment of 3 ( $n = 3$ ) with Bromine.** A Pyrex test tube containing bishomoisodrin (3,  $n = 3$ ) (0.50 g) and bromine (0.10 g) in 18 mL of carbon tetrachloride was irradiated with 16 low-pressure mercury lamps overnight. NMR examination of the crude product then showed complete disappearance of starting material. The product was separated by chromatography on neutral alumina (50 g), elution being with ether–petroleum ether (1:4) and 50-mL fractions being collected. Fractions 1 and 2 contained impure 4 ( $n = 3$ ) (0.20 g, mp 100–105 °C) identified by NMR. Fraction 3 contained a mixture. Fractions 4 and 5 contained a ketone (50 mg), identified by NMR, IR, and mass spectra as 7 ( $n = 3$ ). Fractions 7–9 contained an unknown ketone (IR 1735  $\text{cm}^{-1}$ ) (60 mg), which was not investigated further.

Irradiation of 3 ( $n = 3$ ) in carbon tetrachloride under the same conditions, but in the absence of bromine, gave only starting material.

**Hexacyclo[6.4.1.0<sup>2,7</sup>.0<sup>3,11</sup>.0<sup>6,10</sup>.0<sup>9,12</sup>]-tridecane (5,  $n = 2$ ).** To a solution of 4 ( $n = 2$ ) (3.8 g, 10 mmol) in dry THF (70 mL) was added *tert*-butyl alcohol (20 mL) and lithium wire (3.0 g) cut into pieces. The reaction mixture was refluxed under nitrogen. A vigorous reaction started after a few minutes and the solution was kept at reflux for 3 h; then a further 10 mL of *tert*-butyl alcohol and 1.5 g of lithium were added, and refluxing was continued for another 1 h. After the solution was cooled, excess lithium was removed by filtration and the solution was poured into ice–water (500 g). The product was extracted into ether (5  $\times$  100 mL) and after the ether extracts were washed with water was obtained by evaporation of the solvent as colorless solid, mp 50–58 °C. Sublimation at 80 °C (2 mm) gave waxy crystals (1.20 g, 70%): mp 90–91 °C; NMR  $\delta$  2.0–2.7 (unresolved m, 8 H, methine protons), 1.0–1.8 (unresolved m, 8 H, overlapping of 6 methylene with 2 methine protons); IR (KBr) 2930 (s), 2860 (s), 1450 (m), 1330 (m), 1293 (m), 942 (m), 840 (m), 750 (w)  $\text{cm}^{-1}$ ; mass spectrum,  $m/e$  172 (100, molecular ion), 171 (6), 157 (13), 144 (14), 129 (27), 117 (18), 105 (39), 92 (55), 91 (42), 79 (32), 78 (22), 77 (27).

Anal. Calcd for  $\text{C}_{13}\text{H}_{16}$ : C, 90.64; H, 9.36. Found: C, 90.19; H, 9.65.

**Hexacyclo[7.4.1.0<sup>2,8</sup>.0<sup>3,12</sup>.0<sup>7,11</sup>.0<sup>10,13</sup>]-tetradecane (5,  $n = 3$ ).** A solution of 4 ( $n = 3$ ) (0.80 g, 2 mmol) in dry THF (18 mL) was refluxed with *tert*-butyl alcohol (10 mL) and lithium wire (1.0 g) for 3 h and then with 10 mL more of *tert*-butyl alcohol and 1.0 g more of lithium for 1 h. Workup as above gave an amorphous solid which was sublimed at 130 °C (2 mm) to give colorless waxy crystals (0.22 g, 60%), mp 44–46 °C. A second sublimation raised the melting point: mp 63–64.5 °C; NMR  $\delta$  2.5 (br s,  $W_{1/2}$  = 5 Hz, 4 H), 2.2 (br s,  $W_{1/2}$  = 6 Hz, 4 H), 1.0–2.0 (unresolved m, 10 H, 8 methylene and 2 methine protons); IR (KBr) 2960 (s), 2940 (br s), 2860 (s), 1453 (s), 1444 (s), 1364 (m), 1340 (m), 950 (m), 916 (m), 828 (m), 750 (w)  $\text{cm}^{-1}$ ; mass spectrum,  $m/e$  186 (53, molecular ion), 171 (7), 158 (17), 157 (17), 143 (12), 145 (7), 129 (22), 119 (30), 106 (86), 105 (22), 92 (55), 91 (100), 79 (40).

Anal. Calcd for  $\text{C}_{14}\text{H}_{18}$ : C, 90.24; H, 10.09. Found: C, 90.26; H, 9.74.

**1,2,3,4,11,11-Hexachloro-6,7-epoxy-1,4,4a,5,6,7,8,8a-octa-hydro-endo,endo-1,4-ethano-5,8-methanonaphthalene (6,  $n = 2$ ).** A solution of homoisodrin (3,  $n = 2$ ) (7.6 g, 20 mmol) and *m*-chloroperbenzoic acid<sup>34</sup> (5.0 g, 25 mmol) in chloroform (70 mL) was stirred at room temperature for 2 days. The solution was diluted with 150 mL of chloroform and washed with dilute NaOH

(33) Beynon, J. H.; Saunders, R. A.; Williams, S. E. "The Mass Spectra of Organic Molecules"; Elsevier: Amsterdam, 1968; p 376.

(34) Aldrich technical grade, 85% purity.

solution and water and dried ( $\text{Na}_2\text{SO}_4$ ). Evaporation of solvent left 7.5 g of product (95%), mp 175–178 °C. An analytical sample was obtained as colorless plates by recrystallization from acetone: mp 207–208 °C; NMR  $\delta$  3.2 (m, 2 H), 2.90 (poorly resolved d, 2 H), 2.55 (unresolved m, 2 H), 1.2–2.2 (m, 4 H); mass spectrum,  $m/e$  392, 394, 396, 398 (molecular ion, with an intensity profile characteristic of the  $\text{Cl}_6$  multiplet),<sup>33</sup> 357 (11), 321 (11), 295 (23), 293 (21), 272 (21), 263 (36), 261 (27), 257 (22), 183 (29), 91 (51), 79 (100), 77 (35).

Anal. Calcd for  $\text{C}_{13}\text{H}_{10}\text{Cl}_6\text{O}$ : C, 39.51; H, 2.55. Found: C, 39.62; H, 2.32.

**1,2,3,4,12,12-Hexachloro-6,7-epoxy-1,4,4a,5,6,7,8,8a-octa-hydro-endo,endo-1,4-propano-5,8-methanonaphthalene (6,  $n = 3$ ).** A solution of bishomoisodrin (**3**,  $n = 3$ ) (3.93 g, 10 mmol) and *m*-chloroperbenzoic acid (2.5 g, 25 mmol) in chloroform (30 mL) was stirred at room temperature for 10 days. Workup as above gave 3.52 g (90%) of white solid: mp 130–132 °C; NMR  $\delta$  3.1–3.3 (m, 2 H), 2.80 (s, 2 H), 2.7 (m, 2 H, overlapped with s at 2.80), 1.2–1.8 (unresolved m, 6 H, methylene protons); mass spectrum,  $m/e$  406, 408, 410, 412 (molecular ion, with an intensity profile characteristic of the  $\text{Cl}_6$  multiplet),<sup>33</sup> 371 (16), 335 (17), 355 (51), 357 (34), 319 (20), 309 (19), 307 (17), 271 (24), 263 (28), 265 (25), 235 (29), 237 (36), 221 (21), 219 (26), 193 (24), 136 (21), 123 (22), 117 (43), 105 (42), 91 (59), 79 (100), 77 (46).

Anal. Calcd for  $\text{C}_{14}\text{H}_{12}\text{Cl}_6\text{O}$ : C, 41.09; H, 2.96. Found: C, 41.18; H, 2.81.

**1,8,9,10,11,11-Hexachloropentacyclo[6.2.1.1<sup>3,6</sup>.0<sup>2,7</sup>.0<sup>4,10</sup>]dodecan-5-one (7,  $n = 1$ ).** A mixture of endrin (**6**,  $n = 1$ ) (1.143 g, 3.0 mmol), concentrated hydrochloric acid (4.5 g), and butyl ether (4.5 mL) was heated to 130 °C with vigorous stirring for 24 h. A first crop of **7** ( $n = 1$ ) (0.4 g), mp 245 °C dec, was removed by filtration. The filtrate was diluted with chloroform (50 mL), washed with water, saturated sodium bicarbonate solution, and water, dried ( $\text{Na}_2\text{SO}_4$ ), and concentrated to give a second crop of **7** ( $n = 1$ ) (0.49 g, overall yield 78%). An analytical sample, mp 290–291 °C (lit.<sup>4</sup> mp 285 °C dec), was obtained by recrystallization from ether: IR (KBr) 1752  $\text{cm}^{-1}$ ; NMR  $\delta$  ( $\text{CDCl}_3$ ) 5.01 (s, 1 H, CHCl), 2.9–3.4 (complex m, 5 H, methine), 1.62, 1.85 (center of AB pattern  $J_{AB} \approx 12$  Hz); mass spectrum,  $m/e$  378, 382, 384, 386 (molecular ion, with an intensity profile characteristic of the  $\text{Cl}_6$  multiplet),<sup>33</sup> 343 (13), 345 (21), 347 (14), 349 (5), 315 (44), 317 (67), 319 (43), 321 (14), 281 (21), 250 (20), 209 (16), 147 (17), 113 (16), 79 (17), 67 (100).

**3,4,5,6,11,11-Hexachloropentacyclo[6.2.2.1<sup>3,6</sup>.0<sup>2,7</sup>.0<sup>4,10</sup>]tridecan-9-one (7,  $n = 2$ ).** A mixture of homoendrin (**6**,  $n = 2$ ) (1.185 g, 3.0 mmol), concentrated hydrochloric acid (4.5 g), and butyl ether (4.5 mL) was heated to 130 °C with vigorous stirring for 24 h. Workup as above gave 0.87 g (83%) of **7** ( $n = 2$ ), mp 170–172 °C. Recrystallization from ether raised the melting point: mp 174–175 °C; IR (KBr) 1735, 1720 ( $\text{s}$ )  $\text{cm}^{-1}$ ; NMR  $\delta$  ( $\text{CDCl}_3$ ) 4.67 (s, 1 H, CHCl), 2.6–3.3 (complex m, 5 H, methine protons), 1.6–2.4 (complex m, 4 H, methylene protons); mass spectrum,  $m/e$  392, 394, 396, 398, 400 (molecular ion, with an intensity profile characteristic of the  $\text{Cl}_6$  multiplet),<sup>33</sup> 357 (64), 359 (100), 361 (66), 363 (22), 321 (43), 323 (58), 325 (30), 327 (11), 329 (30), 331 (43), 333 (27), 295 (32), 293 (28), 259 (27), 257 (26), 152 (21), 149 (23), 93 (21), 91 (18), 87 (41), 80 (18), 79 (51).

Anal. Calcd for  $\text{C}_{13}\text{H}_{10}\text{Cl}_6\text{O}$ : C, 39.54; H, 2.56. Found: C, 39.71; H, 2.37.

**3,4,5,6,11,11-Hexachlorotetracyclo[6.3.2.1<sup>3,6</sup>.0<sup>2,7</sup>]tetradecan-9-one (8).** A mixture of bishomoendrin (**6**,  $n = 3$ ) (1.224 g, 3.0 mmol), concentrated hydrochloric acid (4.5 g), and butyl ether (4.5 mL) was heated at 130 °C with vigorous stirring for 24 h. The cooled solution was diluted with ice-water (50 g) and extracted

with ether; the ether solution was washed with water, bicarbonate, and water, dried ( $\text{Na}_2\text{SO}_4$ ), and concentrated. The residue was chromatographed on neutral alumina (50 g). Elution with petroleum ether gave 0.70 g of starting material. Elution with diethyl ether gave 70 mg (5%) of 3,4,5,6,11,11-hexachlorotetracyclo[6.3.2.1<sup>3,6</sup>.0<sup>2,7</sup>]tetradecan-9-one (**8**): mp 200–201 °C; IR (KBr) 1710 (s), 1600 (s)  $\text{cm}^{-1}$ ; NMR  $\delta$  ( $\text{CDCl}_3$ ) 3.16 (q, 2 H), 2.5–2.8 (m, 2 H), 2.33 (t, 2 H), 1.6–2.0 (unresolved m, 6 H, methylene protons); mass spectrum,  $m/e$  406, 408, 410, 412, 416 (molecular ion, with an intensity profile characteristic of the  $\text{Cl}_6$  multiplet),<sup>33</sup> 371 (6), 373 (9), 375 (6), 377 (2), 309 (11), 266 (14), 264 (21), 262 (13), 136 (15), 94 (100), 81 (74), 79 (60), 67 (24), 41 (45).

Anal. Calcd for  $\text{C}_{14}\text{H}_{12}\text{Cl}_6\text{O}$ : C, 41.09; H, 2.96. Found: C, 40.93; H, 2.97.

**3,4,5,6,11,11-Hexachloropentacyclo[6.3.2.1<sup>3,6</sup>.0<sup>2,7</sup>.0<sup>4,10</sup>]tetradecan-9-one (7,  $n = 3$ ).** A solution of **6** ( $n = 3$ ) (3.26 g, 7.9 mmol) in carbon tetrachloride (50 mL) and boron trifluoride etherate (2.0 mL) was heated under reflux for 5 h. The dark brown solution was decolorized by passage down a short column of neutral alumina (30 g) and concentrated. The residue, recrystallized from diethyl ether, gave **7** ( $n = 3$ ) as a white solid (1.43 g, 44%): mp 178–179 °C; IR (KBr) 1720  $\text{cm}^{-1}$ ; NMR  $\delta$  ( $\text{CDCl}_3$ ) 4.55 (s, 1 H, CHCl), 2.7–3.4 (complex m, 5 H, methine protons), 1.2–2.2 (complex m, 6 H, methylene protons); mass spectrum,  $m/e$  406, 408, 410, 412, 414 (molecular ions, with relative intensities in agreement with theory<sup>33</sup>), 371 (63), 373 (100), 375 (65), 377 (21), 335 (32), 337 (41), 309 (40), 307 (33), 271 (31), 273 (32).

Anal. Calcd for  $\text{C}_{14}\text{H}_{12}\text{Cl}_6\text{O}$ : C, 41.09; H, 2.96. Found: C, 41.14; H, 2.91.

**1,8,9,10,11,11-Hexachlorohexacyclo[6.2.1.1<sup>3,6</sup>.0<sup>2,7</sup>.0<sup>4,10</sup>.0<sup>6,9</sup>]dodecan-5-ol (9,  $n = 1$ ).** A solution of half-cage ketone **7** ( $n = 1$ ) (0.67 g) and pyridine (3 mL) was heated under reflux for 36 h. Pyridine was evaporated in vacuo and the crude product was crystallized from methanol–water to give 0.60 g (90%) of **9** ( $n = 1$ ): mp 320 °C dec (lit.<sup>4</sup> mp 330 °C dec); NMR 4.50 (s, OH), 2.8–3.3 (complex m, 5 H), 2.0 (q, 2 H, methylene protons).

**3,4,5,6,11,11-Hexachlorohexacyclo[6.2.2.1<sup>3,6</sup>.0<sup>2,7</sup>.0<sup>4,10</sup>.0<sup>6,9</sup>]tridecan-9-ol (9,  $n = 2$ ).** A solution of half-cage ketone **7** ( $n = 2$ ) (11.8 g, 30 mmol) in pyridine (50 mL) was heated to about 130 °C in a pressure bottle for 10 days. The pyridine was removed by evaporation, and the residue was chromatographed on a column of neutral alumina. Elution with methylene chloride removed successively starting material (0.80 g) and 3,4,5,6,11,11-hexachlorohexacyclo[6.2.2.1<sup>3,6</sup>.0<sup>2,7</sup>.0<sup>4,10</sup>.0<sup>6,9</sup>]tridecan-9-ol (**9**,  $n = 2$ ) (7.0 g, 55%): mp 152–154 °C; IR (KBr) 3550 (sh, s), 3400 (large, s)  $\text{cm}^{-1}$ ; NMR  $\delta$  ( $\text{CDCl}_3$ ) 4.00 (s, 1 H, OH), 2.90 (m, 2H), 2.80 (m, 2 H), 2.20 (unresolved m, 1 H), 1.75 (m, 4 H, methylene protons); mass spectrum,  $m/e$  392 (13), 394 (25), 396 (20), 398 (4), 400 (2, molecular ion, with an intensity profile characteristic of the  $\text{Cl}_6$  multiplet),<sup>33</sup> 357 (62), 358 (11), 359 (100), 360 (15), 361 (65), 362 (10), 363 (21), 365 (4), 207 (13), 209 (18), 211 (9), 213 (3), 94 (26).

Anal. Calcd for  $\text{C}_{13}\text{H}_{10}\text{Cl}_6\text{O}$ : C, 39.54; H, 2.56. Found: C, 39.51; H, 2.90.

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**Registry No.** 1, 3389-71-7; **2** ( $n = 2$ ), 592-57-4; **2** ( $n = 3$ ), 4054-38-0; **3** ( $n = 2$ ), 73454-21-4; **3** ( $n = 3$ ), 73454-22-5; **4** ( $n = 2$ ), 73454-23-6; **4** ( $n = 3$ ), 73454-24-7; **5** ( $n = 2$ ), 71871-52-8; **5** ( $n = 3$ ), 71871-53-9; **6** ( $n = 1$ ), 72-20-8; **6** ( $n = 2$ ), 73454-25-8; **6** ( $n = 3$ ), 73454-26-9; **7** ( $n = 1$ ), 53494-70-5; **7** ( $n = 2$ ), 73454-27-0; **7** ( $n = 3$ ), 73454-28-1; **8**, 73454-29-2; **9** ( $n = 1$ ), 33058-12-7; **9** ( $n = 2$ ), 73454-30-5.