Synthesis of Homopentaprismane and Homohypostrophene and Some Comments on the Mechanism of Metal Ion Catalyzed Rearrangements of Polycyclic Compounds[1]

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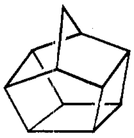
The synthesis of homohypostrophene (tetracyclo[6.3.0.0^{4,11}.0^{5,9}]undeca-2,6-diene) and homopentaprismane (hexacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}.0^{8,11}]undecane) is described. Proofs of structure based on ^{13}C nuclear magnetic resonance spectroscopy are given. The metal ion catalyzed reactions of homopentaprismane are considered. Certain aspects of the mechanism of the silver ion catalyzed rearrangements of polycyclic compounds are considered in some detail.

We have completed the synthesis and unambiguous proof of structure of homopentaprismane (**1**)[2a] and of its progenitor homohypostrophene (**2**).[2b] The skeleton of homopentaprismane has one more carbon–carbon bond (and one more ring) than that of the closely related and well-known pentacyclic diketone **3**.[3] However, direct closure of **3** or a relative to a homopentaprismane derivative, although tried in many laboratories, has not been achieved. Other reactions intervene. For example, attempted pinacol closure (eq 1) leads instead to quantitative reductive cleavage of the cyclobutane ring.[3,4] A previously reported synthesis of homopentaprismane,[2a] supposedly by a direct cyclization approach, is now known to be in error.[5]



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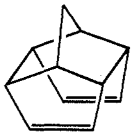

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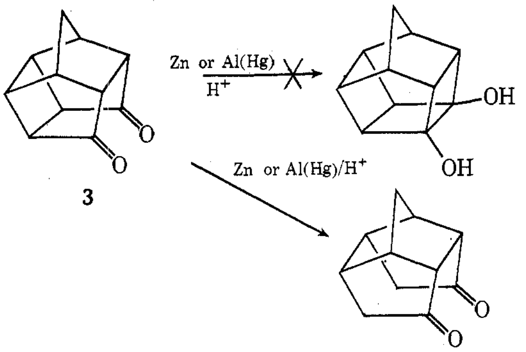


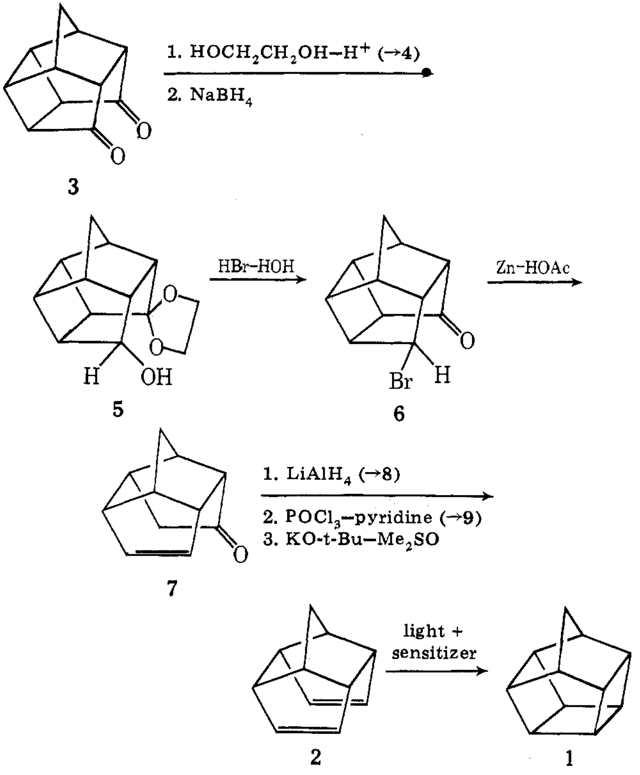
3

(1)

Synthesis. In our successful approach (Scheme I) we make use of the ready reductive cleavage of the cyclobutane ring in a derivative of **3** to establish a good, preparatively useful route to the tetracyclic diene homohypostrophene.[6] The diene is then closed to homopentaprismane by $2\pi + 2\pi$ intramolecular photocycloaddition.

Reaction of **3** with ethylene glycol and toluenesulfonic acid in boiling benzene gives the monoketal **4** in excellent yield. Bisketalization is not a problem. Reduction of **4** with sodium borohydride in ethanol and work-up in dilute hydrochloric acid produces the hydroxy ketal **5**, homogeneous by TLC and GLC after molecular distillation.[7,8] Treatment of **5** with 48% aqueous hydrobromic acid at 80 °C gives the bromo ketone **6** in 90% yield. Reductive cleavage of this bromo ketone with zinc metal powder in boiling acetic acid, the key step in the sequence, gives better than 90% yield of the enone **7**. We find no evidence for any substantial interaction between the chromophoric units in **7**: λ_{max} (cyclohexane) 299 nm (ϵ 17).

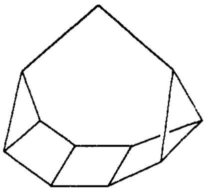
Scheme I



Lithium aluminum hydride reduction of the enone yields the corresponding enol **8**, which can be converted satisfactorily (70–80%) directly to the ene chloride **9** by reaction with phosphorus oxychloride in pyridine on the steam bath. Dehydrochlorination of crude enechloride to homohypostrophene occurs slowly, but effectively, upon reaction under nitrogen with potassium *tert*-butoxide in dimethyl sulfoxide on the steam bath. The pure diene (35% in two steps from the enol) can be isolated by extraction into pentane and separation from sulfurous contaminants by chromatography on alumina followed by careful bulb-to-bulb transfers under high vacuum. The gas-phase ultraviolet spectrum of homohypostrophene, λ_{max} 202 nm, indicates some interaction between the two pairs of sp^2 centers; the photoelectron spectrum will be of interest. Homohypostrophene rearranges slowly at room temperature, probably in Cope fashion, but we have not pursued this aspect of its chemistry. The diene is also somewhat sensitive to oxygen.

Ultraviolet irradiation of homohypostrophene in the presence of suitable sensitizers (xanthone or acetone) gives homopentaprismane. This reaction is not completely clean, but fortunately homopentaprismane is the only volatile product formed in significant quantity. Isolated yields (preparative GLC) of 50% have been obtained.

Proofs of Structure. From the synthesis and the proton NMR data a strong case can be made in the usual manner for assigning the structures homopentaprismane and homohypostrophene to our synthetic products. Much more interesting is the point that *unequivocal, de novo proofs of structure are available from consideration of their* ^{13}C *NMR spectra:* compound 1 (22.63 MHz, $CDCl_3$), δ 40.7 (1 CH_2, t, J = 131 Hz), 42.6 (4 CH, d, J = 149 Hz), 49.0 (4 CH, d, J = 146 Hz), and 51.2 ppm (2 CH, d, J = 140 Hz); compound **2**, δ 31.8 (1 CH_2, t, J = 130 Hz), 49.0 (4 CH, d, J = 143 Hz), 64.9 (2 CH, d, J = 147 Hz), and 137.1 ppm (4 CH, d, J = 164 Hz). Of the possible $C_{11}H_{12}$ structures, only homopentaprismane and its isomer **10** and homohypostrophene and its isomers **11–13** have the correct hydrogen distribution and sufficient symmetry to give rise to the observed ^{13}C spectral patterns. If structure **10, 11**, or **12** pertained, ^{13}C–H coupling constants in excess of 160 Hz would arise from the cyclopropyl CH units (cf.[9] cuneane). All observed coupling constants for the saturated CH units in **1** and **2** are well below this figure. If structure **13** (or **12**) were applicable, the vinyl ^{13}C–H coupling constant would be 170 Hz or greater (cf.[10] cyclobutene). The observed coupling is significantly below this value. It is certain, therefore, that the assigned structures are correct.



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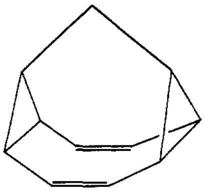

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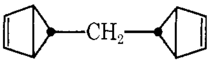
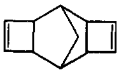
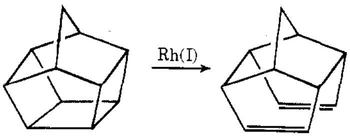


(syn, syn or anti, anti)
12



(bis-endo or bis-exo)
13

Metal Ion Catalyzed Rearrangements. Homopentaprismane is cleaved cleanly to homohypostrophene by rhodium(I) complexes, e.g., $[Rh(norbornadiene)Cl]_2$, acting catalytically (eq 2).[11] The reaction is analogous to that observed for cubane (eq 3), but the rate of reaction of cubane is orders of magnitude greater.[12] It seems clear, intuitively, that the release of strain on opening the cubane system would be greater than on cleaving homopentaprismane. The origin of the difference in rate of reaction may well be here and/or in the different p character of the carbon bonds. $J_{^{13}C-H}$ in cubane is 160 Hz,[13] whereas in homopentaprismane it is only 149 Hz at the relevant carbon atoms; it follows[14] that the p character of the carbon–carbon bonds is greater in cubane than in homopentaprismane. This should increase the ease of oxidative addition to the metal ion and the susceptibility to subsequent rearrangement.



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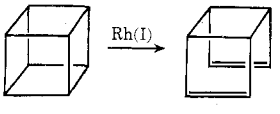
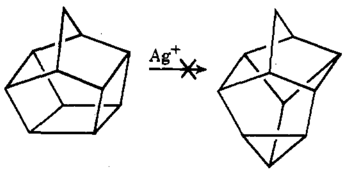


(3)

Silver salts do not rearrange homopentaprismane (eq 4),[15] even under conditions very much more drastic than



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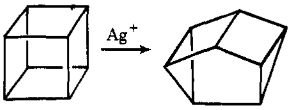


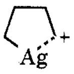
(5)

those required to rearrange cubane (eq 5),[9] or its less reactive relatives.[16] We believe that this observation bears importantly on the mechanism of silver ion catalyzed rearrangements of polycyclic systems.

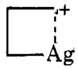
The Chicago school originally proposed,[17] and still favors, a nonconcerted, carbonium ion rearrangement to account for the known silver ion catalyzed rearrangements of relevant systems. The proposed course of these reactions is outlined in simplified form in Chart I for various cubane systems and *syn*-tricyclo[4.2.0.0^{2,5}]octane (I–V).[9,16] For comparison, the hypothetical course of the conversion (unobserved) of homopentaprismane (VIa) to the less strained undecane VId is included. The first and the last steps in the rearrangements are common to each case. At the beginning (a → b), silver is introduced, and the central bond of a bicyclo[2.2.0]hexane subunit is broken. At the end (c → d), silver is extruded, and a cyclopropane ring is closed. In the first four cases, all of which proceed easily, the second step (b → c), in which a bond migrates, is accompanied by the formation of a cyclopropane ring at the expense of two cyclobutane rings—downhill by about 21 kcal/mol. (Note: for simplicity only the strain energies of the small rings are taken into account in these rough calculations.) In the fifth case, the conversion of *syn*-tricyclooctane to tetrahydrosemibullvalene, which also occurs readily, the bond migration in the second step is accompanied by the loss of one cyclobutane ring—downhill by about 24 kcal/mol. Only in the last case, the one that does not occur, is there no net loss of a strained ring in the bond migration step. Without this driving force, the reaction does not go.

We conclude from this simple exercise in bookkeeping that it is altogether likely that the rate-determining step in these silver ion catalyzed rearrangements is the bond migration (b → c). It follows that the first step, the cleavage by the metal, must be reversible. In the case of 4-methylhomocubane the silver-catalyzed rearrangement is known to be preceded by the reversible formation of a "complex" between the homocubane and the metal ion.[16e] We speculate reservedly that this complex may be the ion that subsequently rearranges. We shall examine related cases in the future in detail.

Why should the bond migration step be rate determining? We suggest that there is a significant stabilizing interaction between silver and the carbonium ion in the intermediates Ib–VIb, namely[18]

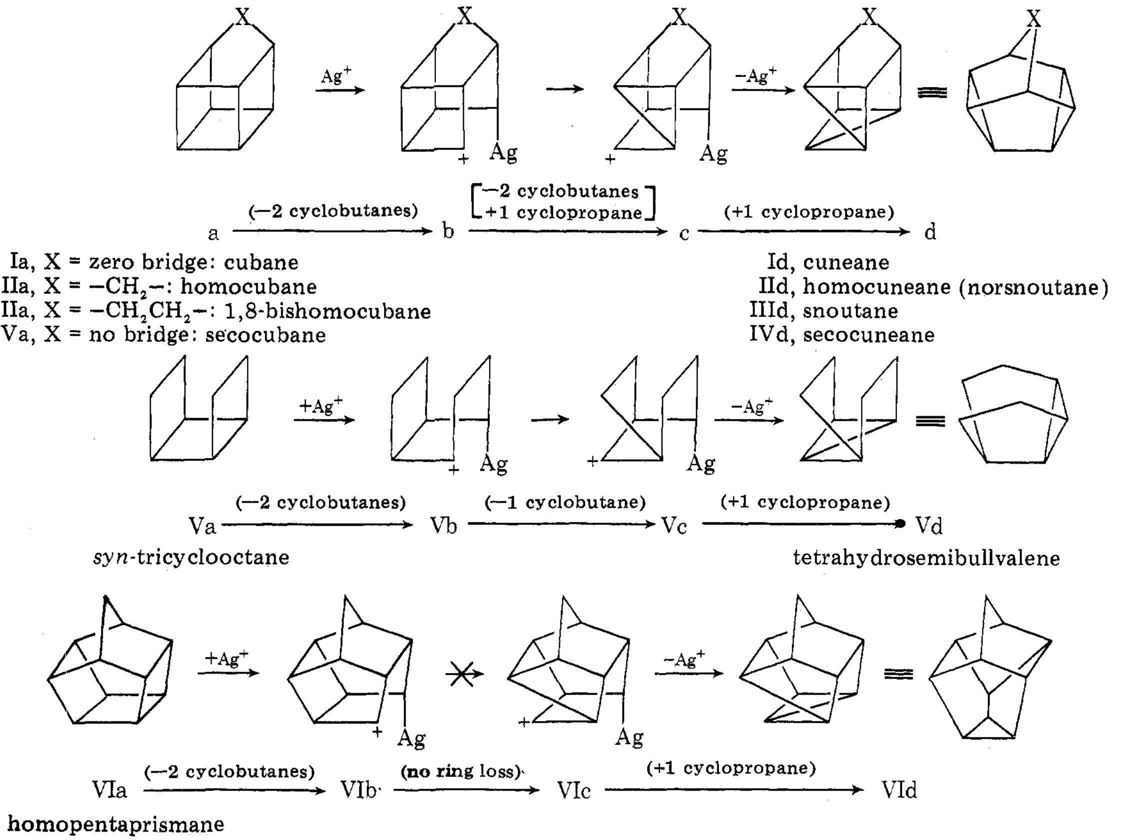


In the rearranged intermediates Ic–VIc this stabilization would be less efficient, for the geometric arrangement



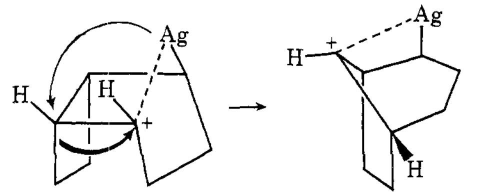
is distinctly less favorable. The decrease of stabilization energy would, *of course, appear (in part) as an increase in the* activation barrier to rearrangement. (Note also that rear-

Chart I



rangement from one silver stabilized ion to the other requires inversion of configuration at the origin and terminus of the migrating bond.) Without a significant difference in the degree of silver interaction with the carbonium ion, VIb and VIc appear approximately isoenergetic (in less stilted drawings), and the origin of an important barrier between them becomes obscure. Similarly, the interaction between silver and the carbonium ion in VIb can account for the lack of rearrangement of this ion into the (D_3)-trishomocubyl series—a rearrangement known to occur easily from this system in the absence of a silver substituent.[19]

Although *syn*-tricyclooctane (Va) is rearranged readily by silver ion, the anti isomer is not. Contrary to some opinions,[16f] this observation is not only not troublesome, but helps confirm our mechanistic interpretation. The bond shift in the rate-determining step of these rearrangements occurs to the back side of the silver bridged ion—inversion at the site is required to account for cubane → cuneane type transformations. This geometric requirement is easily accommodated in the syn series (eq 6), but is not practicable in the anti compound, as inspection of a model will show (eq 7).



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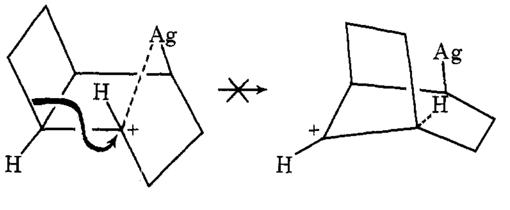
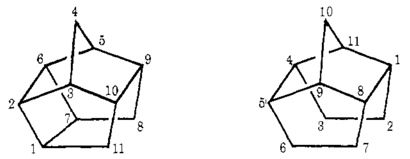


(7)

Experimental Section

The position numbering systems used in the formal naming are illustrated.



Proton magnetic resonance spectra were taken at 270 MHz on solutions in deuteriochloroform and are referenced to internal Me_4Si. Most spectra were recorded for convenience on compressed scale (3 Hz/mm); therefore, quoted shifts are ±0.02 ppm and coupling constants are ±1 Hz, sufficient accuracy for the present purposes. Only interpretations relevant to the stereochemical assignments are given. Further interpretations are either obvious or moot. Infrared spectra were taken on solutions in chloroform unless otherwise noted; positions of interesting absorptions are quoted ±5 cm^{-1}. The high-resolution mass spectrum of each new compound was recorded on an MS-9 spectrometer operating at 50 eV ionization voltage. Each compound exhibited a proper parent peak at *m/e* within 30 ppm of the expected value.

Pentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane-8-11-dione Monoethylene Ketal (4). A mixture of diketone 3[3] (10.0 g, 57.5 mmol), ethylene glycol (3.57 g, 57.6 mmol), *p*-toluenesulfonic acid (125 mg), and 50 ml of benzene was refluxed with good stirring for 5 h. The reaction mixture was then cooled and poured slowly into 50 ml of ice-cold 10% aqueous sodium carbonate. Work-up with methylene chloride and crystallization from ether–hexane afforded 11.07 g (87%) of the desired monoketal: mp 73.0–73.5 °C; ir ν 1750 cm^{-1}; ^{1}H NMR δ 3.91 (4 H, m), 3.0–2.5 (8 H, multiplet sets), 1.88, 1.58 ppm (1 H each, doublet pair, $J \sim 10$ Hz).

***exo*-11-Bromopentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecan-8-one (6).** The monoketal 4 (2.20 g) was dissolved in 25 ml of warm absolute ethanol. The solution was cooled in an ice bath. A freshly prepared, cold solution of sodium borohydride (0.76 g) in 17 ml of water was added with stirring over 6 min. The reaction mixture was left for 2 h in the ice bath and then removed to room temperature for 2 more h. The mixture was put back into the ice bath and 10 ml of 3% hydrochloric acid was added drop by drop. After a standard work-up with methylene chloride, 2.21 g of crude hydroxy ketal 5 was obtained. Molecular distillation at 139 °C (0.25

Torr) gave a clear, homogeneous oil:[7] ^{1}H NMR δ 4.62 [1 H, t, $J \sim 5$ Hz, HC(1)-**H(exo)**C(11)-HC(10)], 3.71, 3.79 (2 H each, m), 3.4 (1 H, bs, OH), 2.9–2.4 (8 H, multiplets), 1.56, 1.91 ppm (1 H each, doublet pair, $J \sim 10$ Hz).

The crude hydroxy ketal was usually taken on without distillation directly to the bromo ketone **6** by stirring it in a large excess of 48% hydrobromic acid at 80° for 3 h. The acid solution was then cooled to room temperature and quenched in iced water. The crystalline precipitate was collected, washed with water, and recrystallized from a small volume of methanol, giving, in various runs, about 90% yield overall of pure **6:** mp 84.5–85.3 °C; ir ν 1760 cm^{-1}; ^{1}H NMR δ 4.28 [1 H, bs, **H(endo)**C(11)Br], 3.29 (1 H, m), 3.15 (2 H, m), 2.98 (1 H, m), 2.79 (2 H, m), 2.61 (1 H, m), 2.40 (1 H, m), 1.67, 1.92 ppm (1 H each, doublet pair, $J \sim 11$ Hz).

Tetracyclo[6.3.0.0^{4,11}.0^{5,9}]undec-2-en-6-one (7). The bromo ketone **6** (17 g) was dissolved in 200 ml of glacial acetic acid. The solution was stirred mechanically (good stirring is essential); zinc powder (27 g) was added. The mixture was refluxed with stirring for 8 h, cooled, and filtered. The filter cake was washed carefully with ether. The filtrate and ether washings together were mixed with water. Standard work-up of the ether layer including washes with aqueous sodium bicarbonate to remove acetic acid gave 10.5 g (92%) of crystalline ene ketone **7** as shiny plates. A pure sample was obtained by crystallization from pentane: mp 192–193 °C; ir (CCl$_4$) ν 2970, 1745 cm^{-1}; ^{1}H NMR δ 6.05, 5.94 (1 H each, both d of d, $J \sim 6$ and 3 Hz), 3.06 (1 H, m), 2.82 (2 H, m), 2.63 (1 H, m), 2.44 (2 H, m), 2.18 [1 H, d of d, $J \sim 19$ and 6 Hz, HC(8)-**H(exo)**HC(7)]; 2.01 [1 H, d, $J \sim 19$ Hz, **H(endo)**HC(7)], 1.83, 1.72 ppm (1 H, each, doublet pair, $J \sim 11$ Hz).

***endo*-Tetracyclo[6.3.0.0^{4,11}.0^{5,9}]undec-2-en-6-ol (8).** A solution of 5.6 g of the ene ketone **7** in 40 ml of anhydrous ether was added under nitrogen to a stirred mixture of 1.5 g of lithium aluminum hydride and 40 ml of ether cooled in an ice bath. The mixture was stirred for 3 h cold and then left overnight at room temperature. The excess reducing agent was destroyed with aqueous sodium hydroxide according to the standard procedure.[20] The precipitate was removed by filtration and washed with ether. The filtrate was washed with water, dried, and concentrated, leaving 5.5 g (97%) of white, crystalline enol **8** sufficiently pure to be taken on in the next step. A pure sample of **8** was prepared by recrystallization from pentane and sublimation: mp 215–216 °C (sealed tube); ir ν 3600, 2975, 1410 cm^{-1}; ^{1}H NMR δ 6.39 (1 H, bs, $W_{1/2} \sim 10$ Hz), 5.94 (1 H, $W_{1/2} \sim 10$ Hz), 4.47 [1 H, 5 lines overlapping d of t (?), spacing ~4 Hz, H$_2$C(7)-**H(exo)**C(6)-HC(5)], 7.9 (1 H, bs, OH), 2.7–2.1 (7 H, multiplets), 1.60 (2 H, bs), 1.53 ppm [1 H, d of d, $J \sim 15$ and 5 Hz, **H(endo)**HC(7)-H(exo)C(6)].

Tetracyclo[6.3.0.0^{4,11}.0^{5,9}]undeca-2,6-diene. Homohypostrophene (2). Phosphorus oxychloride (23 g) was added slowly with swirling to a solution of 4.86 g of the enol **8** in 40 ml of pyridine. The mixture was heated on the steam bath for 5 h. The dark brown solution was then cooled and poured into 200 ml of iced water. This mixture was extracted with pentane, and the extract was washed with 10% hydrochloric acid, 10% sodium bicarbonate solution, water, and saturated brine, in that order, and then dried carefully. The solvent was removed at atmospheric pressure through a 10-cm Vigreux column. The residue was the crude ene chloride **9:** ^{1}H NMR δ 6.09 (2 H, m, $W_{1/2} \sim 5$ Hz), 4.24 [1 H, clean d of d, $J \sim 7$ and 3 Hz, HC(5)-**H(endo)**C(6)-HC(7)], 2.99 (1 H, bs), 2.91 (1 H, bs), 2.54 (1 H, m), 2.43 (3 H, m), 2.89 [1 H, clean d of d, $J \sim 15$ and 7 Hz, HC(6)-**H(endo)**HC(7)], 2.03 [1 H, d + additional smaller couplings, $J \sim 15$ Hz, probably HC(6)-**H(exo)**HC(7)-HC(8)], 1.68, 1.60 ppm (1 H each, doublet pair, $J \sim 12$ Hz).

The ene chloride was used without further purification. It was taken up in 20 ml of dry dimethyl sulfoxide, and this was added with shaking to a solution of 5 g of alcohol-free potassium *tert*-butoxide in 80 ml of dimethyl sulfoxide. The mixture was heated under nitrogen on the steam bath for 8–10 h, then cooled and quenched in water. The product was extracted into purified pentane. The brown-yellow extract was decolorized and freed from sulfurous impurities by passing it through a 1 × 10 cm column of alumina. The clear, colorless eluate was concentrated on the steam bath beneath a 20-cm Vigreux column. Residual pentane was removed by transfer at 20 mm pressure from the sample at room temperature to a trap at −70 °C. The diene was purified by repeated sublimation at high vacuum, keeping the middle cut; the final product (1.6 g, 35% in two steps from enol **8**) had mp 139–140 °C (sealed tube); ir (acetone-d_6) ν 3060, 1590, 843, 730 cm^{-1}; ^{1}H NMR δ 5.86 (4 H, $W_{1/2} \sim 3$ Hz), 3.13 (2 H, $W_{1/2} \sim 3$ Hz), (2.31 (4 H, $W_{1/2} \sim 5$ Hz), 1.64 ppm (2 H, $W_{1/2} \sim 3$ Hz).

Hexacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}.0^{8,11}]undecane. Homopentaprismane (1). A solution of 500 mg of homohypostrophene in 2 ml of benzene containing 10 mg of xanthone was prepared in a standard 1-cm quartz cuvette. The solution was exposed to the focused beam from a 500-W Osram mercury arc filtered through 5 cm of water and a single Pyrex plate 3 mm thick. The photoreaction was followed by GLC on OV-225. Irradiation was continued until the diene concentration had been reduced by 95%. Homopentaprismane was isolated from the reaction mixture by preparative GLC on a 3 ft × 0.25 in. column of 15% OV-225 on 60/80 Gas-Chrom Q at 120 °C. The material was purified by repeated sublimation under high vacuum. The yield of pure material was 40–50% in various runs on this scale: mp 160–161 °C (sealed tube); ^{1}H NMR δ 3.02 (8 H, $W_{1/2} \sim 3$ Hz), 2.70 (2 H, $W_{1/2} \sim 8$ Hz), 1.76 ppm (2 H, $W_{1/2} < 3$ Hz).

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Registry No.—**1,** 25107-14-6; **2,** 30114-57-9; **3,** 2958-72-7; **4,** 58228-93-6; **5,** 58228-94-7; **6,** 58228-95-8; **7,** 58228-96-9; **8,** 58228-97-0; **9,** 58228-98-1; ethylene glycol, 107-21-1.

References and Notes

(1) The synthetic work in this paper was first reported by one of us in an invited lecture at the 155th National Meeting of the American Chemical Society, San Francisco, Calif., April 1968.

(2) For the origin of the trivial names see (a) G. R. Underwood and B. Ramamoorthy, *Chem. Commun.*, 12 (1970); (b) J. S. McKennis, L. Brener, J. S. Ward, and R. Pettit, *J. Am. Chem. Soc.*, **93,** 4957 (1971).

(3) E. Wenkert and J. E. Yoder, *J. Org. Chem.*, **35,** 2986 (1970).

(4) P. E. Eaton, R. A. Hudson, and C. Giordano, *J. Chem. Soc., Chem. Commun.*, 978 (1974).

(5) G. R. Underwood and B. Ramamoorthy, Erratum: *Chem. Commun.*, 600 (1971).

(6) Cf. G. R. Underwood and B. Ramamoorthy, *Tetrahedron Lett.*, 4125 (1970).

(7) Acid-catalyzed reorganization of the hydroxyl and ethylene ketal groups to HOCH$_2$CH$_2$O-C-O-C-H has been observed on occasion.

(8) Assignments of stereochemistry to this compound and the others reported here are based on simple mechanistic considerations strengthened by our analysis of the NMR spectra of these compounds (see Experimental Section).

(9) L. Cassar, P. E. Eaton, and J. Halpern, *J. Am. Chem. Soc.*, **92,** 6366 (1970).

(10) E. A. Hill and J. D. Roberts, *J. Am. Chem. Soc.*, **89,** 2047 (1967).

(11) In a typical run, a CDCl$_3$ solution 0.2 M in **1** and 0.06 M in catalyst was heated at 65 °C. The reaction was monitored by NMR and was complete in less than 3 h.

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corresponds to oxidative addition to silver(I) with formation of silver(III). As has been pointed out,[16d,f] this seems unfavorable energetically. We do not now propose [illegible] as an intermediate. The interaction we are concerned with here is much less extreme.

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