Ten-Membered Rings. Transannular Double-Bond Participation in Acid-Promoted Cyclizations[1,2]

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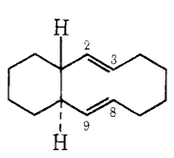
Acid-promoted cyclizations of **1**, **2**, and **3** are described. They occur with great facility in buffered acetic acid because protonation is accompanied by participation of a transannular double bond and there is consequent relief of medium-ring strain as the *trans,syn,trans*-perhydroanthracene system is generated. Two isomeric *trans,syn,trans*-perhydroanthracenes can be produced from **2** and **3**, the ratio of which depends upon the regioselectivity of protonation. The effects of the methyl substituent of **2** are a 1.5-fold increase in rate of cyclization relative to **1** and a 19:1 regioselectivity of protonation which favors generation of methyl-stabilized tertiary carbocation **9** over secondary carbocation **13**. Cyclization of **3** occurs exclusively *via* protonation of the cyclopropane with participation of the double bond (not *vice versa*) and generation of carbocation **15**.

This article reports synthetic work and results of acid-promoted cyclization studies relating to three compounds: *trans,trans*-2,8-*trans*-bicyclo[8.4.0]tetradecadiene (**1**), 2-methyl-*trans,trans*-2,8-*trans*-bicyclo[8.4.0]tetradecadiene (**2**), and *trans*-9-*trans,anti,trans*-tricyclo[9.4.0.0^{2,4}]pentadecene (**3**).



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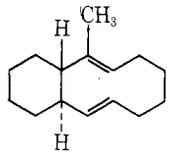

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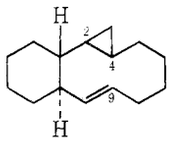

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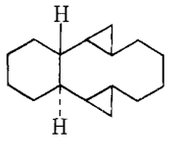

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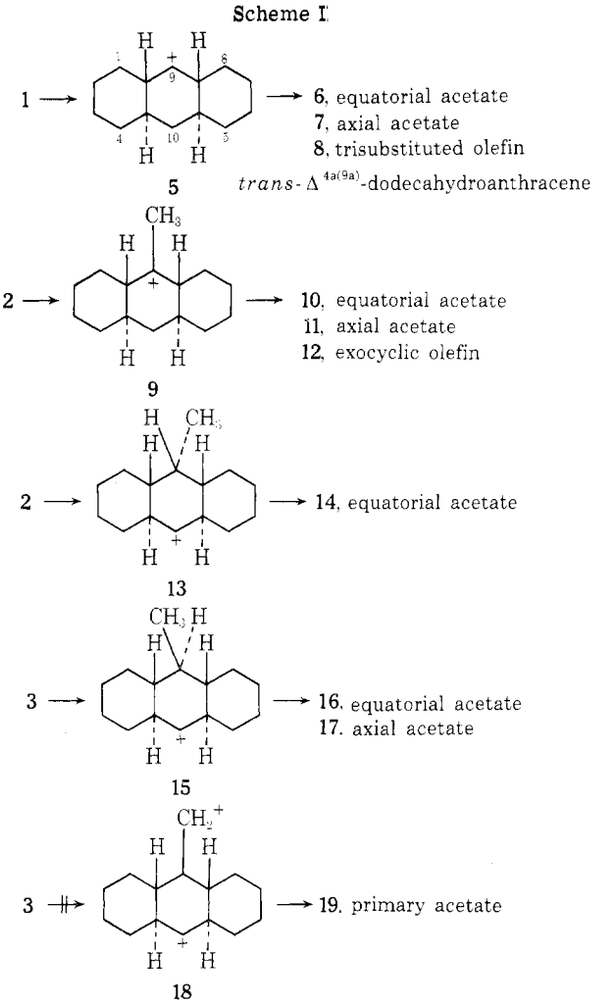
Results and Discussion. The high energy of **1** (medium-ring strain) and its locked conformation[3] (chair-chair-chair) are, in combination, highly favorable to reactions involving overlap of the p orbitals of C-3 and C-8 with the development of a σ bond.[4] The distance separating C-3 and C-8 across the ring is only about 3 Å and the p orbitals on these atoms are well aligned for interaction.[5,6] The anticipated acid-promoted cyclization of **1** to carbocation **5** (see Scheme I) should be facilitated, relative to that of acyclic 1,5-dienes, if protonation involves participation of the transannular double bond for, as the *trans,syn,trans*-perhydroanthracene system is developed, there is a gain of at least 12 kcal mol^{-1} with the relief of ring strain.[7] Indeed **1** is tremendously reactive. Cyclization can be effected in buffered acetic acid at 60°, conditions which are without effect on either *trans*-cyclodecene or *cis,trans*-1,5-cyclodecadiene.[8]

An initial series of cyclizations was carried out with acetic acid containing perchloric acid at room temperature and is mentioned here because it was subjected to the most careful analysis which revealed that all products were indeed derivable from carbocation **5**. Products were identified by comparison with authentic samples synthesized as described in the next section. An exemplary analysis yielded the following data: 80.8% of equatorial acetate **6**, 3.0% of axial acetate **7**, 0.4% of trisubstituted olefin **8**, and 15.0% of the tetrasubstituted olefin *trans*-$\Delta^{4a(9a)}$-dodecahydroanthracene which was formed at least in part under the reaction conditions by hydrogen rearrangement of **8**. The yields given are absolute and correspond to quantitative cyclization, a characteristic which sharply distinguishes 1,5-cyclodecadienes from their acyclic counterparts.[9]

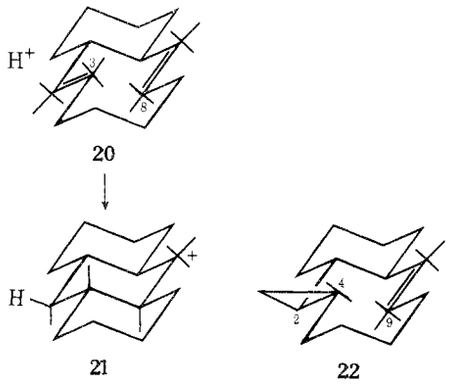
Scheme I



Subsequently, all cyclizations were carried out in buffered acetic acid at 60° and allowed to proceed for approximately 90 hr (close to 6 half-lives). The mixture of equatorial and axial acetates **6** and **7** was produced in at least 81% yield (this yield was obtained after isolation) and in almost the same ratio as in strong acid (94:6 by gc analysis). The olefin fraction was not investigated.

Characterization of the products establishes all stereochemical aspects of cyclization except that of protonation. This was determined by carrying out experiments with deuterium labeling.[10] The synthesis of **1**-*2,9-d*$_2$ is de-

scribed in the next section. Its cyclization in buffered acetic acid yielded an acetate fraction which was converted to the corresponding ketone (**25**) *via* sequential treatment with lithium aluminum hydride and chromic acid. This procedure retained the deuterium atom which was at the site of protonation but removed the other one. The infrared spetrum of the ketone showed C–D doublet maxima at 2124 and 2145 cm^{-1}. The complementary experiment of cyclizing **1** in buffered acetic acid-*O*-*d* was also carried out. It afforded a monodeuterated ketone with C–D doublet maxima at 2149 and 2170 cm^{-1}. Together the two sets of doublets are diagnostic for axial and equatorial C–D, respectively.[11] Thus protonation occurs with equatorial approach to the open face of the double bond antiparallel to the developing carbon–carbon bond (see **20** → **21**). That the stereospecificity of protonation is absolute is suggested by the fact that 2124 cm^{-1} corresponds to maximum absorption for one ketone but base-line absorption for the other.



There are two alkenyl methyl derivatives of **1** and the synthesis of one of them, **2**, is described in the next section. If the overall nature of the reaction with acetic acid were to remain unchanged[12] the effect of the methyl group might be observable in a rate enhancement and also a regioselectivity of protonation which generates the methyl-stabilized tertiary carbocation **9** in preference to secondary carbocation **13**. Evaluation of these two pathways was facilitated by independent synthesis of the principal products expected to be produced from these cations, as described in the next section.

The half-life of **2** in buffered acetic acid at 60° was found to be 10 hr. For comparison that of **1** is 16 hr. Product composition was found to vary with time because of the solvolytic instability of the initially formed tertiary acetates and the analyses cited refer specifically to work-up after a reaction period of 10 half-lives. Of most interest was the presence of 5% of secondary equatorial acetate **14** formed *via* carbocation **13**. The remaining 95% was, as expected, derived from tertiary carbocation **9** and consisted of 25% of equatorial tertiary acetate **10**, 4% of axial tertiary acetate **11**, and 66% of exocyclic olefin **12**.[13]

The rate ratio for cyclization of **2** *vs.* **1** is 1.6:1 and the rate ratio for generating tertiary carbocation **9** *vs.* secondary carbocation **5** is therefore 1.5:1. In addition to this intermolecular comparison there is the intramolecular comparison of forming tertiary carbocation **9** *vs.* secondary carbocation **13** which is associated with a rate ratio of 19:1. The intramolecular ratio is somewhat higher but some of the difference may well be caused by a steric retardation effect of the methyl group in the formation of **13**.[14]

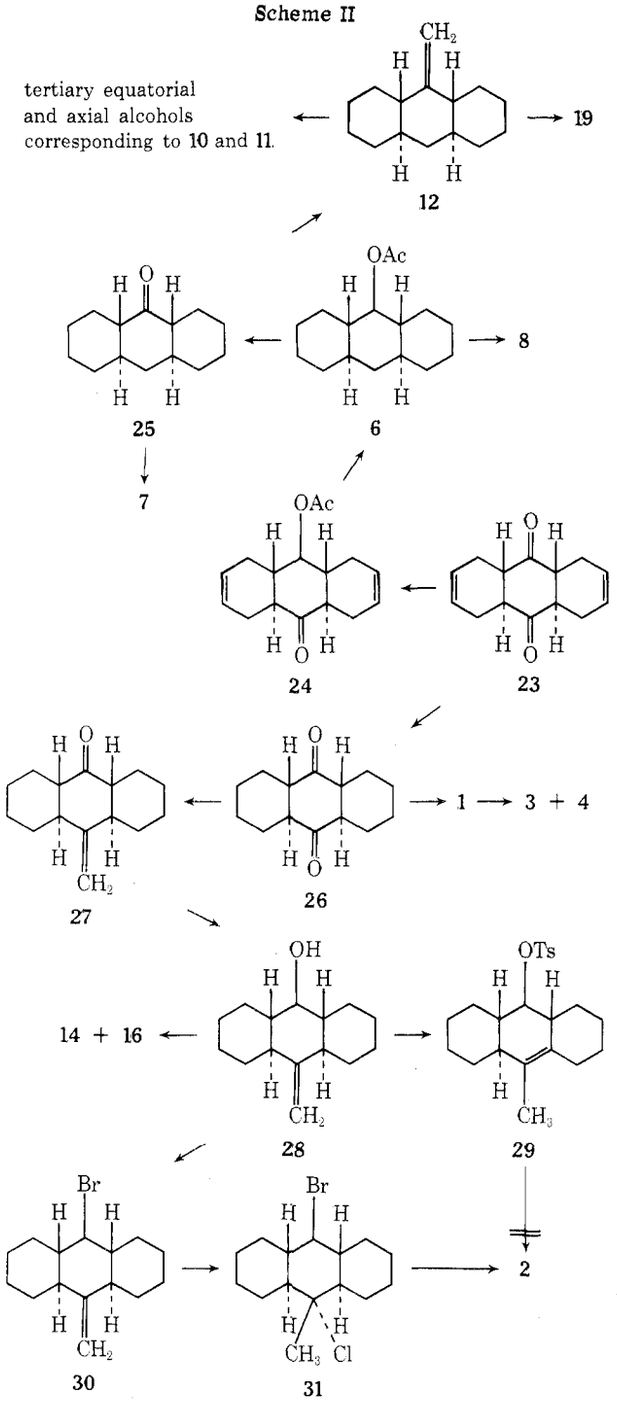
The pattern of reactivity of **2** is described by a large rate increase relative to the corresponding saturated compound (*trans*-cyclodecene) with a small rate increase (2 to 20) for substitution of a methyl group on the participating double bond. In the absence of reference data on protonation of double bonds with acetic acid, a comparison with solvolytic data can be made.[15] The ion pairs formed by solvolytic and protonation routes bear some resemblance. Specifically the transition state for protonation of **1** resembles that of the solvolysis of *trans*-5-cyclodecenyl *p*-nitrobenzoate for which substantial participation of the double bond has been shown (there is a rate increase of 1500 relative to the saturated system).[16] Moreover, several solvolyses involving participation of a double bond show rate increases for methyl substitution of the same order of magnitude found for **2** even though the extents of participation differ greatly. The 2-(3′-cyclohexenyl)ethyl, 2-(3′-cyclopentenyl)ethyl, and 7-*anti*-norbornenyl systems solvolyze with rate increases, relative to the corresponding saturated systems, of 5, 10^2, and 10^{11} but the additional rate increases found upon substituting methyl on the participating double bond are much the same: 7, 7, and 13.[17]

The synthesis of olefinic cyclopropane **3** is described in the next section. The small ring is attached with the stereochemistry shown in **22**. The external cyclopropane bond at C-2 is pseudoequtorial and there is potential interaction of the p-orbital of C-9 with the rear lobe of the external cyclopropane bond of C-4 which should lead to behavior similar to that of **1** and **2**, namely acid-promoted cyclization with generation of the *trans,syn,trans*-perhydroanthracene system. With results of the cyclization of **2** in hand, the more likely of the two pathways leading to the *trans,syn,trans*-perhydroanthracene system was predicted to be protonation of the cyclopropane with participation of the double bond, generating carbocation **15**. The alternative mode of cyclization involving protonation of the double bond with participation of the cyclopropane seemed less likely, not least because of the generation of a less stable (primary) carbocation (**18**).[18] Evaluation of these pathways was assisted by independent synthesis of samples of acetates **16** and **19** as described in the next section. These are the principal acetates which would be produced from carbocations **15** and **18**, respectively.

Reaction of **3** with buffered acetic acid was complete within 6 days at reflux temperature. For comparison, biscyclopropane **4** was unaffected under these conditions. The acetate fraction of the product (58%) was found to consist solely of two components in a ratio of 6:94 with retention times of 12.8 and 15.5 min.[19] Neither component corresponded to **19** which had a coinjection retention time of 14.5 min. Cyclization *via* the pathway leading to carbocation **18** is therefore excluded (it is estimated that 1% of **19** would have been detected). The larger gc peak at 15.5 min corresponded to that of **16** and isolation of the corresponding component and comparison with authentic material established its identity. The smaller gc peak was present in an amount expected for axial acetate **17** produced along with equatorial acetate **16** and this supposition was confirmed indirectly. The acetate fraction obtained from cyclization was subjected to sequential treatment with lithium aluminum hydride, chromic acid, sodium borohydride, and acetic anhydride–pyridine. The expected effect of this sequence on any **16** and **17** originally present is solely to change the ratio in favor of the axial isomer. Experimentally, it was found that, after treatment, the final product still consisted of only two components with retention times unchanged from those of the two components originally present. Their ratio, however, had changed from 6:94 to 79:21. Thus it appears that cyclization of **3** occurs *exclusively via* the pathway with participation of the double bond and generation of carbocation **15**.

Synthetic Work (see Scheme II). Synthesis of **1** was

Scheme II



achieved from **26** using two previously described fragmentation sequences[20] (**26** is derived from the bis adduct of benzoquinone and butadiene *via* **23**). Reduction of **26** with lithium aluminum deuteride gave, by the same sequence, a sample of 1-2,9-d_2.

Simmons–Smith cyclopropanation of **1** afforded **3** as an oil and **4** as a solid. They were readily separated by column chromatography on silica gel impregnated with silver nitrate. In their nmr spectra the vinyl hydrogens of **3** are centered at δ 5.3, downfield from the corresponding signals of **1** which are centered at δ 4.7, and the four external cyclopropane hydrogens of **4** are centered at δ 0.21, downfield from the corresponding two hydrogens of **3** which are centered at δ 0.09. Both differences can be attributed to the shielding effect of the transannular double bond. By contrast, the cyclopropane ring has a negligible effect on the shift of transannular hydrogens.

The synthesis of **2** was more involved. Dione **26** was converted to methylene ketone **27** in 30% yield by treatment with a controlled amount of Wittig reagent. Column chromatography separated **27** from starting dione and the dimethylene compound formed from reaction with 2 equiv of Wittig reagent. Reduction of **27** with sodium in boiling isopropyl alcohol gave a two-component mixture (95:5) from which equatorial alcohol **28** could be crystallized in 70% yield. (Lithium aluminum hydride gave a 60:40 mixture.) Conversion of **28** to a bromo tosylate was readily effected but this compound failed to fragment in the presence of zinc because of rapid 1,2 elimination of hydrogen bromide from the tertiary bromide. The target molecule for fragmentation then became chloro bromide **31**, a molecule in which the degree of substitution of the zinc-reducible bromine has been changed from tertiary to secondary in order to minimize the occurrence of 1,2 elimination. Alcohol **28** was first converted to the corresponding brosylate and the brosylate was treated with potassium bromide in dimethylformamide. This sequence gave a multicomponent mixture from which a pure bromide could be isolated in 30% yield by simple crystallization. Fortuitously, it turned out to be equatorial bromide **30**, presumably formed by two substitutions, the second on the first-formed axial isomer. Bromide **30**, upon treatment with hydrogen chloride in ether, gave a mixture of tertiary chlorides, principally equatorial isomer **31**, which could be isolated by crystallization.

Fragmentation of **31** was effected using Applequist's recipe for the synthesis of spiropentane: zinc dust in boiling aqueous alcohol containing potassium iodide, the disodium salt of ethylenediaminetetraacetic acid, and sodium hydroxide.[21] Pure **31** was first used in the preparation of samples of **2** but it was found that no advantage was thereby gained and subsequently the mixture of equatorial and axial isomers was used. Thereby, with the addition of the appropriate amount of sodium hydroxide,[22] **2** was obtained as an oil in 70% yield after silica gel chromatography. Its nmr spectrum shows a vinyl methyl at δ 1.4 and three vinyl hydrogens in the range 4.5–4.9.

One other synthesis of **2** was attempted but was unsuccessful. The double bond of **28** was isomerized to the endocyclic position, a transformation best carried out on the acetate in liquid sulfur dioxide. Tosylate **29** was then routinely prepared but it failed to fragment to **2** when subjected to Marshall's procedure involving treatment with diborane and then aqueous base[23] and it would appear that diborane does not add in the regiospecific sense which is appropriate for fragmentation. As some slight recompense, reduction of **29** with lithium aluminum hydride yielded an authentic sample of 10-methyl-*trans*-$\Delta^{4a(10)}$-dodecahydroanthracene.

The products formed in acid-promoted cyclizations of **1**, **2**, and **3** were identified by comparison with compounds synthesized as described in the following paragraphs. Hydrogenation of the acetate of **28** yielded a 2:1 mixture of **14** and **16** with the axial methyl isomer **14** predominating as would be expected from delivery of hydrogen to the less hindered side. The major isomer, mp 150–153°, was purified by preparative gc but pure minor isomer, mp 95–96.5°, was obtained only from cyclization of **3**.

Partial reduction of **23** was accomplished with sodium borohydride in pyridine, a combination which afforded a ketol in 19% yield. Acetylation of the ketol gave acetate **24**. Sequential hydrogenation, thioketalization, and desulfurization applied to **24** afforded equatorial acetate **6**. Saponification of **6** and subsequent oxidation gave ketone **25** from

which axial acetate **7** was obtained *via* reduction with sodium borohydride.[24] Careful pyrolysis of **6** afforded trisubstituted olefin **8.** Perchloric acid in acetic acid isomerized **8** to *trans*-$\Delta^{4a(9a)}$-dodecahydroanthracene.

Subjection of ketone **25** to the Wittig reaction afforded exocyclic olefin **12.** Application of the sequence hydroboration–acetylation to **12** yielded a 2:5 mixture of **19** and the more abundant corresponding axial isomer. The individual isomers were separated by preparative gc. Application of the sequence epoxidation–reduction to **12** afforded a 2:3 mixture of axial and equatorial alcohols corresponding to acetates **10** and **11.** The axial alcohol was generated much more selectively by the addition of methyllithium to ketone **25.**

The stereochemical assignments to **14** and **16** are unambigously established by their specific geometric relations to **2** and **3** from which they are respectively formed. The axial methyl of **14** absorbs at δ 0.75 as a doublet with J = 6.5 Hz whereas the equatorial methyl of **16** appears at δ 0.85 as a single broad peak because of a near coincidence of shift of the methyl and C-9 axial hydrogen.

The stereochemical assignments to the acetoxymethyl isomers are well based on nmr coupling data. One of them has acetoxymethyl hydrogens absorbing as a doublet with J = 5 Hz while the corresponding signal of the other isomer (**19**) appears as a single broad peak. A straightforward conformational analysis, based on the effects of 1,3 interactions, reveals that in the equatorial acetoxymethyl isomer the conformer in which the acetate and C-9 axial hydrogen are antiparallel is the most stable (giving a small average J) whereas, in the axial isomer the conformer with the ester and C-9 equatorial hydrogen antiparallel is the least stable (giving a larger average J). Once again the methylene hydrogens which are axial absorb at higher field (δ 3.98) than those which are equatorial (δ 4.16).

The following is a listing of reactions in this series which involve addition to a trigonal carbon at the 9 position and generation of isomers in which a methyl or methylene carbon and a functional group are both present on C-9. The chemical shifts of the methyl or methylene groups of the two isomers are given in δ with that given first corresponding to the major isomer formed. Addition of hydrogen bromide to **12:** 1.49, 1.65. Addition of hydrogen chloride to **30:** 1.30, 1.40. Epoxidation of **12:** 2.46, 2.60. Addition of methyllithium to **25:** 1.06, 0.90. These results, combined with those obtained from the hydroboration of **12** and hydrogenation of **28** which have already been discussed, allow a self-consistent, if not completely satisfactory, set of stereochemical assignments to be made, exemplified by the formulation of **31.** All examples conform to the generalizations that additions to C-9 show a preference for equatorial attack and yield isomers which show a higher field shift for axial methyl or methylene.

Experimental Section

Physical Data. Melting points were determined by the capillary method and are uncorrected. Spectra were recorded using Perkin-Elmer 137 and Beckman IR-8 infrared spectrometers; Cary 11 and 14 ultraviolet spectrometers; Varian A-60 and A-60A nmr spectrometers using tetramethylsilane as an internal reference. Analytical and preparative gas chromatography (gc) were performed on Perkin-Elmer F11 and Varian Aerograph A-90-P units. Peak areas were calculated using a Disc chart integrator.

Materials and Procedures. Solvents were dried and/or distilled before use with the exceptions of ether, methanol, and ethanol. Magnesium and sodium sulfates were used as drying agents. Solvents were removed under reduced pressure using a rotary evaporator. Silica gel used for chromatography was Davison-Grace grade 950, 60–200 mesh. Available procedures for the preparation of special reagents such as Raney nickel, Jones' reagent, activated zinc, and Simmons–Smith reagent were followed.[25] Anhydrous acetic acid was prepared from glacial acetic acid, previously distilled from chromium trioxide, by the sequence: addition of acetic anhydride, reflux, and fractional distillation.

10(e)-Acetoxy-9-keto-$\Delta^{2,6}$-*trans,syn,trans*-decahydroanthracene (24). To a solution of 100.0 g (0.462 mol) of dione **23,** mp 239.0–245.5° dec, in 2500 ml of pyridine, maintained at a water-bath temperature of 75° and in a nitrogen atmosphere, was slowly added, with magnetic stirring, 4.370 g (0.115 mol) of sodium borohydride. After stirring for 7 hr, the resulting yellow-brown reaction mixture was poured into 2500 ml of distilled water and allowed to stand overnight. Filtration of the mixture afforded 5.851 g of recovered dione **23,** mp 211.0–220.0° dec. The filtrate was extracted five times with 500-ml portions of chloroform and the combined organic layers were washed with 500 ml of distilled water and then dried. Evaporation of the solvents under reduced pressure afforded 105.5 g of a yellow-brown gum which contained some suspended crystalline material. Crystallization of the crude product from benzene gave 18.75 g (19%) of light tan crystals, mp 197.5–204.0° dec. Three recrystallizations of 17.18 g from benzene gave 11.80 g of white needles, mp 209.0–212.0° dec, not raised by further crystallization.

Anal. Calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31. Found: C, 77.22; H, 8.45.

Oxidation of the ketol regenerated **23,** with mp undepressed upon admixture with authentic dione.

A solution of 11.33 g (0.052 mol) of the ketol, mp 209.0–212.0° dec, in 300 ml of pyridine (distilled from barium oxide) containing 150 ml (1.57 mol) of acetic anhydride was allowed to stand at room temperature for 24 hr. A deposit of white needles separated from solution. The mixture was diluted with 1500 ml of distilled water and allowed to stand at room temperature for 7 hr. The precipitate was collected, washed with several portions of 2% hydrochloric acid, and dried, thereby affording 13.47 g of white solid, mp 204.0–207.0° dec: nmr ($CDCl_3$) δ 5.65 (broad s, 2), 5.07 (t, 1, J = 8 Hz), and 2.11 (s, 3). Sublimation of the recovered nmr sample at 100° (0.1 mm), followed by crystallization from absolute ethanol, gave an analytical sample, mp 206.0–209.0°

Anal. Calcd for $C_{16}H_{20}C_3$: C, 73.82; H, 7.74. Found: C, 73.98; H, 7.78.

9(e)-Acetoxy-*trans,syn,trans*-perhydroanthracene (6). A suspension of 11.94 g of unsaturated ketol acetate **24,** mp 205.5–208.5° dec, in 300 ml of ethyl acetate was hydrogenated over 1.01 g of 5% palladium-on-calcium carbonate at 40 psi and room temperature for 1.9 hr. The reaction mixture was filtered and the solvent evaporated under reduced pressure to give a white crystalline residue. Crystallization from absolute ethanol afforded 11.45 g (94%) of white crystals, mp 157.5–158.5°: nmr (CCl_4) δ 4.86 (t, 1, J = 9 Hz) and 2.04 (s, 3); ir ($CHCl_3$) 5.79, 5.84 μ.

Anal. Calcd for $C_{16}H_{24}O_3$: C, 72.69; H, 9.15. Found: C, 73.00; H, 9.20.

A suspension of 4.93 g (0.0186 mol) of ketol acetate, mp 157.5–158.5°, in a mixture of 5.0 ml (0.060 mol) of ethanedithiol and 5.0 ml of freshly distilled boron trifluoride etherate, was stirred at room temperature. After a few minutes the mixture became warm and most of the suspended white solid dissolved. Upon continued stirring, the mixture cooled and a white solid separated. After 30 min the mixture was diluted with 20 ml of methanol and cooled to −20°. The resulting solid was collected, washed with several small portions of cold methanol, and dried, thereby giving 6.202 g (98%) of white crystals, mp 141.0–141.5°: nmr (CCl_4) δ 4.36 (m, 1), 3.16 (s, 4), and 1.99 (s, 3); ir ($CHCl_3$) 5.80 μ.

Anal. Calcd for $C_{18}H_{28}O_2S_2$: C, 63.48; H, 8.29; S, 18.83. Found: C, 63.46; H, 8.16; S, 18.71.

A mixture of 5.501 g of thioketal, mp 141.0–141.5°, and *ca.* 70 g of W-4 Raney nickel catalyst in 600 ml of absolute ethanol was heated under reflux for 5 hr. The warm reaction mixture was passed through Filter Cel and the nickel residues were washed with several portions of hot absolute ethanol. Concentration of the filtrate and washings to *ca.* 45 ml followed by cooling to −20° gave 3.520 g of white solid, mp 125.0–179.0°. Sublimation at 60° (0.1 mm) afforded 2.980 g of white powder, mp 123.5–125.0°. Crystallization from absolute ethanol gave 2.658 g (66%) of small white needles, mp 125.5–126.0°: nmr (CCl_4) δ 4.37 (m, 1) and 1.98 (s, 3). Sublimation of the recovered nmr sample at 75° and 0.1 mm, followed by crystallization from absolute ethanol, afforded an analytical sample of **6,** mp 125.5–126.0°.

Anal. Calcd for $C_{16}H_{26}O_2$: C, 76.75; H, 10.47. Found: C, 76.62; H, 10.54.

$\Delta^{4a(10)}$-*trans,syn*-Dodecahydroanthracene (8). A 1.003-g sample of acetate **6,** mp 125.0–126.0°, was sealed under vacuum in

a 2.2 × 16 cm Pyrex tube and heated at *ca.* 400° in a furnace for 20 min. The crude product crystallized on standing at room temperature. Chromatography on 100 g of 60–200 mesh silica gel with hexane elution, followed by crystallization from aqueous acetone, afforded 0.573 g (75%) of white solid, mp 49.0–50.0°. Two additional crystallizations from aqueous acetone afforded 0.456 g of white solid, mp 50.5–51.0°, not raised by further crystallization: nmr (CCl_4) δ 5.01 (broad s, 1). Sublimation of the recovered nmr sample at room temperature and 0.1 mm gave an analytical sample of **8**, mp 50.5–51.0°: uv end absorption (95% ethanol) 210 nm (ϵ 6200); mol wt from the mass spectrum, 190.

Anal. Calcd for $C_{14}H_{22}$: C, 88.35; H, 11.65. Found: C, 88.23; H, 11.65.

$\Delta^{4a(9a)}$-*trans*-Dodecahydroanthracene. A solution of 0.285 g of **8**, mp 50.5–51.0°, in 35 ml of an anhydrous 0.557 *M* solution of perchloric acid in acetic acid, was stirred magnetically under nitrogen at 27° for 3 hr. The resulting light orange solution was diluted with 70 ml of distilled water and was extracted four times with 35-ml portions of benzene. The combined benzene extracts were washed twice with 70-ml portions of distilled water, twice with 70-ml portions of 10% potassium bicarbonate solution, once with 70 ml of distilled water, and then dried. Capillary gc showed that there were present in the product the desired olefin, starting olefin, and acetate **6** in the ratio 1.4:1.3:1.0. Preparative gc at 165° on a 5 ft × 0.25 in. column of SF-96 on 60–80 firebrick afforded an analytical sample, mp 23–24°: nmr (CCl_4) no olefinic hydrogens; uv end absorption (cyclohexane) 210 nm (ϵ 4100); mol wt from the mass spectrum, 190.

Anal. Calcd for $C_{14}H_{22}$: C, 88.35; H, 11.65. Found: C, 88.52; H, 11.45.

9-Keto-*trans,syn,trans*-perhydroanthracene (25). Saponification of 2.448 g of acetate **6**, mp 125.5–126.0°, in 1 *N* methanolic potassium hydroxide afforded, after crystallization from carbon tetrachloride, 1.916 g (94%) of alcohol, mp 169–170°.

Anal. Calcd for $C_{14}H_{24}O$: C, 80.71; H, 11.61. Found: C, 80.82; H, 11.58.

The alcohol afforded a tosylate in good yield *via* the normal pyridine–tosyl chloride method, mp 116–117° dec.

Anal. Calcd for $C_{21}H_{30}O_3S$: C, 69.57; H, 8.34: S, 8.85. Found: C, 69.73; H, 8.08; S, 8.89.

A solution of 1.669 g (8.00 mol) of alcohol, mp 169–170°, in 500 ml of acetone (distilled from potassium permanganate) was cooled at ice-bath temperature and 2.30 ml of Jones' reagent was added rapidly from a buret with magnetic stirring. After stirring at ice-bath temperature for 8 min, the mixture was diluted with 2500 ml of distilled water. The resulting precipitate was collected, washed well with distilled water, and dried, thereby yielding 1.567 g of white powder, mp 117.0–124.0°. Two crystallizations from absolute ethanol afforded 1.079 g (65%) of small white plates, mp 130.5–131.5°. Two additional crystallizations from aqueous ethanol afforded an analytical sample of **25**, mp 130.5–131.5°.

Anal. Calcd for $C_{14}H_{22}O$: C, 81.50; H, 10.75. Found: C, 81.76; H, 10.76.

Ketone **25** afforded an oxime by the normal method, mp 221–222° dec. The ketone was converted to *trans,syn,trans*-perhydroanthracene as follows. A mixture of 0.288 g (1.40 mmol) of **25**, mp 130.5–131.5°, 0.30 ml (3.6 mmol) of ethanedithiol, and 0.30 ml of freshly distilled boron trifluoride etherate in a test tube was homogenized with a stirring rod. The mixture became warm and set to a white paste. After 10 min the mixture was diluted with 10 ml of methanol, cooled to −20°, and filtered. The collected solid was washed with several portions of cold methanol and dried, thereby affording 0.392 g (99%) of white solid, mp 202.0–203.0°. Crystallization from ethyl acetate afforded 0.355 g of white needles, mp 202.0–203.0°: nmr ($CDCl_3$) δ 3.17 (s, 4). A single recrystallization from ethyl acetate gave an analytical sample, mp 202.0–202.5°.

Anal. Calcd for $C_{16}H_{26}S_2$: C, 68.02; H, 9.27; S, 22.70. Found: C, 68.31; H, 9.35; S, 22.78.

A mixture of 0.201 g of thioketal, mp 202.0–203.0°, and *ca.* 4 g of W-4 Raney nickel catalyst in 40 ml of absolute ethanol was heated under reflux for 4 hr. The hot reaction mixture was filtered and the nickel residues were washed with several portions of hot absolute ethanol. Evaporation of solvent under reduced pressure gave a white solid residue which was crystallized three times from acetone to yield 0.054 g (40%) of white plates, mp 88.0–89.0°, undepressed on admixture with authentic *trans,syn,trans*-perhydroanthracene.[26] The infrared and nmr spectra of the two compounds were identical.

9(a)-Acetoxy-*trans,syn,trans*-perhydroanthracene (7). A solution of 0.413 g (2.00 mmol) of ketone **25**, mp 130.5–131.5°, in 80 ml of anhydrous methyl alcohol was cooled at ice-bath temperature and 0.145 g (3.82 mmol) of sodium borohydride added with magnetic stirring. A white precipitate formed after 13 min. Stirring at ice-bath temperature was continued for 22 hr. The reaction mixture was then diluted with 250 ml of distilled water and the resulting precipitate collected, washed with several portions of distilled water, and dried, thereby, giving 0.411 g of white powder, mp 115.0–117.5°. Two crystallizations from aqueous ethanol afforded 0.306 g (73%) of fibrous white needles, mp 122.0–123.0°. Repeated recrystallizations from aqueous ethanol and acetonitrile gave an analytical sample, mp 122.0–122.5°. Oxidation of the alcohol with Jones' reagent regenerated ketone **25**.

Anal. Calcd for $C_{14}H_{24}O$: C, 80.71; H, 11.61. Found: C, 80.70; H, 11.64.

The alcohol afforded a tosylate, but with some difficulty, using a butyllithium–tetrahydrofuran–tosyl chloride procedure, mp 85–85.5 dec.

Anal. Calcd for $C_{21}H_{30}O_3S$; C, 69.57; H, 8.34; S, 8.85. Found: C, 69.75; H, 8.27; S, 8.83.

A solution of 0.160 g (0.766 mmol) of alcohol, mp 122.0–123.0°, in 4.0 ml of pyridine (freshly distilled from barium oxide) was treated with 2.0 ml (21 mmol) of acetic anhydride and allowed to stand at room temperature for 20 hr. The reaction mixture was then diluted with 25 ml of distilled water and allowed to cool at room temperature for 2.6 hr. The precipitate was collected, washed well with 2% hydrochloric acid and then with distilled water, and finally dried, thereby affording 0.176 g of white solid, mp 96.0–103.0°. Preparative gc on a 5 ft × 0.25 in. column of 5% Carbowax 20M on Teflon-6 at 190°, followed by two crystallizations from aqueous ethanol, gave 0.081 g (42%) of white fibrous crystals, mp 109.0–110.0°: nmr (CCl_4) δ 4.91 (broad s, 1) and 2.00 (s, 3). The recovered nmr sample was sublimed at 50° (0.1 mm) and crystallized repeatedly from aqueous ethanol to give an analytical sample of **7**, mp 110.0–111.0°.

Anal. Calcd for $C_{16}H_{26}O_2$: C, 76.75; H, 10.47. Found: C, 76.51; H, 10.49.

9(a)-Hydroxy-9-methyl-*trans,syn,trans*-perhydroanthracene. To a stirred solution of 0.113 g (0.549 mmol) of ketone **25**, mp 128.0–129.2°, in 2 ml of ether under nitrogen at room temperature, was added 1.3 ml of commercial (Foote Chemical) 1.62 *M* methyllithium in ether. The resulting mixture of liquid and white precipitate was stirred under nitrogen for 12 hr. Ether and water were added, the mixture was poured into saturated sodium chloride, the resulting mixture was extracted with ether, and the combined ether extracts were washed with saturated sodium chloride and dried. The ether was removed under reduced pressure to yield 0.123 g (100%) of a light yellow solid: nmr (CCl_4) δ 2.2–0.4 complex with an intense singlet at 1.06 (equatorial CH_3) and a small singlet at 0.90 (axial CH_3). Crystallization from 2-methylbutane gave as a first crop 0.051 g (42%) of axial alcohol as clear prisms, mp 69.5–70.2°.

Anal. Calcd for $C_{15}H_{26}O$: C, 81.02; H, 11.79. Found: C, 81.04; H, 11.66.

9-Methylene-*trans,syn,trans*-perhydroanthracene (12). To a solution prepared from 0.082 g of a 55% oil dispersion of sodium hydride in 1.0 ml of dimethyl sulfoxide was added a solution of 0.647 g (1.81 mmol) of methyltriphenylphosphonium bromide in 2.0 ml of dimethyl sulfoxide. An additional 1.0 ml of dimethyl sulfoxide was used to rinse remaining bromide salt into the reaction flask. The resulting red-green mixture was stirred at room temperature, under nitrogen, for an additional 20 min. Then 4.0 ml of dimethyl sulfoxide and 0.326 g (1.59 mmol) of ketone **25**, mp 128.0–129.2°, were added and the resulting dark amber solution was heated at 50–53° with stirring, for 31 hr. The solution was then cooled and poured into saturated sodium chloride solution. The mixture was extracted with pentane. The combined pentane extracts were thoroughly washed with distilled water and dried. Removal of the pentane yielded 0.405 g of light yellow solid which was chromatographed on 10.6 g of Woelm neutral alumina (activity 1). The use of pentane as eluent afforded 0.187 g of a white solid, mp 52.0–58.0°. Crystallization from anhydrous methanol yielded as a first crop 0.090 g (28%) of olefin **12**, mp 62.5–63.0°: nmr (CCl_4) δ 4.50 (s, 2, $=CH_2$). Ozonolysis of **12** afforded a ketone with properties identical with those of authentic **25**.

Anal. Calcd for $C_{15}H_{24}$: C, 88.16; H, 11.84. Found: C, 88.27; H, 11.71.

Mixture of Isomers of 9-Hydroxy-9-methyl-*trans,syn,trans*-perhydroanthracene. To a stirred solution of 0.229 g of 85% *m*-chloroperoxybenzoic acid in 2.0 ml of chloroform, cooled in an ice–

water bath, was added a solution of 0.151 g (0.740 mmol) of **12**, mp 62.2–63.0°, in 1.0 ml of chloroform. The resulting mixture of clear solution and white precipitate was stirred under nitrogen at room temperature for 12 hr. Ether was added, the solution was poured into water, and the mixture was extracted with ether. The combined ether extracts were washed first with 10% sodium sulfite solution until a negative iodine–starch paper test was observed and then with saturated sodium bicarbonate solution. The ether solution was dried and the ether was removed to yield 0.164 g (100%) of a light yellow solid which was dissolved in 4.0 ml of ether and cooled in an ice–water bath. Solid lithium aluminum hydride, 0.062 g (1.63 mmol), was added and the mixture was stirred under nitrogen at room temperature for 30 min. The mixture was cooled in an ice–water bath, 10 ml of 5% hydrochloric acid was added, and the resulting mixture was extracted with ether. The combined ether extracts were washed with saturated sodium bicarbonate solution and dried, and the ether was removed under reduced pressure to yield 0.163 g (99%) of a light yellow solid: nmr (CCl_4) δ 2.70–0.30, complex with singlets at 1.08 (equatorial CH_3) and 0.91 (axial CH_3). Analysis by gc at 140° on a 150 ft × 0.01 in. column of SF-96 showed axial and equatorial alcohols at 15 and 16 min in the ratio of 42:58.

9(e)-Acetoxymethyl-*trans,syn,trans*-perhydroanthracene (19). A solution of 1.225 g (5.52 mmol) of **12** in 10 ml of tetrahydrofuran was subjected to an exhaustive hydroboration treatment (a total of 2.27 g of sodium borohydride and 4.0 g of boron trifluoride etherate was used). Work-up gave 0.842 g (64%) of a solid which was acetylated in a mixture of 5 ml of acetic anhydride, 5 ml of isopropenyl acetate, and 5 ml of pyridine, heated at 95° for 60 min. Work-up afforded 0.707 g (71%) of a pasty solid which was chromatographed on 10 g of silica gel using 5-ml portions of methylene chloride as eluent: fractions 3–10 gave 0.167 g (18%) of an oily solid. Analysis by gc at 215° on a 10 ft × 0.25 in. column of 20% SF-96 on Anakrom showed two main components (92% of total) with retention times of 16 and 18 min in the ratio 1:2.4. These components were separated by preparative gc on the same column, thereby affording samples of **19** (16 min), mp 122–124° (nmr (CCl_4) δ 2.00 (s, 3) and 4.16 (broad s, 2)), and the corresponding axial epimer (18 min), mp 67–69° (nmr (CCl_4) δ 1.92 (s, 3) and 3.98 (d, 2, J = 5 Hz)).

***trans,trans*-2,8-*trans*-Bicyclo[8.4.0]tetradecadiene-*2,9-d*$_2$** was prepared by following the procedures published for the unlabeled compound.[20] A suspension of 4.400 g (20.0 mmol) of 9,10-diketo-*trans,syn,trans*-perhydroanthracene (**26**) and 1.495 g (37.4 mmol) of lithium aluminum deuteride in 100 ml of tetrahydrofuran was heated at reflux for 16 hr. The mixture was then cooled and excess hydride destroyed by adding saturated ammonium chloride solution. Dilute hydrochloric acid was also added and the total liquid layer was then removed by decantation from the resulting gum. The gum was extracted with ethyl acetate and the ethyl acetate solutions were combined, washed with water and sodium bicarbonate solution, and dried. Filtration and removal of solvent afforded 3.774 g (83%) of diol. This material was dissolved with warming in 90 ml of pyridine. The solution was then cooled, treated with 11.77 g of mesyl chloride, and stored at 5° overnight. The mixture was then poured into ice–water and the resulting solid was collected, washed with dilute hydrochloric acid and then water, and dried, yielding 5.839 g (92%) of dimesylate, mp 129–133° dec. A portion of this material, 1.515 g (3.84 mmol), was mixed in a three-necked flask under nitrogen with 0.803 g of activated zinc powder, 1.995 g of potassium iodide, and 40 ml of dimethylformamide. After 26 hr at 65° the mixture was cooled and residual zinc removed by decantation. The decanted solution was extracted with hexane–water. Work-up of the combined hexane fractions gave 0.631 g (83%) of a colorless oil which was chromatographed on 40 g of silica gel using hexane as eluent and collecting 25-ml fractions. Fractions 4–9 gave 0.34 g (46%) of oily **1-*2,9-d*$_2$**: nmr (CCl_4) δ 4.70 (broad d, 2, J = 10 Hz).

9-Keto-10-methylene-*trans,syn,trans*-perhydroanthracene (27). To a solution prepared from 56.5 g of a 50% oil dispersion of sodium hydride (pentane washed to remove the oil) in 700 ml of dimethyl sulfoxide was added a solution of 420.4 g (1.178 mol) of methyltriphenylphosphonium bromide in 1000 ml of dimethyl sulfoxide. An additional 400 ml of dimethyl sulfoxide was used to rinse remaining bromide salt into the reaction flask. The resulting red-yellow-green mixture was stirred at room temperature for 15 min. Then 3000 ml of dimethyl sulfoxide and 178.7 g (0.810 mol) of solid diketone **26** were added and the resulting dark red solution was heated to maintain an internal temperature of 42 to 48°, with stirring for 27 hr. The solution was cooled to about 18° and rapidly poured into a well-stirred mixture of 5000 ml of distilled water and 500 ml of pentane. The resulting mixture was extracted thoroughly with water and dried. The pentane was removed under reduced pressure to yield 198.6 g of yellow solid. This solid was combined with 17.8 g of comparable material from another run and the resulting 216.4 g of material was digested with 2500 ml of pentane. The mixture was filtered and the filtrate was chromatographed on 3600 g of alumina (80–200 mesh), using successively eleven 1000-ml portions of pentane, twelve 1000-ml portions of pentane–ether (97:3), twenty-six 1000-ml portions of pentane–ether (95:5), and twenty 1000-ml portions of pentane–ether (93:7). Removal of solvent under reduced pressure yielded 6.0 g of white solid from fractions 1–6, 28.1 g from fractions 7–11, 27.7 g from fractions 12–21, 19.6 g from fractions 22–25, 15.6 g from fractions 26–29, 16.0 g from fractions 30–35, 15.0 g from fractions 36–49, 3.2 g from fractions 50–58, and 0.96 g from fractions 59–69.

A sample, 3.317 g, of compound comparable to that of fractions 1–11, but obtained in another run, was crystallized from hexane, thereby affording 1.769 g of 9,10-dimethylene-*trans,syn,trans*-perhydroanthracene, mp 132–134°: ir (KBr) 6.10 (C=C) and 11.35 μ (=CH_2); nmr (CCl_4) δ 4.66 (s, 4, =CH_2).

Anal. Calcd for $C_{16}H_{24}$: C, 88.82; H, 11.18. Found: C, 88.66; H, 11.29.

Crystallization from hexane of the solid obtained from fractions 26–29 and similar fractions from another run afforded 59.02 g (30%) of **27** as hard, white prisms, mp 161.0–162.0°: ir (KBr) 5.90 (C=O), 6.10 (C=C), and 11.35 μ (=CH_2); nmr (CCl_4) δ 4.81 (s, 2, =CH_2).

Anal. Calcd for $C_{15}H_{22}O$: C, 82.52; H, 10.16. Found: C, 82.13; H, 10.16.

9(e)-Hydroxy-10-methylene-*trans,syn,trans*-perhydroanthracene (28) was made by following a similar preparation.[27] To a stirred, boiling solution of 31.55 g (0.144 mol) of **27**, mp 161.0–162.0°, in 5300 ml of isopropyl alcohol was added, in small portions over a 30-min period, 450 g (19.58 mol) of sodium metal. The mixture was heated at reflux for 5 hr and then 2000 ml of methanol was carefully added and the mixture was poured over 12,000 ml of cracked ice. The resulting mixture was extracted with ether, and the combined ether extracts were washed with water and dried. Removal of solvent yielded 31.8 g of a white solid. This material was combined with 31.1 g of comparable material from another run and the mixture was crystallized from hexane, thereby giving 43.9 g (70%) of white needles, mp 170.0–171.0°: nmr (CCl_4) δ 4.58 (broad s, 2). Repeated crystallizations from hexane yielded an analytical sample of **28**, mp 170.9–171.1°. Oxidation with Jones' reagent gave a ketone identical with starting material.

Anal. Calcd for $C_{15}H_{24}O$: C, 81.76; H, 10.98. Found: C, 81.70; H, 11.03.

9(e)-Bromo-10-methylene-*trans,syn,trans*-perhydroanthracene (30). A solution of 2.274 g (10.34 mmol) of **28**, mp 169.0–169.3°, and 3.712 g (14.55 mmol) of *p*-bromobenzenesulfonyl chloride in 25 ml of pyridine was allowed to stand under nitrogen at room temperature for 24 hr. Then 0.4 ml of distilled water was added and the resulting solution was allowed to stand at room temperature for 60 min. This solution was poured into a solution of 250 ml of saturated sodium chloride solution and 1000 ml of 5% hydrochloric acid and the mixture was extracted with ether. The combined ether extracts were washed with 5% hydrochloric acid and saturated sodium bicarbonate solution and dried. The ether was removed to yield 4.234 g (94%) of crude brosylate as an off-white solid, mp 108.0–117.0° dec.

From another run a mixture of 88.1 g (0.201 mol) of comparable crude brosylate and 54.3 g (0.456 mol) of dried, finely ground potassium bromide, in 850 ml of dry dimethylformamide, was heated at 55–65° with vigorous stirring under nitrogen for 20 hr. The resulting mixture was cooled, diluted with water, and extracted with ether. The combined ether extracts were washed thoroughly with water and dried, and the ether was removed under reduced pressure to yield 57.2 g (100%) of crude bromide as a light yellow solid, mp 62–104°, with the nmr spectrum showing no aromatic hydrogen signals.

A portion of this crude bromide (10.2 g) was crystallized from 95% ethanol to give 5.827 g of white solid, mp 90.5–105.5°. Further crystallization from ethyl acetate yielded 2.913 g of bromide **30** as hard, white prisms, mp 110.0–112.0°: ir (KBr) 6.10 (C=C) and 11.30 μ (=CH_2); nmr (CCl_4) δ 4.65 (s, 2, =CH_2), 3.54 (t, 1, J = 9 Hz). Repeated recrystallization from 95% ethanol yielded an analytical sample, mp 113.0–113.7°.

Anal. Calcd for $C_{15}H_{23}Br$: C, 63.60; H, 8.18; Br, 28.21. Found: C, 63.60; H, 8.22; Br, 28.20.

9(e)-Bromo-10(e)-chloro-10-methyl-*trans,syn,trans*-perhydroanthracene (31). A solution of 0.9246 g (3.26 mmol) of **30** in 20 ml of ether, cooled in a Dry Ice–acetone bath, was saturated with anhydrous hydrogen chloride gas over a period of 45 min. The mixture was allowed to warm slowly to room temperature and then to stand at room temperature for 4 hr. The solution was poured over crushed ice and the mixture was extracted with ether. The combined ether extracts were washed with saturated sodium bicarbonate solution and dried. Removal of the ether yielded 1.024 g (98%) of bromo chlorides as a light yellow solid, mp 103–116°: nmr (CCl_4) δ 1.30 (axial CH_3) and 1.40 (equatorial CH_3), the former signal very much larger than the latter. Repeated crystallization of this material from hexane yielded 0.084 g of analytically pure **31**, mp 123.3–124.5°: nmr (CCl_4) δ 3.39 (t, 1, J = 10 Hz).

Anal. Calcd for $C_{15}H_{24}BrCl$: C, 56.34; H, 7.57; Br, 25.00; Cl, 11.09. Found: C, 56.32; H, 7.54; Br, 25.32; Cl, 11.20.

2-Methyl-*trans,trans*-2,8-*trans*-bicyclo[8.4.0]tetradecadiene (2). To 0.690 g (2.16 mmol) of crude **31**, mp 103–116°, and 0.749 g (11.45 mg-atom) of activated zinc dust was added 65 ml of a solution prepared by dissolving 186.1 g (0.50 mol) of the disodium salt of ethylenediaminetetraacetic acid, 43.0 g (1.07 mol) of sodium hydroxide, and 6.78 g (0.04 mol) of potassium iodide in 3000 ml of 95% ethanol and 1050 ml of water. This mixture was heated at reflux, with vigorous stirring, under nitrogen, for 13 hr. Then 6 ml of 0.4 M sodium hydroxide in 75% ethanol was added, and the mixture was heated at reflux, with vigorous stirring, under nitrogen, for an additional 90 min. The mixture was cooled, poured into water, and extracted with pentane. The combined pentane extracts were washed with saturated sodium bicarbonate solution and then water and dried. The pentane was removed under reduced pressure to yield 0.421 g of a clear oil which was chromatographed on 75.0 g of silica gel using 1015 ml of pentane in 29 fractions of 35 ml each. The solvent was removed from each fraction in a stream of nitrogen. Fractions 1–3 yielded 0.010 g of an oil. Fractions 4–7 yielded 0.045 g of **12** (11%), mp 57.5–62.0°. Fractions 8–15 yielded 0.270 g of oily **2** (70%) which revealed only one component when subjected to gc analysis at 140° on a 150 ft × 0.01 in. column of SF-96: ir (film) 6.03 and 10.30 μ; uv_{max} (2-methylbutane, using 0.1 mm cells) 189 nm (ϵ 16,000) with a slight shoulder at *ca.* 210 nm (ϵ 6300); nmr (CCl_4) δ 5.0–4.4 (complex, 3) and 2.6–0.7, showing a broad methyl singlet at 1.40; mol wt from the mass spectrum, 204.

Anal. Calcd for $C_{15}H_{24}$: C, 88.16; H, 11.84. Found: C, 87.88; H, 12.06.

10-Methyl-$\Delta^{4a(10)}$-*trans,syn*-dodecahydroanthracene. Acetylation of crude alcohol **28** with acetic anhydride in pyridine gave a yellow solid crude acetate in quantitative yield. Crystallization of 9.67 g of crude acetate from absolute ethanol yielded 6.70 g (68%) of white solid, mp 120–121°. Repeated crystallization afforded on analytical sample, mp 121–122°: nmr (CCl_4) δ 4.60 (broad, 3) and 1.97 (s, 3).

Anal. Calcd for $C_{17}H_{26}O_2$: C, 77.81; H, 9.99. Found: C, 77.76; H, 10.24.

The double bond of the acetate was isomerized by placing a sample, typically 0.07 g, mp 120–121°, in a cold nmr tube to which was added liquid sulfur dioxide and a trace of tetramethylsilane. The tube was sealed and then heated at 50° with monitoring of the progress of the reaction *via* nmr spectra. Individual runs took variable times (60 hr was not uncommon) and poor results were obtained without nmr monitoring. Combination of the products from three runs afforded 0.200 g of white solid which yielded 0.113 g, mp 97–98°, after crystallization from absolute ethanol: nmr (CCl_4) δ 4.50 (t, 1, J = 9.5 Hz), 1.99 (s, 3), and 1.59 (broad s, 3). One recrystallization gave an analytical sample, mp 98.5–99.5°.

Anal. Calcd for $C_{17}H_{26}O_2$: C, 77.81; H, 9.99. Found: C, 77.99; H, 10.19.

A sample of isomerized acetate, 0.420 g (1.60 mmol), mp 96–98.5°, was saponified in 20 ml of 0.50 M ethanolic potassium hydroxide heated at reflux for 5 hr. The resulting light yellow solution was poured into saturated sodium chloride solution, and the mixture was extracted with ether. The combined ether extracts were washed with water and dried. Removal of the ether yielded 0.346 g (85%) of light yellow solid, showing no carbonyl absorption in the ir spectrum. A sample of this crude alcohol, 0.173 g (0.785 mmol), was converted to the corresponding tosylate by mixing with 0.204 g (1.071 mmol) of *p*-tosyl chloride in 2 ml of pyridine and allowing the mixture to stand at 5° for 76 hr. Work-up afforded 0.285 g (97%) of crude tosylate as a viscous tan oil which eventually solidified: nmr (CCl_4) δ 8–7 (4), 4.30 (t, 1, J = 9 Hz), 2.42 (s, 3), and 1.59 (s, 3).

Repeated reduction of a sample of this tosylate, 0.025 g, with lithium aluminum hydride in ether afforded, after work-up, 0.015 g of an oily, tosylate-free material: nmr (CCl_4) δ 1.55 (s, 3). Although the oil failed to crystallize, gc analysis showed it to be relatively pure; at 150° on a 150 ft × 0.01 in. column of Apiezon L one principal component was visible at 32 min (93%) with four minor components apparent at 22 (3%), 27 (1%), 34 (2%), and 36 min (1%).

9(e)-Acetoxy-10(a)-methyl-*trans,syn,trans*-perhydroanthracene (14). A mixture of 0.125 g of **28** acetate, mp 120–121°, and 0.109 g of platinum oxide, in 20 ml of ethyl acetate, was vigorously stirred at room temperature under an atmosphere of hydrogen for 20 hr. The resulting mixture was filtered and the ethyl acetate was removed from the filtrate under reduced pressure to yield 0.126 g (100%) of a light yellow solid: nmr (CCl_4) δ 4.32 (broad, 1) and 1.97 (s, 3). Analysis by gc at 140° on a 150 ft × 0.01 in. column of SF-96 showed the presence of two components at 32 and 36 min in the ratio 32:68. A sample of the major component was obtained by careful preparative gc at 198° on a 5 ft × 0.25 in. column of 20% SF-96 on 60–80 firebrick. The solid thus obtained, 40 mg, was crystallized twice, first from methanol–ethanol (1:1) and then from methanol to yield 16 mg of white crystals, mp 150–152°; nmr (CCl_4) δ 0.75 (d, 3, J = 6.5 Hz).

Cyclization of 1. A solution of 0.73 g of diene **1**, mp 48–49°, in 90 ml of an anhydrous 0.557 M solution of perchloric acid in acetic acid was stirred magnetically under nitrogen at a bath temperature of 26 ± 2° for 3 hr. The resulting light yellow reaction mixture was diluted with 180 ml of distilled water and extracted four times with 35-ml portions of benzene. The combined benzene extracts were washed twice with 100-ml portions of distilled water, twice with 100-ml portions of 10% potassium bicarbonate solution, once with 100 ml of distilled water, and then dried and concentrated to a small volume under reduced pressure. The residue was diluted to a volume of exactly 50 ml with benzene and analyzed by gc at 203° on a 150 ft × 0.01 in. column of UCON Polar. The following products were identified by the peak enhancement technique (retention times in min in parentheses): **8** (7.5), $\Delta^{4a(9a)}$-*trans*-dodecahydroanthracene (8.2), **7** (20.4), and **6** (22.4). Preparative gc at 222° on a 10 ft × ⅜ in. column of 5% Carbowax 20M on Teflon-6 afforded samples of **4**, **5**, and **7** with properties identical with those of previously prepared authentic compounds. The authentic compounds were used as standards in a quantitative gc analysis which thereby accounted for 100.9% of the products in terms of the material balance as follows: **8** (0.4%), $\Delta^{4a(9a)}$-*trans*-dodecahydroanthracene (15.1%), **7** (3.0%), and **6** (81.6%) and 0.8% of an unidentified olefin at 8.0 min. Samples of **6** and **7** were found to be virtually unchanged after being submitted to the same reaction conditions as were used in the cyclization.

The conditions used for cyclization of **1** in buffered acetic acid are exemplified by the following description of one of the experiments involving deuterium labeling.

A mixture of 0.47 g (2.51 mmol) of **1** in 5 ml of acetic acid-*O*-*d* containing 0.070 g of sodium acetate was stirred at 60° for 95 hr. Extraction with hexane–water afforded after work-up 0.591 g of white solid, mp 115–123°. Crystallization of this solid from hexane afforded 0.265 g, mp 123–124°. The mother liquor was chromatographed on 15 g of acid-washed alumina using 90 ml of hexane and then 90 ml of 3:1 hexane:ether as eluent and collecting 30-ml fractions. Fraction 4 gave 0.239 g of a solid, mp 115–120°, which was combined with the 0.265 g obtained by crystallization (overall, 0.514 g or 81%). This material was treated with 0.304 g of lithium aluminum hydride in 5 ml of tetrahydrofuran first at room temperature for 150 min and then at reflux for 30 min. The mixture was cooled and water was added cautiously and then dilute hydrochloric acid. Extraction with chloroform afforded after work-up 0.390 g (99%) of a white solid, mp 166–168°. A portion of this solid, dized with Jones' reagent. Excess chromic acid was destroyed by adding a drop of methanol. Extraction of the mixture with dichloromethane gave after work-up 0.026 g (90%) of a solid. This was filtered through a column of 3 g of silica gel in 1:1 hexane:ether solution. Removal of solvent afforded 0.026 g of solid **25-9-*d***, mp 128–130°: ir (KBr) 2149 and 2170 cm^{-1} (equatorial C–D stretching).

Cyclization of **1-2,9-d_2** in buffered acetic acid was similarly carried out and the product converted as described above to a sample of **25-9-*d***, mp 128–129°: ir (KBr) 2124 and 2145 cm^{-1} (axial C–D stretching).

Cyclization of 2. A solution of 75.5 mg (0.57 mmol) of diene **2**, 3.3 mg (0.04 mmol) of sodium acetate, and 39.7 mg (0.27 mmol) of *p*-dichlorobenzene (an internal reference for rate measurements) in 0.25 ml of acetic acid was maintained at 60° for 88 hr. Work-up

afforded 99 mg of a white solid. The nmr spectrum showed that 67% of the product consisted of olefin **12**.

A portion of product, 27 mg, was chromatographed on 2.7 g of acid-washed alumina. One 30-ml fraction of pentane and one 30-ml fraction of ether were collected. Removal of the pentane afforded 17 mg of crude **12**, mp 54–60°, which was homogeneous by gc analysis but by nmr analysis only 90% pure (the remainder absorbing in the saturated C–H region).

Another portion of product, 28 mg, was reduced with lithium aluminum hydride. Gc analysis of the product at 140° on a 150 ft × 0.01 in. column of SF-96 showed four components at 7, 11, 12, and 17 min, identified by coinjection as olefin **12** (66%), the alcohol corresponding to axial acetate **11** (4%), the alcohol corresponding to equatorial acetate **10** (25%), and the alcohol corresponding to equatorial acetate **14** (5%).

Another portion of the product was subjected to preparative gc at 197° on a 5 ft × 0.25 in. column of 20% SF-96 on 60–80 firebrick. Samples of **12** and **14** were thereby obtained and found to be identical with authentic compounds previously prepared.

Synthesis and Cyclization of 3. A mixture of 195 mg (3 mequiv) of activated zinc dust and 63 mg (0.33 mmol) of cuprous iodide in 3 ml of ether was stirred for 30 min at room temperature. Solutions of 142 mg (0.75 mmol) of **1** in 0.6 ml of ether and 405 mg (1.5 mmol) of methylene iodide in 0.6 ml of ether were then added consecutively. Ether was added periodically to compensate for evaporation losses. After 24 hr work-up afforded 161 mg of a pale yellow oil. This oil was passed through a column of 3 g of silica gel in a cold room at 5° with a total of 50 ml of pentane. Removal of the pentane gave 109 mg of a colorless oil which was further purified by chromatography on 5 g of silica gel impregnated with 5% silver nitrate. Seven 5-ml fractions of hexane and five 5-ml fractions of 3:1 hexane:ether were collected. Fraction 2 gave a trace of solid **4**. Fractions 4 and 5 gave 14 mg of an oil shown by gc to contain at least four components. Fractions 9–11 yielded 64 mg (42%) of oily **3**, shown to be homogeneous (>95%) by gc at 200° on a 10 ft × 0.25 in. column of 20% SF-96 on Anakrom: nmr (CCl_4) δ 0.09 (broad, 2, cyclopropane CH_2) and 4.9–5.4 (broad, 2); mol wt from the mass spectrum, 204.

A similar reaction, but using relatively more Simmons–Smith reagent (620 mg (9.5 mequiv) of zinc dust, 182 mg (0.96 mmol) of cuprous iodide, and 1.01 g (7.12 mmol) of methylene iodide to 142 mg (0.75 mmol) of **1**) afforded 156 mg of crude oil which was chromatographed in a cold room at 5° on 13 g of silica gel. Sixteen 10-ml fractions of pentane were collected. Fractions 2–4 gave 99 mg of colorless oil which was crystallized from methanol–ethyl acetate at 5°, thereby yielding 44 mg (27%) of **4** as a white solid, mp 38–39°, shown to be homogeneous by gc at 200° on a 10 ft × 0.25 in. column of 20% SF-96 on Anakrom: nmr (CCl_4) δ 0.21 (broad, 4, cyclopropane CH_2); mol wt from the mass spectrum, 218.

A solution of 64 mg of **3** and 32 mg of sodium acetate in 2 ml of acetic acid was heated to reflux for 6 days. Periodically acetic acid was added to compensate for evaporation losses. Work-up afforded 74 mg of a reddish pasty solid which was chromatographed on 15 g of acid-washed alumina. Four 15-ml fractions of hexane and five 15-ml fractions of 3:1 hexane:ether were collected. Fractions 1 and 2 gave 10 mg of oil which was shown by gc analysis to contain at least three components. Fractions 5 and 6 yielded 48 mg (58%) of solid acetates, mp 82–87°, which consisted of two components in a 6:94 ratio with retention times of 12.8 and 15.5 min according to gc analysis at 213° on a 10 ft × ⅜ in. column of 5% Carbowax 20M on Teflon-6. Crystallization from methanol afforded 16 mg of **16**, mp 95–96.5°: nmr (CCl_4) δ 0.85 (broad s, 3), 1.97 (s, 3), 4.25 (broad, 1). The minor gc component was shown not to be **19** by coinjection analysis (14.5 min). Its characterization as **17** was demonstrated as follows. A sample, 25 mg, of the acetate fraction obtained from cyclization was reduced with lithium aluminum hydride in tetrahydrofuran, work-up affording 24 mg of a colorless solid, mp 141–145°, showing no carbonyl absorption in the infrared spectrum. Oxidation of this solid with Jones' reagent gave 22 mg of a solid ketone mixture, mp 97–102°. Reduction of the ketone mixture with sodium borohydride in ethanol yielded 17 mg of a pasty solid which was acetylated with a mixture of acetic anhydride and pyridine. Work-up afforded 17 mg of a pasty solid which was shown by gc coinjection analysis to consist of the same two acetates obtained in the cyclization but in a ratio which had changed from 6:94 to 79:21.

Registry No.—**1**, 1460-23-7; **1**-2,9-d_2, 52759-82-7; **2**, 32427-44-4; **3**, 52747-13-4; **4**, 52747-14-5; **6**, 52747-15-6; **6** deacetyl derivative, 52747-16-7; **6** tosylate derivative, 52747-17-8; **7**, 52747-18-9; **8**, 52747-19-0; **10**, 52747-20-3; **10** deacetyl derivative, 52747-21-4; **11**, 52747-22-5; **11** deacetyl derivative, 52747-23-6; **12**, 52747-24-7; **14**, 52747-25-8; **16**, 52747-26-9; **17**, 52747-27-0; **19**, 52747-28-1; **23**, 36257-83-7; **23** ketol derivative, 20843-80-5; **24**, 52747-29-2; **24** tetrahydro derivative, 52747-30-5; **24** thioketal derivative, 52747-31-6; **25**, 52747-32-7; **25** ketal derivative, 52747-33-8; **25** tosylate derivative, 52747-34-9; **25** oxime, 52747-35-0; **25** thioketal derivative, 52747-36-1; **25**-9-*d* equatorial, 52759-83-8; **25**-9-*d* axial, 52759-84-9; **26**, 52747-37-2; **26** dimesylate derivative, 32687-23-3; **27**, 52747-38-3; **27** dimethylene derivative, 52747-39-4; **28**, 52747-40-7; **28** brosylate, 52747-41-8; **28** acetate, 52747-42-9; **28** isomerized acetate, 52747-43-0; **29**, 52747-44-1; **30**, 52747-45-2; **31**, 52747-46-3; **31** equatorial CH_3, 52759-85-0; ethanedithiol, 540-63-6; $\Delta^{4a(9a)}$-*trans*-dodecahydroanthracene, 52747-47-4; *trans,syn,trans*-perhydroanthracene, 1755-19-7; *p*-bromobenezenesulfonyl chloride, 98-58-8; 10-methyl-$\Delta^{4a(10)}$-*trans,syn*-dodecahydroanthracene, 52747-48-5; acetic acid-*O*-*d*, 758-12-3; *p*-tosyl chloride, 98-59-9.

References and Notes

(1) The investigation was supported by Public Health Service Research Grants GM 09759, 14133, and 16338 from the Division of General Medical Services, U.S. Public Health Service.

(2) The article is abstracted from the Ph.D. Theses of R.A.K. and R.J.K., University of Wisconsin, and the M.A. Thesis of T.O., Wesleyan University.

(3) The conformations of *trans,trans*-1,5-cyclodecadienes are discussed by P. S. Wharton, Y.-C. Poon, and H. C. Kluender, *J. Org. Chem.*, **38**, 735 (1973).

(4) The facile Cope rearrangement of **1** has already been reported by P. S. Wharton and R. A. Kretchmer, *J. Org. Chem.*, **33**, 4258 (1968).

(5) Dreiding models are useful if account is taken of distortions revealed by X-ray data of related *trans,trans*-1,5-cyclodecadienes. See J. McLure, G. A. Sims, P. Coggon, and A. T. McPhail, *Chem. Commun.*, 128 (1970), and F. H. Allen and D. Rogers, *ibid.*, 588 (1967).

(6) Spectroscopically, an interaction is revealed by a transition which is seen as a shoulder at 204 nm, ϵ 2000. *trans,trans*-1,5-Cyclodecadienes, in general, show similar uv behavior. See F. Sorm, *Progr. Chem. Org. Natur. Prod.* **19**, 1 (1961).

(7) See P. S. Wharton and D. W. Johnson, *J. Org. Chem.*, **38**, 4117 (1973).

(8) Under more vigorous conditions, trifluoroacetic acid at room temperature, *cis,trans*-1,5-cyclodecadiene reacts with quantitative cyclization. See J. G. Traynham and H. H. Hsieh, *Tetrahedron Lett.*, 3905 (1969), and J. G. Traynham, G. R. Franzen, G. A. Knesel, and D. J. Northington, *J. Org. Chem.*, **32**, 3285 (1967).

(9) For example, cyclized products are obtained in less than 50% yield from 2,6-octadienes. See H. E. Ulery and J. H. Richards, *J. Amer. Chem. Soc.*, **86**, 3113 (1964).

(10) The use of deuterium to establish the stereochemistry of protonation of 1,5-dienes has been previously reported by Ulery and Richards[9] and A. Nickon, F. Y. Edamura, T. Iwadare, K. Matsuo, F. J. McGuire, and J. S. Roberts, *J. Amer. Chem. Soc.*, **90**, 4196 (1968).

(11) This diagnostic characterization is documented by E. J. Corey, M. G. Howell, A. Boston, R. L. Young, and R. A. Sneen, *J. Amer. Chem. Soc.*, **78**, 5036 (1956).

(12) Generation of a methyl stabilized but uncyclized carbocation which would lead to a 6-5-7 tricyclic system is conceivable but no evidence for this pathway was found.

(13) Analytical figures do not take into account 7% of a high molecular weight saturated hydrocarbon fraction which is thought to have been present in starting diene.

(14) See the data of Taft cited in ref 17b.

(15) Whichever comparison is made there is certainly a large rate difference associated with the direct generation of tertiary *vs.* secondary carbocations. A factor of 10^3–10^4 is given for protonation (isobutylene *vs.* propylene; see ref 14) and 10^6 is estimated as the limiting difference for solvolysis.

(16) H. L. Goering and W. D. Closson, *J. Amer. Chem. Soc.*, **83**, 3511 (1961).

(17) (a) H. Felkin and C. Lion, *Chem. Commun.*, 60 (1968); (b) P. D. Bartlett and G. D. Sargent, *J. Amer. Chem. Soc.*, **87**, 1297 (1965); (c) P. G. Gassman and D. S. Patton, *ibid.*, **91**, 2162 (1969). It should be noted that other homoallylic systems are more sensitive to methyl substitution than is the 7-*anti*-norbornenyl as is emphasized in ref 17a.

(18) Other comparisons are interesting. The literature reveals (a) similar reactivities toward protonation of cyclopropane and propylene and (b) relative participatory powers of double bonds and cyclopropanes which are highly dependent on geometry and vary greatly, some comparisons favoring the double bond and others the ring. See (a) C. D. Lawrence and C. F. H. Tipper, *J. Chem. Soc.*, 713 (1955), and (b) J. B. Lambert, J. W. Hamersma, A. P. Jovanovich, F. R. Koeng, S. A. Sweet, and P. J. Kucinski, *J. Amer. Chem. Soc.*, **92**, 6372 (1970), and several examples cited by B. Capon, *Org. React. Mech.*, 44 (1968).

(19) The hydrocarbon fraction was not investigated.

(20) P. S. Wharton, Y. Sumi, and R. A. Kretchmer, *J. Org. Chem.*, **30**, 234 (1965); P. S. Wharton and G. O. Spessard, *ibid.*, **37**, 548 (1972).

(21) D. E. Applequist, G. F. Fanta, and B. W. Hendrickson, *J. Org. Chem.*, **23**, 1715 (1958).

(22) The amount of sodium hydroxide turned out to be critically important. Excess led to predominant bimolecular elimination of hydrogen chloride and the formation of olefin **12** from subsequent reduction of the C–Br bond. Surprisingly the same olefin was also obtained when no sodium

hydroxide was added, a result which is intriguingly explicable (but unestablished) in terms of fragmentation followed by subsequent cyclization in the weakly acidic medium.

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(24) Several interconversions and cross-checks were carried out in order to make sure that at no stage was the trans,syn,trans stereochemistry of the tricyclic compounds changed. Exemplary is the thioketalization of **25** and subsequent desulfurization to authentic *trans,syn,trans*-perhydroanthracene, the structure of which rests on X-ray evidence. See S. Bog, O. Hassel, and E. H. Vihovde, *Acta Chem. Scand.*, **7**, 1308 (1953).

(25) L. F. Fieser and M. Fieser, "Reagents for Organic Synthesis," Wiley, New York, N.Y., 1967.

(26) See R. K. Hill, J. G. Martin, and W. H. Storch, *J. Amer. Chem. Soc.*, **83**, 4006 (1961).

(27) W. S. Johnson, V. J. Bauer, J. L. Margrave, M. A. Frisch, L. H. Dreger, and W. N. Hubbard, *J. Amer. Chem. Soc.*, **83**, 606 (1961).

Regioselective [4 + 2] and [2 + 2] Cycloadditions of 1-Azirines to Heterocumulenes. Formation and Rearrangements of the Cycloadducts

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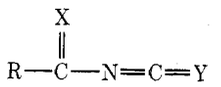
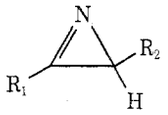
The cycloaddition of 1-azirines to some heterocumulenes is presented. The thermal reaction of representative 1-azirines (**4**) to thiobenzoyl isocyanate (**2**) results in exclusive [4 + 2] cycloaddition. The regiospecificity of the reaction was confirmed by hydrolysis of the cycloadducts **5** to the ureas **6**. Controlled thermolysis of **5a** results in the formation of a novel seven-membered-ring system, a thiadiazepinone (**7**). Compound **7** undergoes a sulfur extrusion reaction thermally to give a pyrimidine ring system (**8**). Benzoyl isocyanate (**1**) also gave [4 + 2] cycloaddition products (**9**). Benzoyl isothiocyanate (**3**), however, gave products (**12**) resulting apparently from a regiospecific [2 + 2] cycloaddition about the C=S bond. The nature of the transition state for the initial [2 + 2] addition is discussed. Structural identification came from mass spectral and nmr studies, particularly ^{13}C nmr.

Heterocumulenes containing a carbonyl or related unsaturation adjacent to the cumulative bonds such as **1**, **2** and **3**, offer the possibility of entry into complex heterocyclic



1, R = Ph; X = O; Y = O
2, R = Ph; X = S; Y = O
3, R = Ph; X = O; Y = S

systems through thermal symmetry-allowed [$_\pi4_s$ + $_\pi2_s$] or [$_\pi2_s$ + $_\pi2_a$] pericyclic reactions. The small ring nitrogen heterocycle, 1-azirine (**4**), may participate as a component in



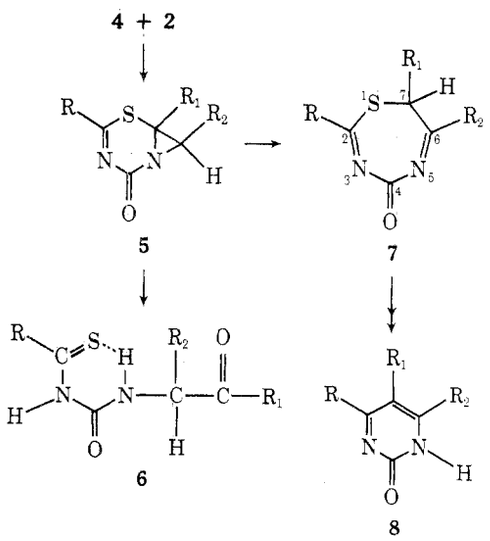
4a, R_1 = Ph; R_2 = Ph
b, R_1 = Ph; R_2 = CH_3
c, R_1 = Ph; R_2 = H

these cycloadditions by utilizing its reactive π bond.[1-4] The possibility of regioselectivity resulting from the inherent polarization in both components enhances the complexity of these reactions. We wish to report on such cycloadditions and to provide evidence that minor structural changes in the heterocumulenes can produce gross changes, not only in the preferred mechanistic pathway for the formation of the adducts, but also in the thermal stability of the final products. A brief announcement of some of our results was made earlier.[11]

Results and Discussion

Thiobenzoyl isocyanate (**2**) can be generated from 2-phenylthiazoline-4,5-dione by thermal extrusion of carbon monoxide.[5-8] When a solution of freshly generated **2** in *p*-xylene was treated with 2,3-diphenyl-1-azirine (**4a**)[9,10] at room temperature for 12 hr, and the reaction mixture after solvent removal was subjected to preparative layer chromatography, a white crystalline compound was obtained, mp 154–155°.[11] Its mass spectral parent ion (*m/e* 356) and fragmentation pattern established the presence of the azirine and thiobenzoyl isocyanate moieties within the structure and that the yield of adduct was high (85%). At least three possibilities exist for the mode of addition:[12] (i) $_\pi4_s$ + $_\pi2_s$ cycloaddition, (ii) $_\pi2_s$ + $_\pi2_a$ adduction, (iii) initial nucleophilic attack by the lone pair of the azirine nitrogen on the highly reactive electrophilic carbon of the carbonyl of the isocyanate and subsequent 1,3-bond scission and cyclization in one or more ways. That the product was actually the result of an exclusive [$_\pi4_s$ + $_\pi2_s$] cycloaddition (**5a**) came from its PFT carbon-13 nmr spectral evidence. The aziridine carbons appeared at δ 53.31 and 56.60, the carbonyl carbon at 173.46, and the imine carbon at 162.94.

The question of the direction or regiospecificity of the cycloaddition and further substantiation of structure was provided in an elegant way by the acid-catalyzed hydrolysis of **5a** to the urea **6a**, yellow plates, mp 199–201°. Dramatic



proof for this mode of ring opening was provided by the observation of three different carbonyl-type carbons (>C=O, N—C(=O)—N, C=S) as suggested by chemical shift correlations in the ^{13}C nmr spectrum. Further confirmation