Synthesis of [4]Peristylane and Functionalized Derivatives of This Hemispherical Ring System

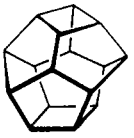
Leo A. Paquette,* John W. Fischer, Alan R. Browne, and Christopher W. Doecke

Contribution from the Evans Chemical Laboratories, The Ohio State University, Columbus, Ohio 43210. *Received June 30, 1984*

Abstract: The Diels–Alder addition of (*p*-tolylsulfonyl)acetylene to tricyclo[5.2.1.$0^{2,6}$]deca-2,5,8-triene proceeds with high below-plane π-facial stereoselectivity. Following selective peracid oxidation of the central double bond in the adduct, [2 + 2] photocyclization was effected to generate the cyclobutane ring. Arrival at the [4]peristylane framework resulted upon treatment of the photoproduct with periodic acid in refluxing aqueous methanol. Once removal of the arenesulfonyl group was accomplished, the pair of carbonyl groups were reduced and tosylated prior to ultimate lithium aluminum hydride promoted displacement of this functionality. Thus, the desired fourfold-symmetric bowl-shaped hydrocarbon has been made available in 10 laboratory steps. [4]Peristylane-2,6-dione has been functionalized in ways that were expected to allow "belting" of the framework across these two positions. Although this goal has been achieved with bridges such as $-(CH_2)_2S(CH_2)_2-$ and $-(CH_2)_2SO_2(CH_2)_2-$, no smaller chain lengths have yet been arrived at.

The recently completed total synthesis of dodecahedrane[1,2] has caused increased attention to be paid to the acquisition of other polyhedral molecules. Particularly in the last decade, research in this area has expanded significantly and notable progress has been forged.[3] Nevertheless, access to a significant number of important target molecules remains to be achieved. One of our more immediate objectives has been [4]perisylane (**1**), suitable

1



2

derivatives of which could prove to be viable precursors to *p*-[$4^2.5^8$]decahedrane (**2**).[4] The framework of **1** is made up of 12 carbon atoms and 16 carbon–carbon bonds. The "floor" of the structure is comprised of a cyclobutane ring that is "walled in" by four mutually fused cyclopentane units. The net effect is a fairly rigid hydrocarbon network whose eight-membered ring is connected via alternate carbons to the four. The fluted periphery and molecular topology that result are comparable to, though different in molecular dimension from, those of the already known [3]- and [5]peristylanes (**3**[5,6] and **4**[7]).

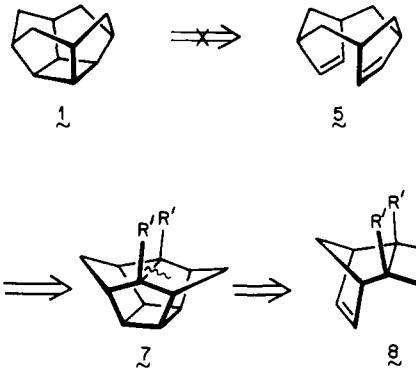
3

4

In this paper, we detail an expedient synthesis of **1**[8] and compare its spectral properties to those of **3** and **4**. Additionally, pilot studies are reported dealing with the chemical embellishment of functionalized [4]peristylanes. As the advance on **2** begins to unfold, it becomes increasingly clear that interconnective bonding between pairs of methylene carbons along the periphery of **1** introduces enhanced levels of strain. Under these circumstances, normally predictable chemical transformations sometimes proceed in unexpected ways. For these reasons, the ultimate elaboration of **2** should be viewed as a synthetic challenge of major dimensions.

Retrosynthetic Considerations. The structural feature inherent to **1** that most uniquely differentiates it from **3** and **4** is its cyclobutane ring. Since proximal double bonds are known to engage in [2 + 2] cycloaddition when photoactivated,[9] little imagination is required to regard **5** as a proper precursor-in-thought to **1**. However, Dreiding models of **5** reveal this hydrocarbon to suffer serious nonbonded steric strain. Since this diene could realistically prove to be more difficult to synthesize than **1**, this retrosynthetic strategy was not followed up.

The preceding difficulty can in principle be surmounted if one views the target as becoming available from a doubly functionalized progenitor molecule such as **6**. This concept holds added



1 **5** **6** **7** **8**

fascination since **6** could also serve as a starting point for the preparation of **2**. On the assumption that cleavage of the appropriate bond in **7** poses no special problems, one is led ultimately to **8**. We had earlier demonstrated that two molecules somewhat resembling **8** were capable of facile [2 + 2] photocycloaddition.[10,11] Furthermore, tricyclo[5.2.1.$0^{2,6}$]deca-2,5,8-triene (**9**)[12] had been shown to undergo Diels–Alder cycloaddition to dimethyl acetylenedicarboxylate[10] and methyl propiolate[13] with complete below-plane π-facial stereoselectivity.[15] The resultant adducts

(1) (a) Ternansky, R. J.; Balogh, D. W.; Paquette, L. A. *J. Am. Chem. Soc.* **1982**, *104*, 4503. (b) Paquette, L. A.; Ternansky, R. J.; Balogh, D. W.; Kentgen, G. *Ibid.* **1983**, *105*, 5446.

(2) For an outline of the chronology with which our ideas and experimentation evolved, see: Paquette, L. A. In "Strategies and Tactics of Organic Synthesis"; Lindberg, T., Ed.; Academic Press: New York, 1984; pp 175–200.

(3) Eaton, P. E. *Tetrahedron* **1979**, *35*, 2189.

(4) For a discussion of the use of this trivial nomenclature, consult footnote 4 of ref 8.

(5) Nickon A.; Pandit, G. D. *Tetrahedron Lett.* **1968**, 3663.

(6) Garratt, P. J.; White, J. F. *J. Org. Chem.* **1977**, *42*, 1733.

(7) (a) Eaton, P. E.; Mueller, R. H. *J. Am. Chem. Soc.* **1972**, *94*, 1014. (b) Eaton, P. E.; Mueller, R. H.; Carlson, G. R.; Cullison, D. A.; Cooper, G. F.; Chou, T.-C.; Krebs, E.-P. *Ibid.* **1977**, *99*, 2751.

(8) Preliminary communication: Paquette, L. A.; Browne, A. R.; Doecke, C. W.; Williams, R. V. *J. Am. Chem. Soc.* **1983**, *105*, 4113.

(9) Kricka, L. J.; Ledwith A. *Synthesis* **1974**, 539.

(10) Paquette, L. A.; Carr, R. V. C. *J. Am. Chem. Soc.* **1980**, *102*, 7553.

(11) Paquette, L. A.; Carr, R. V. C.; Charumilind, P.; Blount, J. F. *J. Org. Chem.* **1980**, *45*, 4922.

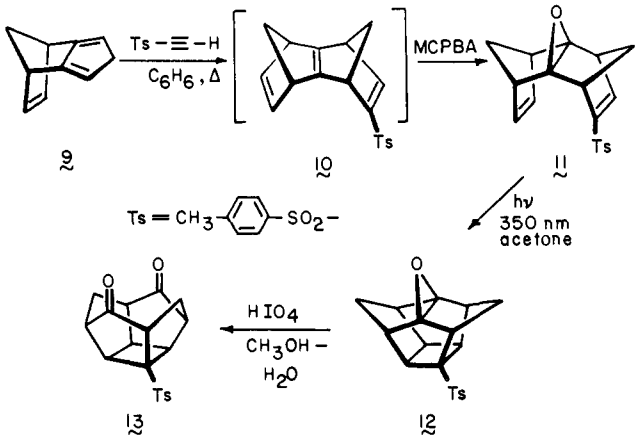
(12) Alder, K.; Flock, F. H.; Janssen, P. *Chem. Ber.* **1956**, *89*, 2689.

(13) (a) Paquette, L. A.; Carr, R. V. C.; Böhm, M. C.; Gleiter, R. *J. Am. Chem. Soc.* **1980**, *102*, 1186. (b) Böhm, M.; Carr, R. V. C.; Gleiter, R.; Paquette, L. A. *Ibid.* **1980**, *102*, 7218.

0002-7863/85/1507-0686$01.50/0

possess a central double bond in addition to the parallel and spatially syn-locked norbornenyl moieties. The brevity of this scheme was equally appealing and work was therefore initiated along these lines.

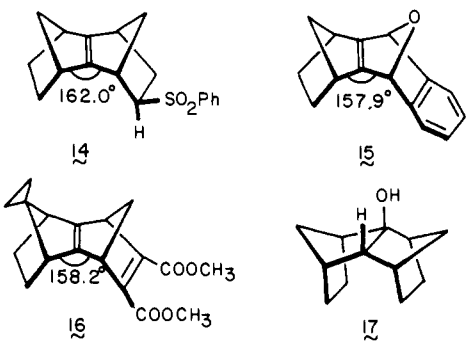
Construction of the [4]Peristylane Framework. Triene **9** was heated with (*p*-tolylsulfonyl)acetylene[14] in benzene solution under an inert atmosphere to give **10**. Because of the tendency of **10** to undergo air oxidation, a property shared by this general class of compounds,[10,15] no attempt was made to isolate the adduct per se. Rather, the substance was directly subjected to controlled peracid oxidation. Epoxide **11** was subsequently isolated in 98%



overall yield as a homogeneous colorless crystalline solid. The conversion to **11** simultaneously revealed the stereochemical course of the cycloaddition and further compressed the remaining π systems in a face-to-face arrangement.

The syn orientation of the methano bridges in **11** was made particularly apparent upon inspection of its ^1H and ^{13}C NMR spectra. The widely differing chemical shifts of the inner and outer protons at both sites (δ 2.22 and 1.38, nearly degenerate pairs in $CDCl_3$ at 90 MHz) testify to the pronounced diamagnetic anisotropy experienced by the two that are proximate to the epoxide ring.[16,17] Additionally, the pair of methylene bridge carbons (45–47 ppm) is appreciably shielded,[18,19] in satisfyingly close agreement with features exhibited by related molecules.[15]

Although *syn*-sesquinorbornenes such as **14** are recognized to be folded out of plane in a downward direction by dihedral angles approximating 15°,[20-22] the effect is more pronounced when an



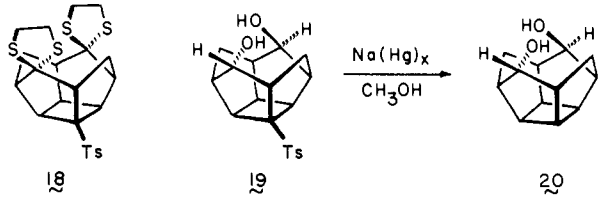
additional double bond is present as in **15**[23] and **16**,[24] presumably due to the absence of a pair of hydrogen atoms on the underside of the molecule. Saturation of the *syn*-sesquinorbornene central double bond from the exo face necessitates adoption of tetrahedral character at these centers. The net consequence of this hybridization change is a major increase in the level of nonbonded steric repulsion. A recent analysis of **17** by X-ray crystallography has revealed the intimate details of this heightened steric interaction.[25] This compression is believed to be the root cause of the enormously high solvolytic reactivity of the derived *p*-nitrobenzoate, the most reactive tertiary system known to date.[26]

The presence of the arenesulfonyl group, so necessary for facilitating the earlier Diels–Alder reaction, was now deployed to advantage a second time. Upon irradiating acetone solutions of **11** through Pyrex in a Rayonet apparatus with 350-nm light, ready conversion to **12** occurred.[27] This end result confirmed that the initial [4 + 2] addition had indeed taken place from the below-plane surface of **9**.

The exceptional susceptibility of **17** to ionization under acidic conditions suggested that conversion of **12** to the 1,2-diol would equally be driven by relief of ring strain. Futhermore, the unique structural features of this molecule require that capture of solvent water occur with retention of configuration. This being the case, the use of periodic acid as hydration catalyst should be followed in course by cleavage of the *cis*-diol to deliver **13**.[28] In actual fact, heating **12** with this oxidizing agent in refluxing methanol for 18 h afforded the desired diketo sulfone in 95% yield.

The Hemispherical Hydrocarbon. From the standpoint of minimal manipulation, the most desirable sequence from **13** to **1** would involve reductive removal of the carbonyl groups followed by desulfonylation. As we were not able to develop Wolff–Kishner conditions conducive to efficient deoxygenation of the diketo sulfone, **13** was transformed into dithioketal **18** only to find that desulfurization with Raney nickel likewise could not be satisfactorily achieved.

As a consequence, we proceeded to reduce **13** with triethylsilane and gaseous boron trifluoride[29] at 0 °C and obtained **19**, although in less than satisfactory yield. Longer reaction times and somewhat higher temperatures did not improve matters. When the subsequent reduction of **19** with 6% sodium amalgam in anhydrous methanol was found to deliver **20** with less than 50% efficiency,



a more synthetically viable pathway to **1** was sought.

A high level of success was achieved when desulfonylation was implemented first. Carbonyl protection was now required, and recourse was therefore made to ketal **21a**. Treatment of this intermediate with lithium in ethylamine[30] and ensuing acid hy-

(14) Bhattacharya, S. N.; Josiah, B. M.; Walton, D. R. M. *Organometal. Chem. Synth.* **1970**, *1*, 145.
(15) Paquette, L. A.; Kravetz, T. M.; Böhm, M. C.; Gleiter, R. *J. Org. Chem.* **1983**, *48*, 1250.
(16) Paquette, L. A.; Fristad, W. E.; Schuman, C. A.; Beno, M. A.; Christoph, G. G. *J. Am. Chem. Soc.* **1979**, *101*, 4645 and references cited therein.
(17) Paquette, L. A.; Charumilind, P.; Böhm, M. C.; Gleiter, R.; Bass, L. S.; Clardy, J. *J. Am. Chem. Soc.* **1983**, *105*, 3136.
(18) Zefirov, N. S.; Kasyan, L. I.; Snedenkov, L. Y.; Shashkov, A. S.; Cherepanova, E. G. *Tetrahedron Lett.* **1979**, 949.
(19) Paquette, L. A.; Carr, R. V. C.; Arnold, E.; Clardy, J. *J. Org. Chem.* **1980**, *45*, 4907.
(20) Watson, W. H.; Galloy, J.; Bartlett, P. D.; Roof, A. A. M. *J. Am. Chem. Soc.* **1980**, *103*, 2022.
(21) Hagenbuch, J.-P.; Vogel, P.; Pinkerton, A. A.; Schwarzenbach, D. *Helv. Chim. Acta* **1981**, *64*, 1819.
(22) This subject has been treated theoretically: Houk, K. N.; Rondan, N. G.; Brown, F. K.; Jorgensen, W. L.; Madura, J. D.; Spellmeyer, D. C. *J. Am. Chem. Soc.* **1983**, *105*, 5980 and relevant references cited therein.
(23) Bartlett, P. D.; Combs, G. L., Jr. *J. Org. Chem.* **1984**, *49*, 625.
(24) Paquette, L. A.; Green, K. E.; Gleiter, R.; Schafer, W.; Gallucci, J. C., unpublished results.
(25) Paquette, L. A.; DeLucca, G.; Ohkata, K.; Gallucci, J. C., unpublished results.
(26) Paquette, L. A.; Ohkata, K.; Carr, R. V. C. *J. Am. Chem. Soc.* **1980**, *102*, 3303.
(27) Compare: (a) Cookson, R. C.; Crundwell, E. *Chem. Ind. (London)* **1958**, 1004. (b) Prinzbach, H.; Sedelmeier, G.; Kruger, C.; Goddard, R.; Martin, H.-D.; Gleiter, R. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 171. (c) Jones, G., II; Becker, W. G.; Chiang, S.-H. *J. Photochem.* **1982**, *19*, 245; *J. Am. Chem. Soc.* **1983**, *105*, 1269.
(28) (a) Nagarkatti, J. P.; Ashley, K. R. *Tetrahedron Lett.* **1973**, 4599. (b) Mori, K. *Tetrahedron* **1978**, *34*, 915. (c) Kim, M. Y.; Starrett, J. E., Jr.; Weinreb, S. M. *J. Org. Chem.* **1981**, *46*, 5383.
(29) Fry, J. L.; Orfanopoulos, M.; Adlington, M. G.; Dittman, W. R., Jr.; Silverman, S. B. *J. Org. Chem.* **1978**, *43*, 374.

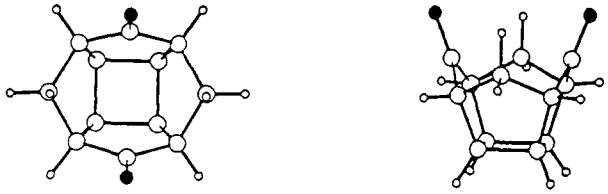
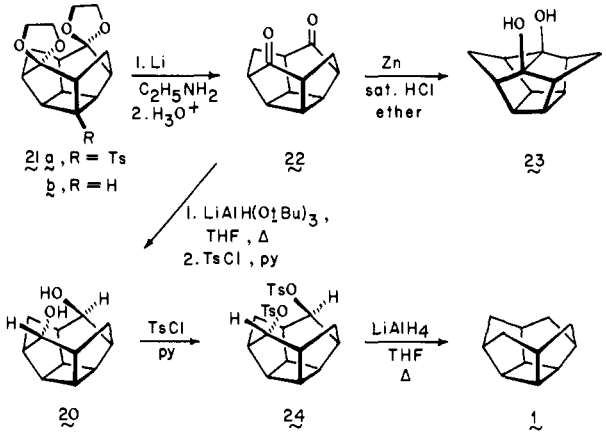


Figure 1. A top and side view of [4]peristylane-2,6-dione (**22**).[32]

drolysis marked arrival at [4]peristylane-2,6-dione (**22**) in 69% overall yield from **13**. The C_{2v} symmetry of this diketone was unmistakingly revealed by its four-line ^{13}C NMR spectrum. Molecular models suggested that **22** might well adopt a pouch-shaped ground-state conformation.[31] Thus, the apparent need of the "inside" methylene hydrogens to move apart as far as possible could lead to a compression of the two carbonyl groups since these sites lack a comparably high nonbonded steric interaction. These considerations led us to determine its X-ray crystal structure.[32] Interestingly, almost perfect C_{2v} symmetry was found (Figure 1). However, whereas the four-membered ring and both five-membered rings bearing the ketone groups are essentially planar, the other two five-membered rings exist in half-chair conformations.

Notwithstanding, the carbonyl functions in **22** are capable of facile transannular interaction. For example, the action of zinc in ether saturated with dry hydrogen chloride on **22** resulted in pinacolization and conversion to diol **23**.

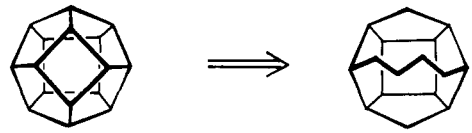
To avoid this complication, **22** was reduced with lithium tri-*tert*-butoxyaluminum hydride. Diol **20** was isolated in quantitative yield. The endo,endo configuration of the hydroxyl groups was



clearly indicated on the basis of the observed coupling constant between the C*H*OH protons and the neighboring hydrogens (J = 8 Hz, ca. 10° dihedral angle). If the OH groups were outside, the relevant angle would be on the order of 100–110° and the resulting spin–spin interaction would be quite small.[7] The bistosylation of **20** proceeded smoothly. Conversion to [4]peristylane (**1**) was completed by exposure of **21** to lithium aluminum hydride in refluxing ether for 8 h. At higher temperatures and/or longer reaction times, **1** was rather rapidly destroyed.

The waxy crystalline target hydrocarbon was expectedly volatile, though unexpectedly high melting (>225 °C). Its 200-MHz ^1H NMR spectrum (in $CDCl_3$) consists of only four groups of absorptions, each of equal area: multiplets at δ 2.98–2.91 and 2.65–2.54, a doublet of triplets (J = 13.7 and 9.9 Hz) at δ 2.15, and a sharp doublet (J = 13.7 Hz) at δ 1.65. The proton-decoupled ^{13}C NMR spectrum has absorption lines of approximately equal intensity at 48.44, 46.85, and 46.31 ppm, again in accord with the fourfold symmetry of the molecule. A comparison of these carbon chemical shifts with those of [3]peristylane (47.13, 40.25, 37.08 ppm)[6] and [5]peristylane (63.1, 48.6, 43.5 ppm)[7] is informative.

Preliminary Attempts at the "Belting" of [4]Peristylane. The successful conversion of **22** to *p*-[$4^2.5^8$]decahedrane (**2**) could rest on the development of a successful strategem for "capping" of the [4]peristylane framework. In simplest terms, **2** can be viewed as a derivative of **1** that carries four interlocked carbon atoms annealed to the superstructure. Antithetic dissections of **2** to **25** are



2 25

conceptually possible, though the task of experimental reconstruction is hardly trivial. Nevertheless, considerable useful information could well be gained by examining methods for "belting" [4]peristylanes, i.e., bridging the gap with chains of varied atomic length. The adoption of **22** as precursor molecule of choice was obviously predicated on its symmetry and ketonic character.

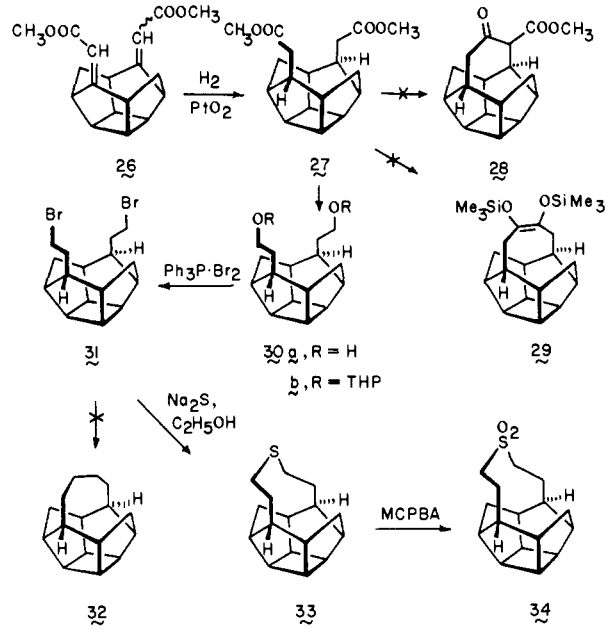
When **22** was subjected to Wadsworth–Emmons condensation[34] with excess trimethyl phosphonoacetate, bis-homologated α,β-unsaturated diester **26** was obtained as a mixture of geometric isomers. Direct catalytic hydrogenation of this material afforded **27** as a clear, colorless oil. The stereochemical homogeneity of this product was evident from its simplified ^1H NMR spectrum, which is reasonable only for a structure having two planes of symmetry. Concordant with steric factors prevailing within **26**, the delivery of hydrogen should have occurred from its exo surface to force the acetic ester residues into the interior of the molecular cavity in **27**.

Despite the *apparent* proximity of the functional groups in **27**, we were unable to effect Dieckmann[35] or acyloin cyclization[36] of the diester. Various bases and reaction conditions were examined and considerable attention was paid to optimization of these parameters (high dilution, etc.), but to no avail. This inability to construct a three- or four-carbon belt in the manner indicated by **28** and **29** is taken to be a reflection of the severe nonbonded steric interactions that necessarily come into being as the carbon atoms destined to be linked begin to align themselves into the geometry necessary for condensation.

These complications caused us to focus attention instead on the conversion of **27** to dibromide **31**. Following diisobutylaluminum hydride reduction to alcohol **30a**, the sequence was continued by conversion to the bis(tetrahydropyranyl) ether **30b** prior to treatment with triphenylphosphine dibromide.[37] As previous experience had suggested,[38] this two-step process delivered **31** most efficiently. The functionality in **31** offers multiple options for further chemical reaction. Pursuit of the coupling scheme first described by Whitesides and Gutowski[39] was initially undertaken. Thus, **31** was allowed to react with excess magnesium metal and the resulting double Grignard reagent was exposed to silver triflate with appropriate control of the dilution factor. Although mixtures of hydrocarbons did result, GC–MS analysis of these oils gave no evidence for the presence of a compound having the molecular weight required for **32**.

Notwithstanding, reaction of **31** with sodium sulfide under high-dilution conditions[40] did lead successfully to sulfide **33** in 43% yield. The ^1H NMR spectrum showed only three regions

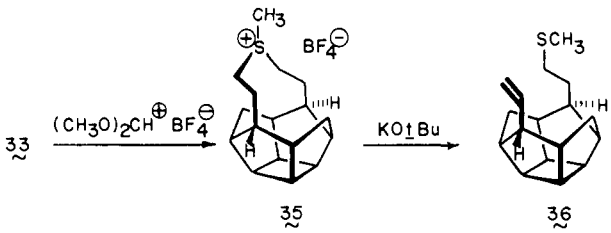
(30) Grieco, P. A.; Masaki, Y. *J. Org. Chem.* **1974**, *39*, 2135.
(31) For a more highly pronounced example of this behavior, consult: Christoph, G. G.; Engel, P.; Usha, R.; Balogh, D. W.; Paquette, L. A. *J. Am. Chem. Soc.* **1982**, *104*, 784.
(32) Engel, P.; Fischer, J. W.; Paquette, L. A. *Z. Kristallogr.* **1984**, *166*, 225.
(33) Toda, M.; Hirata, Y.; Yamamura, S. *J. Chem. Soc., Chem. Commun.* **1969**, 919.
(34) Wadsworth, W. S., Jr. *Org. React.* **1977**, *25*, 73.
(35) Schaefer, J. P.; Bloomfield, J. *J. Org. React.* **1967**, *15*, 1.
(36) Bloomfield, J. J.; Owsley, D. C.; Nelke, J. M. *Org. React.* **1976**, *23*, 259.
(37) (a) Schwarz, M.; Oliver, J. E.; Sonnet, P. E. *J. Org. Chem.* **1975**, *40*, 2410. (b) Sonnet, P. E. *Synth. Commun.* **1976**, *6*, 1211.
(38) (a) Park, H.; King, P. F.; Paquette, L. A. *J. Am. Chem. Soc.* **1979**, *101*, 4773. (b) Hales, N. J.; Paquette, L. A. *J. Org. Chem.* **1979**, *44*, 4603.
(39) Whitesides, G. M.; Gutowski, F. D. *J. Org. Chem.* **1976**, *41*, 2882.
(40) Friedman, P.; Allen, P. *J. Org. Chem.* **1965**, *30*, 780.



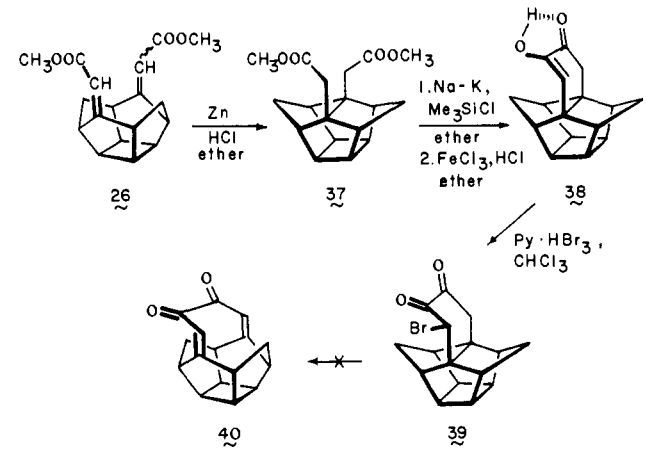
of absorption in the ratio of 4:8:10, as expected for the relative proportion of α-thio, methylene, and methine protons within the molecule. In agreement with the C_{2v} symmetry, the proton-decoupled ^{13}C NMR spectrum showed only six lines for the 16 carbon atoms. The acquisition of **33** realistically constituted the first *chemical* proof of the stereochemical assignments to **27**, **30**, and **31**.

We now concentrated our efforts on the possible ring contraction of **33** via the Ramberg–Bäcklund reaction[41] or Stevens rearrangement.[42] When attempts to involve **33** in sequential α-chlorination/oxidation[43] did not give rise to the desired α-chloro sulfone, **34** was prepared and subjected to the action of potassium *tert*-butoxide in carbon tetrachloride.[44] Extensive experimentation generated no evidence for formation of the ring-contracted cycloalkene.

Having been thwarted in these attempts, we turned to the preparation of sulfonium salt **35** by reaction of **33** with dimethoxycarbenium tetrafluoroborate.[45] When **35** was treated in turn with strong bases such as potassium *tert*-butoxide, however, the desired Stevens rearrangement sequence involving initial α-proton abstraction was not followed. Instead, β-elimination was kinetically favored and **36** was obtained.



Bridging of [4]peristylane by a four-carbon chain clearly proved to be more difficult than we had anticipated. A possible means of overcoming the complications encountered to this point suggested itself. Thus, *temporary* installation of a central bond not only introduces a strategically important control element that has been heretofore lacking but also substantially alters the molecular geometry in a beneficial way. To illustrate these points, let us consider the facile reduction of **26** to **37**. This easily executed reaction proceeds smoothly to generate a functionalized bishomopentaprismane in quantitative yield. The benefits derived from



the presence of the intraannular double bond can be seen in the readiness with which **37** undergoes acyloin condensation (compare the recalcitrance of **27**). Direct oxidation of the acyloin product furnished α-diketone **38**, which expectedly exists as its monoenolized, internally hydrogen bonded tautomer. Conversion of **38** to the corresponding α-bromo derivative with pyridinium hydrobromide perbromide was straightforward. Unfortunately, all attempts to achieve 1,4-dehydrobromination within **39** have come to naught. The stereoelectronic alignment necessary to the success of this Grob-type fragmentation appears to be present. Also, **40** does not appear to be substantially more strained than **29** or **32**. However, an untoward element in this synthetic logic is realization that the CHBrCO proton is the most acidic within **39** and could well be removed first. Subsequent fragmentation of this enolate system is rather unlikely. At the experimental level, **39** was not recovered intact following exposure to base.

Summary

Thermal and photochemical cycloaddition methodology has been demonstrated to provide a ready and remarkably efficient synthetic entry (4 steps, 93% overall yield) to the [4]peristylane ring system. Removal of the arenesulfonyl and carbonyl groups in **13** so as to arrive at parent hydrocarbon **1** requires an additional series of six laboratory manipulations. The "belting" of ketone **22** has been briefly explored and so far found to be feasible only when five atoms are spanned across the molecular hemisphere. The desired shortening of these chains necessitates compression of internal angles and engenders heightened nonbonded steric interactions. Although these topographical changes may ultimately be useful for arrival at **2**, they clearly will require that suitable reactions, perhaps photochemical in type, be applied to achieve contraction of the chain. Further development of this and related chemistry is planned.

Experimental Section

3-((4-Methylphenyl)sulfonyl)[2,5:7,10]dimethano-11-oxatricyclo-[4.4.1.0^{1,6}]undeca-3,8-diene (11). A magnetically stirred solution of **9** (1.70 g, 13 mmol) and *p*-tolylsulfonylacetylene (2.34 g, 13 mmol) in dry benzene (45 mL) was heated at reflux under dry nitrogen for 18 h. The reaction mixture was cooled, diluted with dry dichloromethane (25 mL), and stirred at 0 °C while sodium bicarbonate (1.5 g) and then *m*-chloroperbenzoic acid (2.8 g of 85% purity, 13.9 mmol) were added. After 1 h at this temperature, 5% sodium bicarbonate solution was added and the layers were separated. The aqueous phase was extracted with dichloromethane and the combined organic phases were washed with 10% sodium bisulfite solution and brine prior to drying. Evaporation gave **11** as a semisolid after trituration with ethyl acetate (4.15 g, 98%). Recrystallization from ethyl acetate delivered off-white crystals: mp 150–151 °C; IR (KBr, cm^{-1}) 2980, 1315, 1300, 1289, 1145, 1087, 851, 820, 811, 730, 668, 588, 563, 548; ^1H NMR (90 MHz, $CDCl_3$) δ 7.53 (ABq, $\Delta\nu_{AB}$ = 0.41, J = 8 Hz, 4 H), 6.89 (d, J = 3 Hz, 1 H), 6.66 (dd, J = 5.5 and 3 Hz, 1 H), 6.08 (dd, J = 5.5, 3 Hz, 1 H), 3.33–3.00 (m, 4 H), 2.42 (s, 3 H), 2.22 (br t, J = 7 Hz, 2 H), 1.38 (br t, J = 7 Hz, 2 H); ^{13}C NMR ($CDCl_3$, ppm) 154.12 (s), 153.51 (d), 145.20 (d), 144.49 (s), 141.05 (d), 137.11 (s), 129.90 (d), 127.82 (d), 75.33 (s) 74.90 (s), 53.63 (t), 52.15 (t), 47.29 (d), 46.69 (d), 45.76 (d), 45.59 (d), 21.59 (q).

(41) Paquette, L. A. *Org. React.* **1977**, *25*, 1.
(42) See ref 41, footnotes 107–116 for examples.
(43) Paquette, L. A.; Wingard, R. E., Jr.; Philips, J. C.; Thompson, G. L.; Reed, L. K.; Clardy, J. *J. Am. Chem. Soc.* **1971**, *93*, 4508 and relevant references cited therein.
(44) See ref 41, footnotes 93–102.
(45) Borch, R. F. *J. Org. Chem.* **1969**, *34*, 627.

Anal. Calcd for $C_{19}H_{18}O_3S$: C, 69.91; H, 5.56. Found: C, 69.72; H, 5.53.

2-((4-Methylphenyl)sulfonyl)-11-oxaheptacyclo[7.3.1.0^{2,8}.0^{3,7}.0^{4,12}.0^{6,10}.0^{10,12}]tridecane (12). A solution of **11** (200 mg) in acetone (2 mL) was irradiated in a Pyrex tube (3-mm i.d.) in a Rayonet apparatus equipped with 350-nm bulbs for 2.5 h. Solvent evaporation gave **12** (200 mg, 100%) as colorless crystals: mp 138–139 °C (from ethyl acetate); IR (KBr, cm^{-1}) 2970, 1594, 1308, 1295, 1285, 1140, 762; ^{1}H NMR (90 MHz, $CDCl_3$) δ 7.53 (ABq, $\Delta\nu_{AB}$ = 0.42, J = 8 Hz, 4 H), 3.20–2.97 (m, 3 H), 2.77–2.20 (series of m, 4 H), 2.39 (s, 3 H), 1.70–1.20 (series of m, 4 H); ^{13}C NMR ($CDCl_3$, ppm) 144.87 (s), 134.57 (s), 129.91 (d), 129.09 (d), 71.12 (s), 63.98 (s), 62.43 (s), 43.93 (d), 43.06 (d), 42.62 (d), 39.03 (d), 38.79 (d), 38.40 (d), 37.47 (d), 33.40 (t), 21.60 (q) (one C overlapped or not observed).

Anal. Calcd for $C_{19}H_{18}O_3S$: C, 69.91; H, 5.56. Found: C, 69.69; H, 5.68.

9-(*p*-Tolylsulfonyl)[4]peristylane-2,6-dione (13). A magnetically stirred solution of **12** (1.90 g, 5.8 mmol) in 10% aqueous methanol (50 mL) was treated with periodic acid (2.5 g, 11 mmol) and heated under reflux for 18 h. The resulting purple mixture was added to water (50 mL) and extracted with dichloromethane (3 × 50 mL). The combined organic layers were washed with 20% sodium bisulfite solution (2 × 50 mL) and brine (50 mL) prior to drying and evaporation. There was obtained 1.9 g (95%) of **13** as an off-white solid after trituration with ethyl acetate. Recrystallization from this solvent delivered colorless crystals: mp 181.5–183 °C; IR (KBr, cm^{-1}) 2925, 1725, 1594, 13.3, 1398, 1220, 1140, 1066, 1011, 850, 821, 751, 666; ^{1}H NMR, $CDCl_3$) δ 7.60 (ABq, $\Delta\nu_{AB}$ = 0 '2, J = 8.3 Hz, 4 H), 3.97 (q, J = 8.6 Hz, 2 H), 3.55 (q, J = 8.6 Hz, I), 2.91 (dd, J = 8.6, 2.4 Hz, 1 H), 2.84 (dd, J = 8.6, 2.4 Hz, 1 H), /3 (q, J = 8.3 Hz, 2 H), 2.47 (s, 3 H), 2.34 (d, J = 13.3 Hz, 1 H), 2.24 (d, J = 13.3 Hz, 1 H), 2.16 (dt, J = 13.3, 8.9 Hz, 1 H), 1.75 (dt, J = 13.3, 8.9 Hz, 1 H); ^{13}C NMR ($CDCl_3$, ppm) 225.30 (s), 221.90 (s), 154.64 (s), 133.31 (s), 130.31 (d), 129.16 (d), 75.12 (s), 55.83, 53.85, 53.27, 52.70, 45.67, 44.58, 41.58, 41.13, 39.86, 21.71 (q); mass spectrum, m/z calcd (M^+) 342.0926, obsd 342.0937.

Anal. Calcd for $C_{19}H_{18}O_4S$: C, 66.64; H, 5.30. Found: C, 66.51; H, 5.40.

Ketalization of 13. A mixture of **13** (2.6 g, 7.6 mmol), *p*-toluenesulfonic acid (1.0 g) and ethylene glycol (10 mL) in dry benzene (100 mL) was heated at reflux under a Dean–Stark trap for 2 days. The cooled solution was poured with stirring into 10% sodium carbonate solution (100 mL), the organic phase was separated, and the aqueous layer was further extracted with benzene (2 × 50 mL). The combined benzene solutions were washed with brine, dried, and evaporated to give, after trituration with ethyl acetate, 3.2 g (97%) of **21a** as a colorless solid. Recrystallization from ethyl acetate afforded small needles, mp 193–195 °C.

Anal. Calcd for $C_{23}H_{26}O_6S$: C, 64.16; H, 6.09. Found: C, 64.12; H, 6.09.

[4]Peristylane-2,6-dione (22). Ketal **21a** (2.9 g, 6.7 mmol) was placed in a 250-mL three-necked flask equipped with a dry ice condenser. Ethylamine (120 mL) was condensed in the flask and the resulting solution was stirred at 0 °C while lithium metal (2.5 g cut into small pieces) was added. After the color had turned blue, excess Li metal was removed and the reaction mixture was carefully treated with saturated ammonium chloride solution. After the excess lithium had reacted, additional ammonium chloride solution (100 mL) was introduced and the mixture was extracted with ether (3 × 50 mL). The combined organic extracts were washed with brine, dried, and evaporated to give **21b** as a pale yellow oil that was taken up in tetrahydrofuran (30 mL) and stirred with 2 M hydrochloric acid (10 mL) for 3 h. Water (100 mL) was added, and the product was extracted into dichloromethane (3 × 50 mL). The combined extracts were washed with brine, dried, and evaporated to leave a pale yellow semisolid. MPLC of this material on silica gel (elution with 35% ethyl acetate in petroleum ether) provided **22** as colorless needles: mp >300 °C (sublimes i· sealed tube) (from ethyl acetate), 0.90 g (71%); IR (KBr, cm^{-1}) 30(35, 2865, 1725, 1446, 1227, 1158, 861, 705; ^{1}H NMR (300 MHz. .) δ 3.52–3.47 (m, 4 H), 2.71–2.66 (m, 4 H), 2.65 ($^1/_2$ABq, J Hz, 2 H), 2.16–2.05 (m, 2 H); ^{13}C NMR ($CDCl_3$, ppm) 22 ', 42.7, 41.8.

Anal. Calcd fc $_2O_2$: C, 76.57; H, 6.43. Found: C, 76.69; H, 6.64.

Transannular Re e Cyclization of 22. Anhydrous ether (15 mL) was saturated at 0 ' ith dry hydrogen chloride. Diketone **22** (28.7 mg, 0.15 mmol) was added followed by portionwise introduction of activated zinc powder (1.5 g) during 10 min. The resultant mixture was stirred at 0 °C for 1 h and at room temperature for 1 h before being poured into ice water. Neutralization was effected with solid sodium carbonate and the mixture was extracted with ether (2×). Drying and solvent removal furnished **23** as a pale yellow solid. Trituration with hot hexane left a white solid (21.4 mg, 74%). Recrystallization from hexane afforded colorless needles: mp >300 °C (sealed tube); IR (KBr, cm^{-1}) 3300, 2970, 2875; ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.62–2.54 (m, 4 H), 2.48 (br s, 2 H), 2.29 (m, 4 H), 2.04 (d, J = 10.7 Hz, 2 H), 1.42 (d, J = 10.7 Hz, 2 H); mass spectrum, m/z calcd (M^+) 190.0994, obsd. 190.1021.

Anal. Calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.56; H, 7.39.

***endo*,*endo*-[4]Peristylane-2,6-diol (20).** Lithium tri-*tert*-butoxyaluminum hydride (3.35 g, 13.18 mmol) was dissolved with stirring in dry tetrahydrofuran (6 mL) under nitrogen. A solution of **22** (323 mg, 1.72 mmol) in the same solvent (4 mL) was rapidly added dropwise at room temperature, and this mixture was heated at reflux for 7 h, cooled, and treated with saturated ammonium chloride solution. The inorganic salts were filtered off and washed 3 times with tetrahydrofuran. The combined filtrates were dried and evaporated. The residue was triturated with boiling ethyl acetate, filtered, and again evaporated. There was obtained 335 mg (100%) of **20** as fine colorless plates: mp >300 °C (from ethyl acetate–hexane, 1:2); IR (KBr, cm^{-1}) 3240, 2965, 2950, 1115, 1100, 970; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.31 (t, J = 9.5 Hz, 2 H), 3.00–2.93 (m, 4 H), 2.76–2.62 (m, 4 H), 2.47–2.42 (m, 4 H), 1.52 (t, J = 14.9 Hz, 2 H), 1.47 (t, J = 14.9 Hz, 2 H); ^{13}C NMR ($CDCl_3$, ppm) 77.96, 49.71, 45.24, 28.40.

Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 74.99; H, 8.38.

***endo*,*endo*-[4]Peristylane-2,6-diol Ditosylate (24).** A solution of **20** (176 mg, 0.92 mmol) and *p*-toluenesulfonyl chloride (699 mg, 3.66 mmol) in dry pyridine (7 mL) was stirred at room temperature for 48 h, poured into ice water, and extracted with dichloromethane (3×). The combined extracts were washed twice with 10% hydrochloric acid, saturated sodium bicarbonate solution, and brine, then dried, and evaporated. The resulting off-white solid was recrystallized from hexane–ethyl acetate (6:4) to give **24** as clear colorless needles: mp 152.5–153.5 °C (327 mg, 71%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81 (d, J = 8.3 Hz, 2 H), 7.34 (d, J = 8.3 Hz, 2 H), 4.64 (t, J = 7.9 Hz, 2 H), 2.93–2.82 (m, 4 H), 2.63–2.47 (m, 6 H), 2.45 (s, 6 H), 1.46 (t, J = 11.8 Hz, 2 H), 1.41 (t, J = 11.8 Hz, 2 H).

Anal. Calcd for $C_{26}H_{28}O_6S_2$: C, 62.38; H, 5.64. Found: C, 62.38; H, 5.64.

[4]Peristylane (1). Lithium aluminum hydride (260 mg, 6.53 mmol) was slurried in anhydrous ether (50 mL) under argon while solid **24** (327 mg, 0.65 mmol) was added in one portion. This mixture was stirred at room temperature for 10.5 h and at the reflux temperature for 8 h, cooled, and treated with saturated ammonium chloride solution. The inorganic solids were separated by filtration and washed with ether (3×). The combined organic layers were washed with 10% sodium thiosulfate solution (2×) and brine, dried, and filtered. The majority of the solvent was removed by distillation at atmospheric pressure. Cooling at this juncture caused precipitation of 50 mg of unreacted **24**. The filtrate was subjected to preparative TLC on silica gel (pentane elution). The base-line material consisted of additional recovered **24** (135 mg) while the band with R_f 0.95 was **1**. Sublimation at 50 °C and 760 torr gave **1** as a colorless crystalline solid: mp >225 °C (sealed tube); 5.5 mg (9%); ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.98–2.9 (m, 4 H), 2.65–2.54 (m, 4 H), 2.19 (t, J = 9.9 Hz, 2 H), 2.12 (t, J = 9.9 Hz, 2 H), 1.65 (d, J = 9.9 Hz, 4 H); ^{13}C NMR ($CDCl_3$, ppm) 48.44, 46.85, 46.31; mass spectrum, m/z calcd (M^+) 160.1252, obsd 160.1316.

Wadsworth–Emmons Homologation of 22. Sodium hydride (2.5 g of 50% oil suspension, 50 mmol) was placed in the reaction flask and washed twice with dry benzene. The solid reagent was then slurried in dry benzene (150 mL) as (trimethylphosphono)acetate (9.15 g, 50 mmol) was added dropwise. When vigorous gas evolution had ceased, the reaction mixture was stirred at room temperature for 3 h under a nitrogen atmosphere. Diketone **22** (1.88 g, 10 mmol) was introduced and heating at the reflux temperature was maintained for 14 h. After cooling, the contents were poured into water (200 mL), the organic phase was separated, and the aqueous layer was extracted with ether (2 × 200 mL). The combined organic solutions were washed with water (100 mL) and brine (100 mL) prior to drying and evaporation. The residual yellow oil (3.0 g) was chromatographed on Florisil to give **26** as an oily mixture of geometric isomers (1.50 g, 50%).

This material was dissolved in glacial acetic acid (20 mL), platinum oxide (50 mg) was added, and the mixture was hydrogenated in a Parr apparatus under 50 psi for 2.5 days. Filtration through Celite to remove the catalyst was followed by neutralization with saturated sodium bicarbonate solution and ether extraction (3 × 100 mL). The combined ether layers were washed with water (100 mL) and brine (100 mL), dried, and evaporated. There was obtained 1.40 g (94%) of **27** as a clear colorless oil: IR (neat, cm^{-1}) 2940, 1740, 1430, 1260, 1160, 1000; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.66 (s, 6 H), 2.98 (m, 4 H), 2.53 (d, J =

7.7 Hz, 8 H), 2.30 (m, 2 H), 1.78–1.50 (m, 4 H); mass spectrum, m/z calcd (M^+) 304.1668, obsd 304.1711.

***endo,endo*-2,6-Bis(2-bromoethyl)[4]peristylane (31).** Diisobutyl aluminum hydride (25.3 mL of 1.0 M in hexane, 25.3 mmol) was added dropwise to a magnetically stirred solution of **27** (1.75 g, 5.76 mmol) in anhydrous tetrahydrofuran (40 mL) at 0 °C under nitrogen. After 1 h at this temperature, the reaction mixture was stirred at 22 °C for 4 h, treated with Rochelle's salt to destroy the excess hydride, and allowed to stand overnight. Water (50 mL) was introduced and the product was extracted into ether (3 × 50 mL). The combined organic layers were washed with water (50 mL) and brine (50 mL) prior to drying. Solvent removal under reduced pressure afforded 1.61 g of viscous oil that crystallized on standing. Purification by silica gel chromatography (elution with 25% ethyl acetate in petroleum ether) gave 1.30 g (92%) of **30a** as a colorless solid: IR ($CHCl_3$, cm^{-1}) 3350, 2910; ^1H NMR (300 MHz, $CDCl_3$) δ 3.63 (t, J = 7.2 Hz, 4 H), 2.93 (m, 4 H), 2.42 (br s, 6 H), 1.9–1.6 (m, 8 H), 1.49 (dt, J = 15, 11.5 Hz, 2 H); ^{13}C NMR ($CDC)_3$, ppm) (t), 48.67 (d), 47.25, (2d), 33.09 (t), 27.51 (t).

A solution of **30a** (80 mg, 0.32 mmol), dihydropyran (0.12 mL, 1.3 mmol), and pyridinium tosylate (10 mg) in dry dichloromethane (15 mL) was stirred under nitrogen at 20 °C for 2 days. Additional dichloromethane (20 mL) was added prior to washing with water (3 × 10 mL) and brine (10 mL). Drying and solvent evaporation afforded 200 mg of a pale yellow viscous oil, which was purified by MPLC on silica gel (elution with 10% ethyl acetate in petroleum ether). There was isolated 110 mg (83%) of **30b** as a white solid, mp 54–55 °C, spectral analysis of which showed it to be a mixture of diastereomers: IR (KBr, cm^{-1}) 2980, 1440, 1015, 900; ^1H NMR (300 MHz, $CDCl_3$) δ 4.56 (t, J = 4 Hz, 2 H), 3.70 (m, 4 H), 3.40 (m, 4 H), 2.91 (br s, 4 H), 2.46 (br s, 4 H), 2.0–1.25 (m, 2 H); ^{13}C NMR ($CDCl_3$, ppm) 98.97, 67.42, 62.40, 48.84, 48.67, 47.91, 47.30, 30.90, 30.03, 27.57, 25.60, 19.75; mass spectrum, m/z calcd (M^+) 416.2926, obsd 416.2916.

Bromine (0.23 mL, 4.5 mmol) was added dropwise to a cold (0 °C) magnetically stirred solution of triphenylphosphine (1.18 g, 4.5 mmol) in dry dichloromethane (10 mL) under nitrogen. After 15 min, **30b** (420 mg, 1 mmol) dissolved in the same solvent (5 mL) was added dropwise. The reaction mixture was stirred at 0 °C for 2 h and at room temperature for 16 h. Following dilution with dichloromethane (20 mL), the dark brown solution was washed with water (3 × 20 mL) and brine (20 mL), dried, and evaporated. Purification of the brown residue by chromatography on silica gel (elution with petroleum ether) afforded 250 mg (67%) of **31** as a colorless crystalline solid: mp 73–74 °C (from ethyl acetate); IR (KBr, cm^{-1}) 146, 1435, 1110, 620; ^1H NMR (300 MHz, $CDCl_3$) δ 3.43 (t, J = 7 Hz, 4 H), 2.98 (m, 4 H), 2.52 (br s, 4 H), 2.05 (m, 6 H), 1.76–1.54 (m, 4 H); ^{13}C NMR ($CDCl_3$, ppm) 49.4., 48.12, 47.14, 33.31, 33.14, 27.51.

Anal. Calcd for $C_{16}H_{22}Br_2$: C, 51.36; H, 5.93. Found: C, 51.34; H, 6.01.

Cyclic Sulfide 33. A 5-mL syringe was charged with a solution of **31** (40 mg, 0.11 mmol) in 100% ethanol (5 mL). A second 5-mL syringe was charged with a solution of sodium sulfide nonahydrate (51 mg, 0.22 mmol) in 90% ethanol (5 mL). The syringes were fitted to a syringe pump, and their exit needles were led down a condenser to a flask contg. boiling 100% ethanol (40 mL). The solutions were simultaneously added over a 20-h period to the rapidly stirred reaction mixture. After the addition was completed, heating was continued for another 4 h. The cooled reaction mixture was poured into water (50 mL) and extracted with ether (2 × 50 mL). The combined ether layers were washed with water (50 mL) and brine (50 mL) prior to drying and solvent removal. There was isolated 13.1 mg (43%) of **33**: mp 257–260 °C dec; IR (KBr, cm^{-1}) 2940, 2865, 1410, 1275; ^1H NMR (200 MHz, $CDCl_3$) δ 2.97 (m, 4 H), 2.51 (m, 8 H), 2.0–1.4 (series of m, 10 H); ^{13}C NMR ($CDCl_3$, ppm) 51.73, 48.73, 47.30, 32.60, 31.83, 27.83; mass spectrum, m/z calcd (M^+) 246.1442, obsd 246.1431.

Anal. Cald for $C_{16}H_{22}S$: C, 77.99; H, 9.00. Found: C, 77.90; H, 8.96.

Oxidation of 33. A solution of *m*-chloroperbenzoic acid (23 mg, 0.11 mmol) in dichloromethane (2 mL) was added dropwise to a cold (0 °C) solution of **33** (13 mg, 0.05 mmol) in the same solvent (3 mL) under nitrogen. The reaction mixture was stirred at room temperature for 13 h and poured into water (10 mL). The aqueous phase was extracted with dichloromethane (2 × 10 mL), and the combined organic layers were washed with 10% sodium thiosulfate (10 mL) and saturated sodium bicarbonate solutions (10 mL), water (10 mL), and brine (10 mL). Drying and solvent evaporation afforded 12.5 mg (90%) of sulfone **34** as a white solid: mp >350 °C dec; IR (KBr, cm^{-1}) 2940, 1300, 1115; ^1H NMR (300 MHz, $CDCl_3$) δ 3.04 (m, 8 H), 2.55 (br s, 4 H), 2.15–1.50 (series of m, 10 H); m/z calcd (M^+) 278.1340, obsd 278.1326.

Methylation and Attempted Stevens Rearrangement of 33. A solution of **33** (50 mg, 0.2 mmol) and dimethoxycarbenium tetrafluoroborate (1 mL) in benzene (6 mL) was stirred at room temperature under a nitrogen atmosphere for 32 h. The thick white precipitate of **35** was separated from solvent by decantation and dissolved in dry tetrahydrofuran (10 mL). Following the addition of potassium *tert*-butoxide (224 mg, 2 mmol), the mixture was stirred at room temperature for 24 h, poured into water (20 mL), and extracted with chloroform (3 × 20 mL). The combined organic layers were washed with water (20 mL) and brine (20 mL), dried, and evaporated. The residual viscous yellow oil was purified by chromatography on Florisil (elution with petroleum ether). There was isolated 21 mg (21%) of **36** as a colorless viscous oil: IR (neat, cm^{-1}) 3060, 2940, 1635, 1460, 1430, 1420, 905; ^1H NMR (200 MHz, $CDCl_3$) δ 6.2–6.0 (m, 1 H), 5.2–4.95 (m, 2 H), 3.10–2.85 (m, 4 H), 2.8–2.3 (m, 8 H), 2.10 (s, 3 H), 2.0–1.5 (m, 6 H); mass spectrum, m/z calcd (M^+) 260.1608, obsd 1598.

Transannular Reductive Cyclization of 26. An ethereal solution (5 mL) of **26** (50 mg, 0.17 mmol) and zinc dust (2.5 g) was added to ether (20 mL) that had been saturated with hydrogen chloride at 0 °C for 1 h. The reaction mixture was stirred for 1 h at 0 °C and 1 h at room temperature, diluted with ether (100 mL), and neutralized with saturated sodium bicarbonate solution. The organic phase was washed with water (100 mL) and brine (100 mL), dried, and evaporated. There was obtained 50 mg (99%) of **37** as a colorless viscous oil: IR ($CDCl_3$, cm^{-1}) 2960, 1735, 1440, 1330, 1200; ^1H NMR (300 MHz, $CDCl_3$) δ 3.64 (s, 6 H), 2.58 (br s, 4 H), 2.41 (br s, 4 H), 2.21 (s, 4 H), 1.80 (d, J = 11 Hz, 2 H), 1.39 (d, J = 11 Hz, 2 H); ^{13}C NMR ($CDCl_3$, ppm) 172.89, 63.32, 51.35, 50.37, 43.10, 37.96, 35.55; mass spectrum, m/z calcd (M^+) 302.1543, obsd 302.1518.

Acyloin Cyclization–Oxidation of 37. To a rapidly stirred mixture of sodium–potassium alloy (from 140 mg of Na and 230 mg of K) and chlorotrimethylsilane (5 mL) in anhydrous ether (150 mL) was added a solution of **37** (150 mg, 0.5 mmol) in the same solvent (10 mL) via syringe pump over a period of 40 h. Upon completion of the addition, the purple reaction mixture was stirred for an additional 4 h and carefully filtered through Celite (careful—pyrophoric residue). The filtrate was concentrated, redissolved in 10 mL of ether, added dropwise to a stirred mixture of ferric chloride (290 mg, 1.5 mmol) and concentrated hydrochloric acid (6 drops) in ether (10 mL), and heated at reflux for 1 h. Following cooling to 0 °C, saturated ammonium sulfate solution (15 mL) was added, and the layers were separated. The aqueous phase was extracted with ether (20 mL), and the combined organic solutions were washed with water (20 mL) and brine (20 mL), dried, and concentrated. The residue was purified by preparative TLC on silica gel (elution with 5% ethyl acetate in petroleum ether) and 38.2 mg (32%) of **38** was obtained as a white solid: mp 137.5–138.5 °C; IR (CCl_4, cm^{-1}) 3474, 2860, 2780, 1715, 1680, 1655, 1420, 1235; ^1H NMR (300 MHz, $CDCl_3$) δ 6.02 (s, 1 H), 5.96 (s, 1 H), 2.77–2.68 (m, 4 H), 2.66 (s, 2 H), 2.26 (m, 2 H), 2.08 (m, 2 H), 1.77 (d, J = 11 Hz, 2 H), 1.44 (d, J = 11 Hz, 2 H); ^{13}C NMR ($CDCl_3$, ppm) 195.32, 146.66, 121.35, 55.38, 53.74, 44.38, 43.30, 42.33, 38.13 (two quaternary carbons not observed); mass spectrum, m/z calcd (M^+) 240.1150, obsd 240.1119.

To arrive at bromide **39**, equimolar amounts of **38** and pyridinium hydrobromide perbromide in chloroform solution were stirred at 0 °C for 3 h and washed with 10% sodium thiosulfate solution and brine, followed by drying and solvent evaporation. The resulting pale yellow oil, which exhibits a sharp one-proton singlet at δ 3.7, was generally used without further purification.

Acknowledgment. The financing of this research by the National Institutes of Health via Grant AI-11490 is deeply appreciated.