that was identified with a previously described sample by comparison of IR and NMR spectra.

E. Thermal Stability. After a solution of 170 mg (1.12 mmol) of the enone **2** in 10 mL of anhydrous PhH had been refluxed under a N_2 atmosphere for 10 days, the solution was concentrated to leave 165 mg (97%) of the unchanged enone **2**, $n^{25}D$ 1.5272, that was identified with an authentic sample by comparison of IR and NMR spectra. Similarly, a solution of 160 mg (1.0 mmol) of the enone in 5 mL of decalin (bp ~190 °C) was refluxed under a N_2 atmosphere for 48 h. After the mixture had been chromatographed on a short silica gel column with an EtOAc–hexane eluent (1:1 (v/v)), distillation of the later fractions separated 104 mg (65%) of the unchanged enone **2**, $n^{25}D$ 1.5272, that was identified with an authentic sample by comparison of IR spectra. Examination of the recovered decalin and the distillation residue failed to indicate the presence of any other product such as a nonconjugated ketone formed by cycloaddition.

Registry No. **2**, 70562-48-0; **3b**, 70562-49-1; **4**, 1121-66-0; **6**, 66921-76-4; **7**, 70562-50-4; **9**, 66077-95-0; **10**, 70562-51-5; **11**, 70562-52-6; **12**, 70562-53-7; **14**, 70562-54-8; **15**, 70562-55-9; **19**, 70576-36-2; **20**, 70576-35-1; **21a**, 70562-56-0; **21b**, 70562-57-1; **22**, 70562-58-2; methyl 1-methoxy-8-hydroxybicyclo[4.3.1]dec-7-ene-7-carboxylate, 70562-59-3; methyl 1-cyano-8-hydroxybicyclo[4.3.1]dec-7-ene-7-carboxylate, 70562-60-6; methyl 1-bromo-8-hydroxybicyclo[4.3.1]dec-7-ene-7-carboxylate, 70562-61-7; *tert*-butyl 1-methoxy-8-hydroxybicyclo-[4.3.1]dec-7-ene-7-carboxylate, 70562-62-8; cycloheptanone, 502-42-1; $HOCH_2CH_2OH$, 107-21-1; 2-bromocycloheptanone ethylene ketal, 70562-63-9; 2-cycloheptanone ethylene II ketal, 184-26-9; ethyl acetoacetate, 141-97-9; *tert*-butyl acetoacetate, 1694-31-1.

Peristylenones and Norperistylenones: Highly Reactive Intermediates. Synthesis of Dodecahedrane Precursors. 2[1f,g]

Philip E. Eaton,* Gerald D. Andrews, Ernst-Peter Krebs, and Atsutaka Kunai

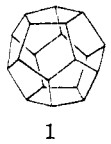
Contribution from the Department of Chemistry, Searle Chemistry Laboratory, The University of Chicago, Chicago, Illinois 60637

Received January 17, 1979

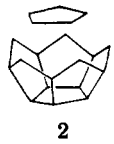
The synthesis of substituted, functionalized peristylanes (hexacyclo[7.5.1.$0^{3,13}$.$0^{5,12}$.$0^{7,11}$.$0^{10,14}$]pentadecane) and norperistylanes (hexacyclo[6.6.0.0^{2,6}.$0^{3,13}$.$0^{4,12}$.$0^{10,14}$]tetradecane) designed as dodecahedrane precursors is described. Included are pentafunctional peristylanes, e.g., 4,8,15-tris(diethylamino)peristylane-2,6-dione, tetrafunctional norperistylanes, e.g., norperistylane-5,7,9,11-tetrone, and norperistylanes and peristylanes carrying carbon substituents, e.g., 7,9-dicarbomethoxynorperistylane-5,11-dione and 4-(2,5-dioxocyclopent-1-yl)peristylane-2,6-dione, the last containing all of the 20 carbons needed for dodecahedrane. These compounds were prepared by way of Michael additions to peristylenones and norperistylenones. In turn, these α,β-unsaturated ketones were made from the saturated systems reported earlier by elimination of $H_\alpha X_\beta$ or by decomposition of phenyl selenoxide derivatives. Peristylenones and norperistylenones are shown to be exceptionally reactive compounds, forming Diels–Alder adducts with furan at room temperature. This is accounted for by recognizing that the π system in these compounds must be twisted from planarity, away from full p-orbital overlap, by the geometric demands of the molecular skeleton. Some spectroscopic evidence to this point is given. The synthesis of a peristylane bearing a bulky endo carbon substituent is described. The NMR spectrum of this compound is compared to that of the less hindered exo isomer to obtain an idea of the conformational preferences of the endo substituent in the congested peristylane cavity. Useful procedures are described for the oxidative degradation of a β-alkyl-substituted acetylacetone to the alkyl carboxylic acid and for the hydrolysis and decarboxylation of a methyl nitroacetate. A new method is given to trap phenylselenenic acid, a product of phenyl selenoxide eliminations, before it consumes the desired olefin product in unwanted side reactions.

Introduction

Dodecahedrane (1), the organic chemist's transliteration



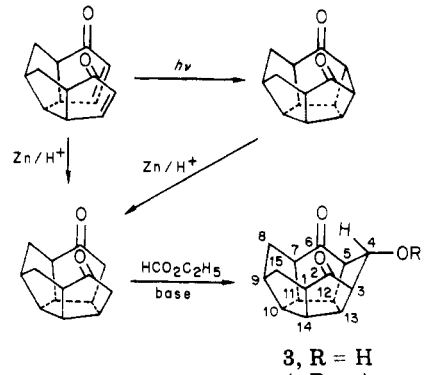
1



2

of the twelve-faced Platonic solid, presents a significant challenge. A number of interestingly different approaches to its synthesis have been devised, and reports of progress are increasingly frequent.[1] This paper is concerned with a portion of our own continuing efforts, in particular, with the chemistry of the peristylane system.[1f,g] As is evident from the drawing, peristylane (2) differs (conceptually) from dodecahedrane only by a well-placed cyclopentane ring. Clearly, adding this ring correctly requires proper site preparation, i.e., the introduction of useful functionality on each of the methylene groups of peristylane.

Chart I



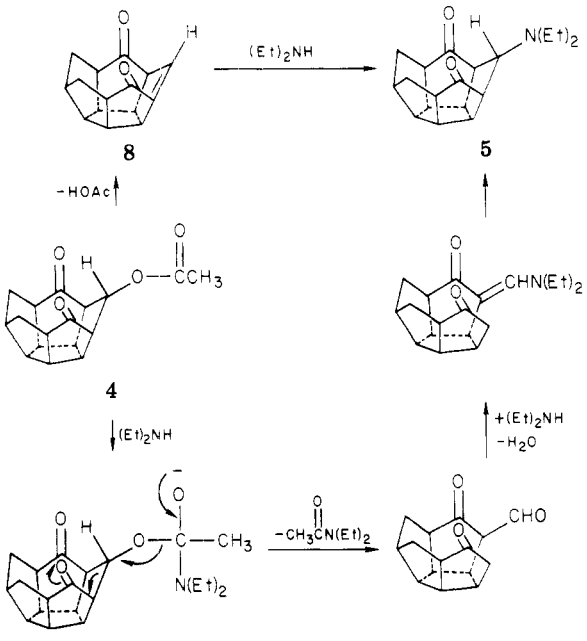
3, R = H
4, R = Ac

The synthesis of the peristylane system,[1g] the last steps of which are given in Chart I, is such that first entry occurs

(1) (a) R. B. Woodward, T. Fukunaga, and R. C. Kelley, *J. Am. Chem. Soc.*, **86**, 3162 (1964); (b) I. T. Jacobson, *Acta Chem. Scand.*, **21**, 2235 (1967); (c) N. J. Jones, W. D. Deadman, and E. LeGoff, *Tetrahedron Lett.*, 2087 (1973); (d) D. McNeil, B. R. Vogt, J. J. Sudol, S. Theodoropulos, and E. Hedaya, *J. Am. Chem. Soc.*, **96**, 4673 (1974); (e) L. A. Paquette, S. V. Ley, and W. B. Farnham, *J. Am. Chem. Soc.*, **96**, 311 (1974); L. A. Paquette, W. B. Farnham, and S. V. Ley, *ibid.*, **97**, 7273 (1975); L. A. Paquette, I. Itoh, and W. B. Farnham, *ibid.*, **97**, 7280 (1975); L. A. Paquette, M. J. Wyvratt, O. Schualler, D. F. Schneider, W. J. Begley, and R. M. Blankenship, *ibid.*, **98**, 6744 (1976); L. A. Paquette, I. Itoh, and K. B. Lipkowitz, *J. Org. Chem.*, **41**, 3524 (1976); L. A. Paquette, R. A. Snow, J. L. Muthard, and T. Cynkowski, *J. Am. Chem. Soc.*, **100**, 1600 (1978); (f) P. E. Eaton and R. H. Mueller, *ibid.*, **94**, 1014 (1972); (g) P. E. Eaton, R. H. Mueller, G. R. Carlson, D. A. Cullison, G. F. Cooper, T.-C. Chou, and E.-P. Krebs, *ibid.*, **99**, 2751 (1977). For a review of various efforts, see P. E. Eaton, *Tetrahedron*, in press.

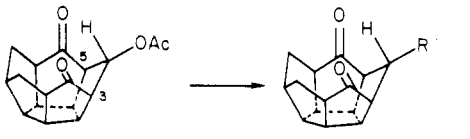
0022-3263/79/1944-2824$01.00/0

Chart II



at 4-hydroxyperistylane-2,6-dione (**3**), best handled as the corresponding acetate, **4**.[2] At this point, three of the five methylene groups of the parent hydrocarbon are functionalized; we deal now with the problem of functionalizing the other two.

Peristyl-3-ene-2,6-dione. The key to solving this problem was the early observation that the acetate group of **4** is remarkably easily replaced by simple nucleophiles.



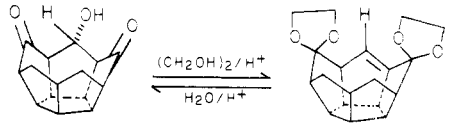
4

5, R = $N(CH_2CH_3)_2$
6, R = $-OCH_2CF_3$
7, R = $-OCH_3$

Thus, for example, reaction of **4** with diethylamine gives the amine derivative **5** in excellent yield. Similarly, reaction with trifluoroethanol and base gives the trifluoroethyl ether **6**.[3] Related conversions include hydrolysis of **5** to alcohol **3** and formation of methyl ether **7** on reaction of **5** with methanol and ammonium chloride. In each case, it is clear from the ^1H NMR spectra that the stereochemistry at C-4 is preserved; that is, the substituent occupies the exo position, away from the confines of the peristylane cavity. This follows from the small nuclear coupling ($J < 2$ Hz) of the C-4 hydrogen to the adjacent methine protons at C-3 and C-5, appropriate for a dihedral angle near 110°.[4] Had inversion occurred, exo → endo, the dihedral angle of concern would have been near 10° and the coupling constant much larger.

The ready replacements at position 4, as we shall show, occur via intermediate **8** (Chart II), peristyl-3-ene-2,6-dione, a strained enone of noteworthy reactivity. We admit, however, that this hypothesis was dismissed at first thought for a model of the peristylene system "showed" it to be very strained, and it was already known that double bonds in equivalent locations in much less rigid bicyclo[3.3.0]octanes are distinctly unfavorable.[5] As we were unable initially to detect enone **8** in these reactions or to prepare it by pyrolysis of **4**, we devised a more complex explanation for conversions like **4** → **5** involving reverse aldol ring opening, substitution, and reclosure as outlined, for example, in Chart II. Such a scheme requires for the case illustrated production of *N,N*-diethylacetamide—a stable, readily identifiable compound. In the real event, quantitative conversion of **4** → **5**, none of this acetamide is formed.

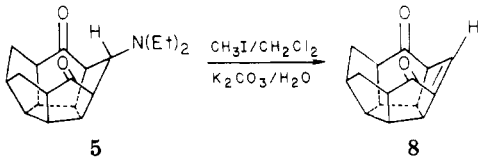
Fortunately, just at this time, we found that it was possible to make and isolate stable peristyl*enes* much more simply than expected. Thus, reaction of **3** or **4** with ethylene glycol and acid under standard ketalizing conditions gives peristylene **9**.[1g] This compound is quite



3 **9**

stable, melting at 99–100 °C without decomposition. On hydrolysis in aqueous acid it gives back hydroxydione **3**, presumably via Michael addition of water to an intermediate enone. This implies, of course, that **8** is a reasonable compound.

In due course, we were able to find suitable conditions for the preparation and isolation of peristylenone **8**. Reaction of 4-(diethylamino)peristylane-2,6-dione (**5**) with methyl iodide in the two-phase system methylene chloride–aqueous potassium carbonate at room temperature works well. Apparently, the methylene chloride soluble amine is transformed in the organic phase to the quaternary ammonium salt which then passes into the water layer. Here, elimination of triethylamine generates the water-insoluble enone which moves to the hydrophobic haven of the methylene chloride in which the concentration of available nucleophile is low. Evaporation of the methylene chloride followed by high-pressure LC purification of the residue gives unsaturated ketone **8** in 80% yield, pure by analytical TLC.



5 **8**

Peristyl-3-ene-2,6-dione (**8**) is a white, crystalline compound, mp 195 °C (dec). Of particular interest in its 270-MHz ^1H NMR spectrum (see Experimental Section) is the one-proton, high-field signal centered at δ 1.22, about 0.5 ppm above the highest field absorption of the parent dione, of peristylane itself, or of peristyl*ene* **9**. Clearly, some special conformational feature must be invoked to understand this resonance. We find from consideration of molecular models of **8** that flattening of the α,β-unsaturated ketone subunit to achieve the greatest degree

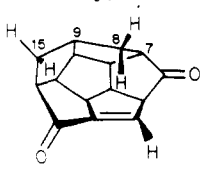
(2) See footnote 2 of ref 1g for the nomenclature of these systems. The numbering for the parent hydrocarbons is applied, without regard for the substitutent hierarchy, to the present cases to avoid confusion.

(3) Trifluoroethanol/base behaves very differently from ethanol/base. The fluorinated alcohol is more acidic (pK_a = 12.4)[3a] and much less nucleophilic.[3b] Its salts are less basic and less destructive than those of ethanol. Although trifluoroethoxide is a poor nucleophile in S_N2 reactions, it is an effective addend in Michael reactions.[3c] See: (a) R. Filler and R. M. Schure, *J. Org. Chem.*, **32**, 1217 (1967); (b) W. S. Trahanovsky and M. P. Doyle, *Tetrahedron Lett.*, 2155 (1968); (c) F. L. Scott, *Chem. Ind. (London)*, 224 (1959).

(4) M. J. Karplus, *J. Chem. Phys.*, **30**, 11 (1959); *J. Am. Chem. Soc.*, **85**, 2870 (1963).

(5) H. Stetter, I. Krüger-Hansen, and M. Rizk, *Chem. Ber.*, **94**, 2702 (1961); P. E. Eaton, C. Giordano, G. Schloemer, and U. Vogel, *J. Org. Chem.*, **41**, 2238 (1976).

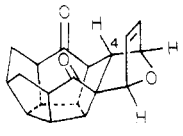
of parallel p-orbital overlap forces the endo hydrogen on C-8 inward toward the shielding region of the π system (drawing 8a). Concurrently, the dihedral angle between



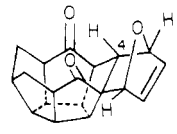
8a

this proton and the adjacent methine protons at C-7 and C-9 is increased to about 150°. Thus, H(endo)C-8 should be shifted upfield, and its coupling to the vicinal protons should increase over that observed ($J \simeq 2$–4 Hz) in less distorted peristylanes in which the dihedral angle is nearer 110°. Indeed, the high-field resonance at δ 1.22 is split, in addition to the usual geminal coupling, into a triplet with J = 10 Hz. Part and parcel of the conformational change which moves H(endo)C-8 inward is movement of H(endo)C-15 outward (away from the peristylene cavity) and reduction of the dihedral angle to the vicinal protons from about 110° to, perhaps, 90°. In accord, the doublet resonance (geminal coupling) at δ 1.90 for H(endo)C-15 is only slightly broadened by vicinal coupling, quite different from that of H(endo)C-8.

Enone 8 is stable to storage as a solid for months at 0 °C. In concentrated solution (>0.5 M), polymerization beyond dimerization occurs, and after a few days at room temperature the enone is completely gone. The strained double bond is quite reactive. Diels–Alder addition to furan occurs rapidly at room temperature. Two adducts, 10 and 11, are formed in a ratio of roughly 3:1. The major



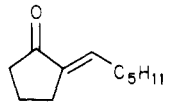
10



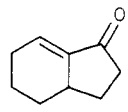
11

adduct is assigned the stereochemistry illustrated (Diels–Alder endo transition state), for neither NMR signal (δ 4.76, 4.59) for the protons at the oxide bridgeheads is coupled noticeably to the proton at C-4. Appropriately, the dihedral angle between HC-4 and the adjacent bridgehead proton is near 90° in this isomer. The minor adduct 11, the result of an exo addition, has a dihedral angle of near 0° between these protons and, in accord with the Karplus relation,[4] an oxide bridgehead proton (δ 5.04) is coupled significantly (J = 4.9 Hz) to HC-4.

The ease of reaction of enone 8 with furan is noteworthy. Most cyclic enones will not undergo Diels–Alder reactions with furan and certainly not under such mild conditions.[6] The present case is reminiscent of the reactions of highly strained unsaturated compounds like *trans*-2-cyclooctenone in which full π overlap of the carbon–carbon double-bond p orbitals is prevented by the geometric constraints of the molecule.[7] Indeed, the C–C double bond of 8 is probably twisted in a similar way, but to a lesser extent. The infrared spectrum of 8 indicates that the C–C double bond is weakened (ν 1600 cm^{-1}) in comparison to that of model enones 12 and 13 (ν 1650 cm^{-1}).[8] Steric constraints in 8 also appear to reduce the conjugation



12

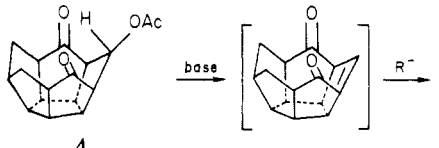


13

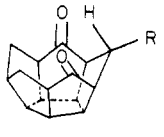
between the double bond and its adjacent ketone group;[9] the extinction coefficient for the ultraviolet $\pi \rightarrow \pi^*$ absorption (λ_{max}^{THF} 256 nm, ϵ 5100) is much reduced in comparison to that of 12 (λ_{max} 252 nm,[10] ϵ 11 300).[8a] Loss of effective conjugation probably also accounts for the fact that the usual ordering of the α- and β-vinyl carbon signals of a conjugated enone, β at much lower field,[11a] is reversed in the ^{13}C NMR spectrum of 8. The vinyl carbon positions (α at δ 150.1, singlet; β at δ 132.5, doublet, $J_{^{13}C-H}$ = 170 Hz) are not much different from those expected for quaternary and tertiary vinyl carbons.[11b]

Although the enone subunit in 8 is distorted geometrically from that of the classical conjugated α,β-unsaturated ketone, Michael additions to it still occur with ease. For example, and in accord with our explanation of the conversion 4 → 5, diethylamine adds readily to 8 giving 5 quantitatively.

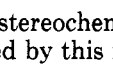
More interesting to us synthetically are the additions of carbon nucleophiles that can ultimately be made part of the carbon frame of dodecahedrane itself. The enone is an excellent acceptor in the sense of the Michael reaction for stabilized carbanions. For example, reaction of acetate 4 with dimethyl malonate and sodium methoxide in methanol at room temperature results in attachment of the malonate moiety, $CH(COOCH_3)_2$, to the peristylane giving compound 14, mp 145–146 °C, in 92% yield. Presumably, this reaction proceeds by addition of dimethyl malonate anion to enone 8, generated on site by base-induced elimination of acetic acid from 4. Similarly, we have also used the enone to "C-alkylate" methyl nitroacetate, acetylacetone, and cyclopentane-1,3-dione obtaining 15, 16, and 17, respectively, each characterized spectroscopically. Attention is drawn particularly to the last of these, compound 17, which contains all 20 carbon atoms needed for dodecahedrane.



4 8



14, R = $-CH(CO_2CH_3)_2$
15, R = $-CH(NO_2)COOCH_3$
16, R = $-CH(O{=}CCH_3)_2$
17, R =



As illustrated, we have assigned exo stereochemistry to the C-4 carbon substituents introduced by this method. This is in accord with the earlier heteroatom examples 5–7,

(6) M. P. Kunstman, D. S. Tarbell, and R. L. Autrey, *J. Am. Chem. Soc.*, 84, 4115 (1962); W. G. Dauben and H. O. Krabbenhaft, *ibid.*, 98. 1992 (1976); F. Kienzle, *Helv. Chim. Acta*, 58, 1180 (1975).

(7) P. E. Eaton and K. Lin, *J. Am. Chem. Soc.*, 86, 2087 (1964).

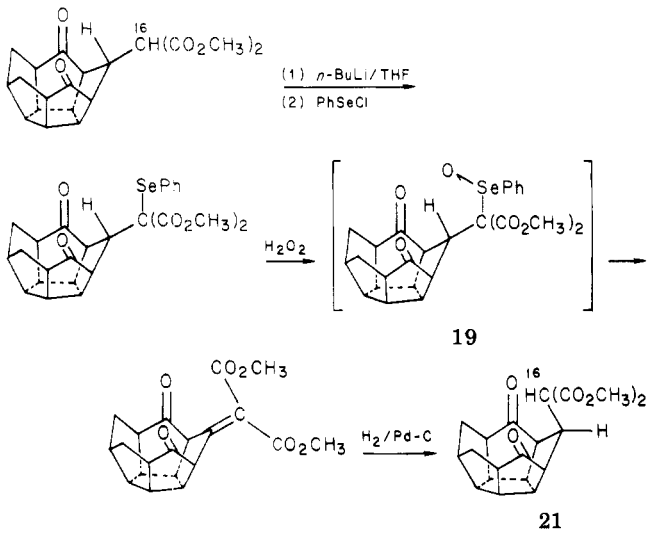
(8) (a) Sadtler Research Laboratories, "Ultraviolet Spectra", No. 19456 and "Standard Infrared Prism Spectra", No. 42356; (b) L. A. Paquette, R. P. Henzel, and R. F. Eizember, *J. Org. Chem.*, 38, 3257 (1973).

(9) See the discussion in Chapter 15 of H. H. Jaffe and M. Orchin, "Theory and Applications of Ultraviolet Spectroscopy", Wiley, New York, 1962.

(10) Corrected for the change in solvent from the reported λ_{max}^{MeOH} 245 nm.

(11) (a) J. Jautelat, J. B. Grutzner, and J. D. Roberts, *Proc. Natl. Acad. Sci. U.S.A.*, 65, 288 (1970); K. Nakanishi, R. Crouch, I. Miura, X. Diminguez, A. Zamudio, and R. Villarreal, *J. Am. Chem. Soc.*, 96, 609 (1974); (b) Cf. M. G. Venegas and R. D. Little, *Tetrahedron Lett.*, 309 (1979).

Chart III



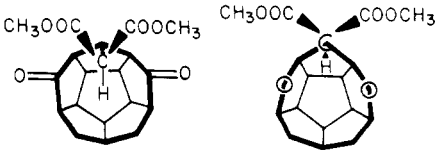
direct NMR evidence (vide infra), and the convincingly simple notion that Michael additions to enone **8** should occur preferentially to the less hindered, outer side of the peristylane rim.

Endo Substituted Peristylanes. It should be obvious on reference to drawings **2** and **17** that, if we are to use peristylanes like **14–17** to complete the skeleton of dodecahedrane, we must invert the attachment at C-4 from exo to the less stable endo stereochemistry. We have devised an appropriate methodology for the systems at hand and illustrate it here for the inversion of the malonate group of **14**.

Treatment of the dimethyl malonate adduct **14** with 1 equiv of *n*-butyllithium in THF followed by 1 equiv of phenylselenenyl chloride gives fairly cleanly and in good yield the phenyl selenide **18**, mp 189–190 °C (Chart III). As the kinetic acidity of the malonate proton is very much greater than that of those α to the peristylane ketone groups, there is little uncertainty about the direction of selenenylation. This is confirmed by the ^{1}H NMR spectrum of **18** which shows clearly that the product has mirror-plane symmetry. As expected, the selenide is easily oxidized by hydrogen peroxide in THF to the corresponding selenoxide **19**. This material is not isolated; it undergoes spontaneous loss of phenyl selenenic acid to give olefin **20**, a beautifully crystalline, stable compound, mp 177–178 °C. Its assigned structure is fully consistent with the analytical and spectroscopic data. This sequence of reactions for the introduction of a double bond by way of selenium-containing intermediates is derived, of course, from the exceedingly nice studies of Sharpless, Reich, and their co-workers,[12] of which we have made much use. In the case at hand, the overall yield for **14** → **20** is a satisfying 70%.

Catalytic hydrogenation of **20** in ethyl acetate over neutral 10% palladium-on-carbon[1g] results in hydrogen delivery to the less hindered, outer face of the molecule, giving "inside", endo malonate **21**, mp 210 °C (dec). Although this reduction is very slow, the ultimate yield is very good. The structure of the product follows unambiguously from its origin and spectral comparison to its progenitor, **14**. The ^{13}C NMR spectra of these configurational isomers confirm the presence of a mirror plane of symmetry in each. In the ^{1}H NMR spectra, as anticipated, the resonance for the proton at C-4 in **14** is nearly unsplit, $J < 2$ Hz, by the adjacent protons at C-3 and C-5 (dihedral angle about 110°) but is strongly coupled, $J = 9.1$ Hz, in isomer **21** (dihedral angle approximately 10°). There are remarkable differences in the position and coupling of the malonate proton (HC-16) in the two isomers. In **14**, in which the malonate group is exo—in an environment not unlike that of any simple malonate derivative—the proton at C-16 appears at δ 3.58, an ordinary position. Its coupling to the adjacent proton at C-4 is 5.8 Hz, like that in many such sp^3–sp^3-bound systems in which rotation about the bond is essentially unhindered on the NMR time scale, and no particular conformer predominates greatly. In isomer **21**, however, in which the malonate group is endo and cannot avoid interaction with much of the peristylane structure, the C-16 proton is shifted downfield by 1.09 ppm to δ 4.67, 0.9 ppm *below* even the methyl ester signals. This large deshielding can only arise from the influence of the induced anisotropic magnetic fields about the ketone groups of the peristylane.

As inspection of a Büchi model shows, a peristylane conformation like **21a** of fivefold symmetry (ignore



21a 21b

functionality/hybridization) or a small distortion therefrom places the C-16 proton of **21** in the shielding cones of the ketone groups at C-2 and C-6. Just the opposite is required to rationalize the ^{1}H NMR spectrum of this compound. A substantial distortion from fivefold symmetry in which C-2 and C-6 are moved inward and nearer and C-4 out and away from the center, as in **21b**, is needed to put the proton of C-16 into an environment of average deshielding, near the ketone oxygen and to the side of the plane orthogonal to that of C–C(=O)–C and passing through the carbonyl group. Conformation **21b** accomplishes this fairly well and has the further advantage of reducing the bulk steric interactions of the endo malonate substituent with the other atoms along the peristylane rim.[13]

Rotation about the C-4, C-16 bond in **21** is hindered by the bulky attachments; rotomers in which one or the other carbomethoxy groups on C-16 approach being "inside" the peristylane bowl are distinctly unfavorable sterically. We can confidently expect that "on the average" the proton on C-16 is likely to occupy the inside position. This being the case, the average dihedral angle between HC-16 and HC-4 is near 180°, and the coupling constant between these two protons should be larger than in isomer **14** in which rotation is less hindered and the average angle smaller. Indeed, the observed HC-16, HC-4 coupling constant in **21** is 12.2 Hz, more than double that in **14**.

The ketone carbons of **14** and **21** appear substantially shifted in the ^{13}C NMR spectra—in **14** at δ 208.1, a fairly normal position; in **21** at δ 223.1, notably further downfield. Steric compression against the closely placed proton at C-16 might account for this downfield shift. A more in-

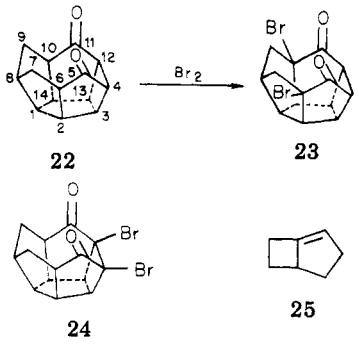
(12) K. B. Sharpless, R. F. Lauer, and A. Y. Teranishi, *J. Am. Chem. Soc.*, **95**, 6137 (1973); H. J. Reich, J. M. Renga, and I. L. Reich, *ibid.*, **97**, 5434 (1975). For additional references and contributors see the excellent review article by D. L. J. Clive, *Tetrahedron*, **34**, 1049 (1978).

(13) The change in ^{1}H NMR chemical shift of HC-16 on changing solvent from chloroform to benzene is much larger for **21** (+0.51 ppm) than for **14** (+0.12 ppm). This fits nicely with the location of HC-16 relative to the carbonyl groups in conformation **21b**. See the discussion of benzene-induced chemical shifts by P. Laszlo in *Prog. NMR Spectrosc.* **3**, 348–390 (1967).

teresting possibility is hydrogen bonding of this proton to a ketone oxygen, decreasing the electron density at the ketone carbon. Unfortunately, resolution of the separate infrared absorptions of the carbonyl groups in **14** and **21** has not been possible, and we are unable to offer independent evidence for this idea.

Norperistylenones. The facile formation of the enone subunit on the peristylene rim suggests that it might be possible to introduce this group into the more strained norperistylane system. This would permit functionalization of the methylene groups of norperistylane and open the way to new dodecahedrane precursors.

Bromination of norperistylane-5,11-dione **22** in methylene chloride at room temperature in the dark gives quickly and quantitatively a single dibromide, mp 195 °C (dec). The rate of further reaction with bromine is insignificant. The C_{2v} symmetry of the product is clear from its ^{1}H NMR spectrum. Thus, the compound is either **23** or **24**. The latter is exceedingly unlikely for its formation would require repeated enolization of **22** toward the cyclobutane ring, a process known to be very difficult even in much less constrained bicyclo[3.2.0]heptane systems;[14] olefins like **25** are quite strained.[15] In accord, the ^{1}H NMR resonances for the methylene groups of the dibromide are much simplified from those of its parent; that is, the couplings with protons at C-6 and C-10 are gone. Thus, the product is **23**, the needed 6,10-dibromide.

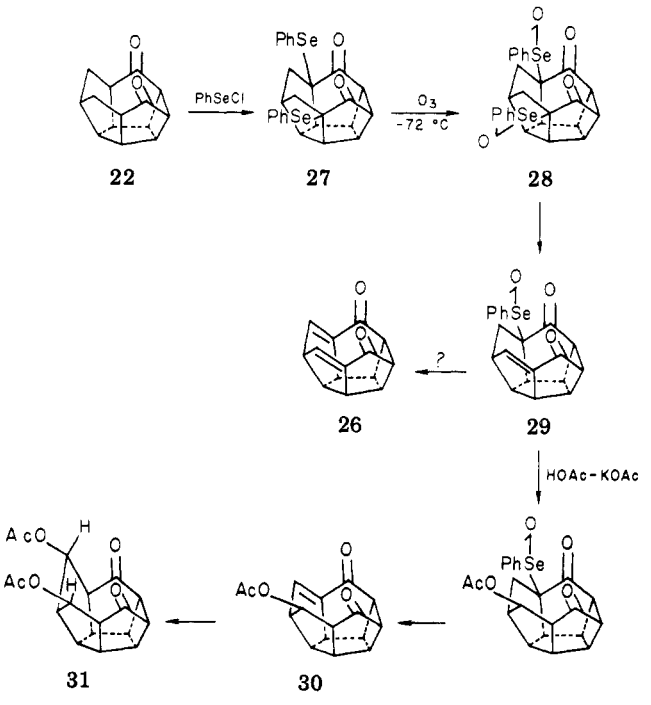


22 23 24 25

The easy bromination of **22**, presumably via intermediate enols, bodes well for the introduction of enone units on the norperistylane rim. Nonetheless, all our attempts to eliminate HBr from **23** were thwarted. Either **23** was untouched or, when the conditions were escalated sufficiently, the products were hopelessly mangled.

Although there are many other choices for the preparation of an α,β-unsaturated ketone by elimination of $X_\alpha H_\beta$, after this experience it seemed to us that none but the elimination of a phenylselenenic acid, X = PhSe → O would be sufficiently easy to be useful in the case at hand.[12] This reaction is a concerted cis elimination, often proceeding spontaneously below room temperature, and does not require the presence of complicating reagents. In a speculative venture, it might even be possible to generate double enone **26**.[16] For our purposes it seemed more prudent, remembering the reactivity of **8**, to arrange for alternating elimination/addition reactions, so that only one enone unit need be present in any of the intermediates in our plan (Chart IV). Conveniently, the presence of Michael nucleophiles to trap the intermediate enones should not interfere with the projected selenoxide eliminations.

Chart IV



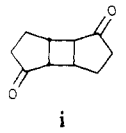
22 27 28 26 29 31 30

Reaction at 50 °C of norperistylane dione **22** with 2 equiv of phenylselenenyl chloride in ethyl acetate is complete, without added catalyst, in less than 1 h. As expected from the formation of dibromide **23**, the requisite enol intermediates form readily. A single bis(selenide), mp 220–220.5 °C, is obtained in 90–95% yield. The ^{1}H NMR spectrum of this product is similar in the high-field region to that of dibromide **23** and leads to structure assignment **27**.

Conversion of **27** to the corresponding bis(selenoxide), **28**, is done most conveniently by low-temperature oxidation with ozone—a fast, clean reaction free of reagents difficult to remove. Compound **28** is not isolated for it decomposes rapidly near room temperature. In one case, we followed this decomposition by ^{1}H NMR. Elimination to a mono enone occurs (**29**?), but in the absence of suitable trapping agents this material disappears unproductively before elimination of the second selenoxide group.

Many attempts of varying success were made to trap the enones produced in the decomposition of **28**. A simple and productive method is to bring the bis(selenoxide) to room temperature in glacial acetic acid containing potassium acetate. This gives diacetate **31** in 65–85% yield. The reaction side products contain phenyl selenide groups and grow in importance with prolonged reaction time. We interpret this to mean that phenylselenenic acid, PhSeOH, a product of the desired reaction, and a potentially reactive electrophile,[17] adds in a secondary reaction to an enol of **31**. Reactions of this sort have been prevented in much simpler cases by performing the selenoxide elimination in the presence of a secondary amine, thus tying up the

(14) Neither acid- nor base-induced proton/deuteron exchange occurs at the ring junctions α to the carbonyls of compound i. Unpublished results, this laboratory.



i

(15) The system has been prepared only by rearrangement of norbornan-7-ylidene, a high-energy species: R. A. Moss and J. R. Whittle, *Chem. Commun.*, 341 (1969).

(16) Indeed, the ion corresponding to **26** is the base peak or at least a major peak in the mass spectra of **30**, **31**, **34**, **36**, and **37**.

(17) H. J. Reich, S. Wollowitz, J. E. Trend, F. Chow, and D. F. Wendelborn, *J. Org. Chem.*, **43**, 1697 (1978). No doubt, the presence of acetic acid magnifies the problem in our case.

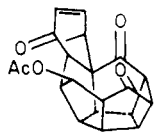
selenenic acid as its amide.[17] Since this is not useful here—the amine reacts with **28**[18]—we devised an alternate, rather better, solution to the problem. We now trap PhSeOH before it damages the desired product by running the elimination reaction in the presence of an excess of ethyl vinyl ether or vinyl acetate, both of which are easy to come by, easy to remove, and highly reactive toward electrophiles. For the case at hand, the method substantially improves the yield and quality of the reaction. Decomposition of bis(selenide) **28** in acetic acid containing potassium acetate and 20–30 equiv of vinyl acetate gives norperistylane diacetate **31** in essentially quantitative yield, uncontaminated with norperistylane selenides. The other reaction product is $PhSeCH_2CH(OAc)_2$, readily separable from the desired product by chromatography. Its structure follows in straightforward fashion from the ^1H NMR spectrum.

Diacetate **31**, the first norperistylane functional at all of the methylene carbons of the parent hydrocarbon, is a stable, crystalline solid, mp 178–180 °C. The ^{13}C NMR spectrum (10 lines for 18 carbons) testifies to its mirror-plane symmetry. The ^1H NMR spectrum establishes that the acetates are attached to CH groups (δ 5.37, singlet, 2 H), the protons of which are endo to the ring cavity (acetates exo) for they are not coupled significantly to the adjacent protons, in accord with the near 110° dihedral angle.

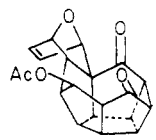
Diacetate **31** offers many useful reaction possibilities. Hydrolysis with hydrochloric acid in THF at 45 °C gives slowly diol **32**, mp 260 °C, which is hardly soluble in organic solvents. Oxidation of **32** with Jones' reagent gives **33**, norperistylane-5,7,8,11-tetrone, a high-melting, very insoluble material: IR (KBr) ν 1770, 1720 cm^{-1}. More to the point of the present paper, treatment of diacetate **31** with a suspension of potassium carbonate in chloroform gives back slowly the norperistylenone **30** from which it must have come (Chart IV).

The spectroscopic data for **30** (e.g.: ^1H NMR δ 5.87 (br s, 1 H, **HC**=C), 5.53 (s, 1 H, **HC**OAc); IR ($CHCl_3$) ν 1740, 1610 cm^{-1}) are consistent with the assigned structure. As with peristylenone **8**, but more dramatically, the intensity of the enone $\pi \rightarrow \pi^*$ transition (λ_{max}^{THF} 240 nm, ϵ 3400) is much lower than usual for model conjugated α,β-unsaturated ketones. The chromophore is very distorted in **30**; the substantial blue shift in its absorption wavelength maximum shows clearly that the ethylenic and carbonyl π bonds are not nearly parallel to one another. Presumably the strain in this system is such that the ethylene unit is also twisted within itself.[19]

Comparison of molecular models indicates that norperistylenone **30** is more strained and more severely distorted about the enone subsystem than is peristylenone **8**. Yet, operationally at least, **30** is more "stable" than **8**, there being little problem with its polymerization at room temperature. Our surprise at this merely reflects the difficulty of predicting reaction pathways open to strained, twisted enones contained within fairly complex molecules. Norperistylenones do, however, react readily with nucleophiles (vide infra), and, as expected, **30** undergoes Diels–Alder addition to furan quickly at room temperature. Two adducts, **34** and **35**, are formed in a ratio of about 3:1. The configurations are assigned based on ^1H NMR analysis as discussed earlier for compounds **10** and **11**. The major



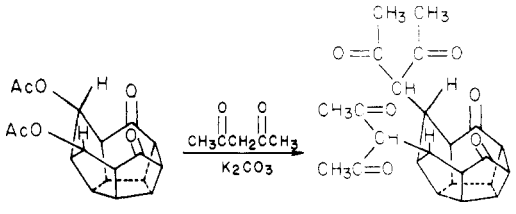
34



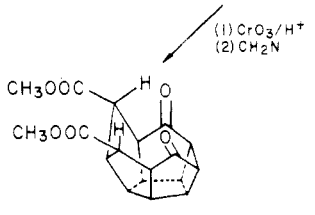
35

adduct is the product of addition via the familiar endo transition state.

The ease of formation of **30** from diacetate **31** and its undoubted reactivity in Michael additions (e.g., **30** → **31**) suggests that **31** can be used as a parent for norperistylanes carrying carbon substituents, just as the peristylane **4** was used to make **14**–**17**. Our initial effort was to achieve the attachment of the cyanide group by generating the enone from **31** in the presence of cyanide ion. This was totally frustrating and without success. Fortunately, the use of other carbon nucleophiles was much more fruitful. For example, reaction of diacetate **31** with potassium carbonate and neat acetylacetone (pentane-2,4-dione) gives 7,9-bis(acetylacetonyl)norperistylane-5,11-dione (**36**) in 97%



31 36



37

yield. It seems certain that this transformation proceeds by alternating elimination–addition reactions starting with the conversion of **31** → **30**.

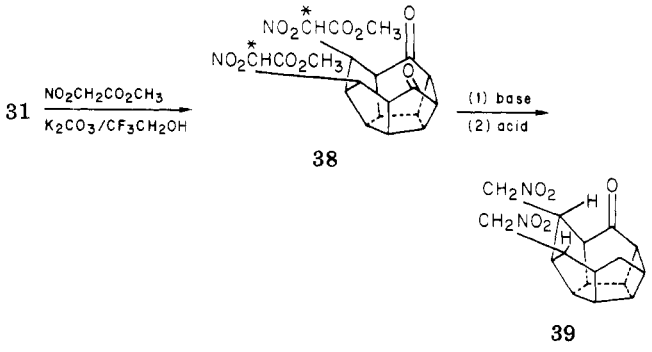
Compound **36** is an easily isolable, crystalline solid, mp 178–180 °C. Its structure, like those of the other compounds in the series, follows convincingly from the NMR data (see Experimental Section). Usefully, the acetylacetone substituents on **36** can be degraded to carboxylic acid groups by oxidation via the enol of the β-diketone system. This reaction is slow, for like most acetylacetones carrying a bulky group (here a norperistylane) at the central carbon, the enol tautomer is sterically unfavored and present in only small amounts.[20] Still, patient oxidation of **36** with Jones' reagent for 2 days gives the expected diacid, isolated as the corresponding dimethyl ester, **37**, in 81% yield.

In a complementary sequence, reaction of compound **31** with methyl nitroacetate and potassium carbonate in trifluoroethanol gives bis(methyl nitroacetate)norperistylane **38**. This is, of course, a mixture of three diastereomers due to configurational differences at the new (starred) centers. This is apparent in the 270-MHz ^1H NMR spectrum where, for example, there are four closely spaced lines for the ester methyl group resonance. Simplification of the nitroacetate substituent was achieved

(18) In fact, decomposition of **28** in the presence of diethylamine gives 7,9-bis(diethylamino)norperistylane-5,11-dione.

(19) Poor overlap of the individual chromophores in an enone system and twisting within the carbon–carbon double bond change the electronic spectrum in different ways.[9] A better understanding of the chromophore in **30** awaits completion of an X-ray analysis of the molecular geometry.

(20) For example, J. B. Conant and A. F. Thompson, *J. Am. Chem. Soc.*, **54**, 4039 (1932). Appropriately, degradation with sodium periodate, so useful in the case of cyclic, highly enolized β diketones, fails completely with **36** (cf. M. L. Wolfram and J. M. Bobbitt, *ibid.*, **78**, 2489 (1956).



by gentle hydrolysis of the methyl esters in dilute base and subsequent decarboxylation of the nitro acids to bis(nitromethyl)norperistylane **39**.[21] This compound will ultimately provide access to the corresponding bis(aminomethyl)- and bis(aldehydo)norperistylanes.

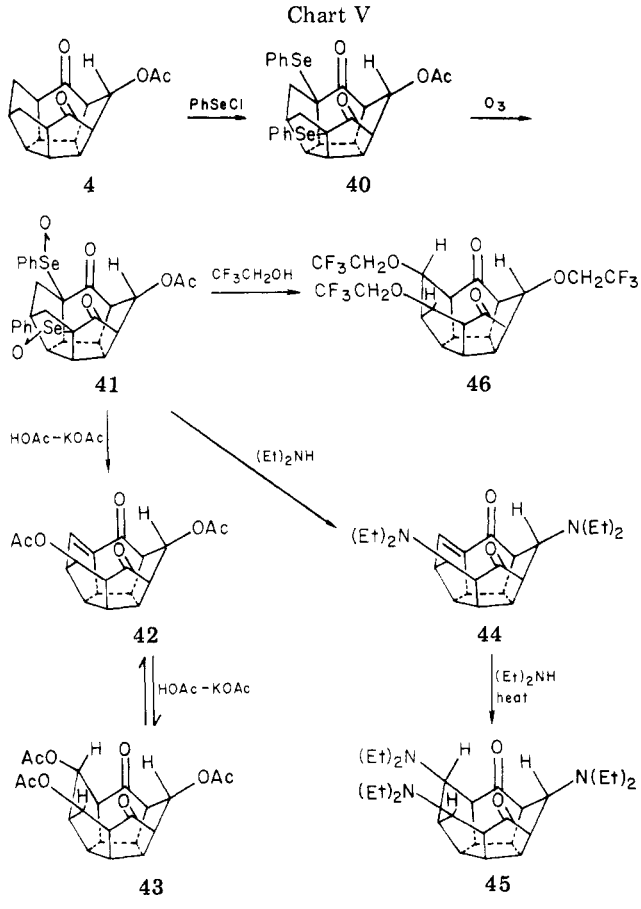
These reaction sequences in which both methylene groups of the parent norperistylane **22** are functionalized proceed in excellent overall yield. Diester **37** and the bis(nitromethyl) compound **39** are obtained in 78 and 79% overall yields, respectively, from **22**. The whole process is altogether satisfactory for the production in quantity of useful norperistylanes.

More Highly Functionalized Peristylanes. Application of these methods to peristylane **4** opens the way to peristylanes functional at the five methylene carbons of the parent hydrocarbon (Chart V). Reaction of **4** with 2 equiv of phenylselenenyl chloride in ethyl acetate is rapid. It is clear from the ^{1}H NMR spectrum of the major product, isolated in 69% yield, that the two selenide groups enter symmetrically—either at C-3 and C-5 or at C-1 and C-7. The latter is in fact the case, for the ^{1}H NMR of the methylene groups at C-8 and C-15 is much simplified from that of **4** in accord with the removal of protons from C-1 and C-7. Thus, the compound is assigned structure **40**.

Oxidation of bis(selenide) **40** with ozone in methylene chloride at dry-ice temperature gives (presumably) the corresponding bis(selenoxide) **41**. This is not isolated but is let decompose in acetic acid–potassium acetate near room temperature. Little product free of phenyl selenide groups can be isolated unless excess vinyl acetate is added initially to the reaction mixture to trap phenylselenenic acid. With this precaution, the sequence goes well, if somewhat astray. It is clear from spectroscopic examination of the crude that the major product is the olefin diacetate **42** rather than the expected triacetate **43**. Apparently, the equilibrium **42** ⇌ **43**, possible in acetic acid–potassium acetate, favors **42**. We are not at all sure why this should be the case, for the double bond in **42**, like that in peristylenone **8**, is surely strained and open to nucleophilic additions. (Indeed, **42** is not stable but polymerizes fairly readily at room temperature.) It seems that small conformational differences along the peristylane rim, arising in the different ordering of the four sp^2 carbons of **8** and **42**, are more significant than obvious.

On the notion that the problem with **42**/**43** is only a matter of the relative leaving group ability vs. the nucleophilicity of acetate, we ran the decomposition of **41** in diethylamine. The major product, characterized spectroscopically, is bis(diethylamino)peristylenedione **44**; this is easily converted to tris(diethylamino)peristylanedione

Chart V



45 if warmed with diethylamine. Similarly, but more directly, decomposition of **41** in trifluoroethanol–potassium carbonate–ethyl vinyl ether gives the desired saturated tris(trifluoroethyl) ether, **46**. Thus, we have in hand suitable methods for the preparation of peristylanes functional at all the methylene carbons as required for the tactical use of this system as a precursor of dodecahedrane.

Experimental Section

Unless otherwise noted, proton magnetic resonance spectra were taken at 270 MHz of solutions in deuteriochloroform and are referenced to internal Me_4Si. In general, spectra were recorded for convenience on a compressed scale (3 Hz/mm); for this reason, the shifts given are no better than ±0.02 ppm, and the coupling constants are no better than ±1 Hz, sufficiently precise for most of our work. In some cases, expanded scales were used and coupling constants are then reported precise to the tenth, ±0.1 Hz. Carbon magnetic resonance spectra were run at 22.63 or 15.09 MHz of solutions in deuteriochloroform by using standard pulse techniques and white noise or gated decoupling and are referenced to internal Me_4Si; chemical shifts are reported to ±0.2 ppm. Approximate relative strengths are given parenthetically for methine and methylene carbon signals. Infrared spectra were taken of solutions in chloroform unless otherwise noted; positions of interesting absorptions are quoted ±5 cm^{-1}. Ultraviolet spectra were recorded on a Cary 14; solvents are as noted. High-resolution mass spectra were recorded on a computer-interfaced MS-902 spectrometer operated at 50-eV ionization voltage.

Vapor-phase chromatographic analysis was done on a Varian Aerograph 1700 dual-column gas chromatograph equipped with a temperature programmer. Stainless steel columns, 5 ft × $^1/_8$ in., containing 5% OV-225 on 70/80 mesh Varaport 30, 5% SE-30 on 60/80 mesh Chromosorb W, or 5% Carbowax 20M on 60/80 mesh Chromosorb G were employed. Analytical thin-layer chromatography was performed on precoated silica gel or alumina plates with a fluorescent indicator supplied by Quantum Industries or Macherey-Nagel Co. Visualization was accomplished under ultraviolet light or with iodine vapor. High-pressure column chromatography was done on fine-particle silica gel with a system

(21) Use of the methyl ester is essential. The rate of hydrolysis of the ethyl ester is so significantly lower that damaging, secondary reactions compete successfully. Acid-catalyzed hydrolysis and degradation of the *tert*-butyl ester analogue of **38** to **39** was explored without substantial reward.

home built around columns, valves, plumbing, and pumps supplied by Altex. Both ultraviolet absorption and refractive index detection systems were employed.

The removal of solvent in vacuo refers to the evaporation of solvent at aspirator pressure on a Büchi rotary evaporator. The 0.75% ethanol in commercial chloroform was not removed prior to use, even for chromatographic operations.

Melting points were measured on a Hoover Unimelt apparatus and were not corrected. Elemental analyses were performed by Micro-Tech Laboratories, Inc.

***exo*-4-(Diethylamino)hexacyclo[7.5.1.$0^{3,13}$.$0^{5,12}$.$0^{7,11}$.$0^{10,14}$]pentadecane-2,6-dione (5).** A solution of peristylanedione acetate **4**[1g] (196 mg, 0.69 mmol) and diethylamine (1 mL, freshly distilled from KOH) in methylene chloride (10 mL) was stirred for 30 min under nitrogen and then extracted with saturated aqueous sodium bicarbonate solution (10 mL). The extract was back-washed with methylene chloride (2 × 5 mL). The combined methylene chloride solutions were dried (Na_2SO_4), filtered, and concentrated to give 201 mg of a light yellow solid. Crystallization from ethyl acetate gave 170 mg (83%) of faintly yellow needles of **5**: decomposition at 165–170 °C; IR ν 1730 cm^{-1}; ^1H NMR δ 4.06 (1 H, br s, HC-4), 3.66 (2 H, m), 3.53 (1 H, q, J = 10 Hz, HC-10), 3.37 (2 H, br q, J = 10 Hz), 2.9–2.6 (5 H, m), 2.39 (4 H, q, J = 7 Hz, NCH_2CH_3), 2.06 (2 H, d of t, J = 14, 10 Hz, H(exo)C-8,15), 1.59 (2 H, d of t, J = 14, 5 Hz, H(endo)C-8,15), 1.17 (6 H, t, J = 7 Hz, NCH_2CH_3); ^{13}C NMR δ 207.5 (C=O), 76.7 (1), 62.8 (1), 59.6 (2), 55.3 (4), 52.2 (2), 47.2 (1), 44.2 (2), 36.9 (2), 13.4 (2); m/e 299.1823 ($C_{19}H_{25}NO_2$ requires 299.1885).

***exo*-4-(2,2,2-Trifluoroethoxy)hexacyclo-[7.5.1.$0^{3,13}$.$0^{5,12}$.$0^{7,11}$.$0^{10,14}$]pentadecane-2,6-dione (6).** A solution of amine **5** (22 mg, 0.067 mmol) and methyl iodide (0.1 mL) in 2,2,2-trifluoroethanol (1 mL) was stirred for 15 min under nitrogen. Potassium carbonate (18 mg, 0.13 mmol) was added, and the mixture was stirred overnight. It was acidified (1 M HCl, 1 mL) and then extracted with methylene chloride (3 × 5 mL). The extract was dried, filtered, and concentrated to give 26.7 mg of a cloudy oil. This was chromatographed on a 10 × 250 mm, 5-μm silica gel high-pressure LC column with 5:95 ethyl acetate–methylene chloride to give 18.3 mg (76%) of **6** as a colorless, crystalline solid. The same material was produced when acetate **4** was heated in trifluoroethanol with potassium cyanide: mp 101–102 °C; ^1H NMR δ 4.44 (1 H, s, HC-4), 3.87 (2 H, q, J = 8.6 Hz, OCH_2CF_3), 3.75 (2 H, m), 3.60 (1 H, q, J = 10 Hz, HC-10), 3.40 (2 H, q of m, $J \sim 10$ Hz), 3.02 (2 H, br d, J = 10.3 Hz, HC-3.5), 2.9–2.6 (3 H, m), 2.10 (2 H, d of d of d, J = 14.5, 10.6, 9.3 Hz, H(exo)C-8,15), 1.65 (2 H, d of t, J = 14.5, 4.2 Hz, H(endo)C-8,15); m/e 326.1128 ($C_{17}H_{17}F_3O_3$ requires 326.1130).

Hexacyclo[7.5.1.$0^{3,13}$.$0^{5,12}$.$0^{7,11}$.$0^{10,14}$]pentadec-3-ene-2,6-dione (8). A solution of amine **5** (136 mg, 0.46 mmol) and methyl iodide (0.5 mL) in methylene chloride (5 mL) was stirred gently overnight under a solution of potassium carbonate (75 mg, 0.55 mmol) in water (15 mL) under nitrogen. After 15 min, both layers became cloudy but cleared by the end of the reaction time. The layers were separated, and the aqueous one was extracted twice with methylene chloride (5 mL). The combined organic phase was dried (Na_2SO_4), filtered, and then concentrated at room temperature in vacuo to leave 135 mg of light yellow, partly crystalline oil. This material was chromatographed on silica gel with 15:85 ethyl acetate–methylene chloride to give 81.3 mg (79%) of white, crystalline enone **8** which starts to soften at 195 °C but does not melt up to 260 °C: IR ν 1725 (v br), 1600 cm^{-1}; UV (THF) λ_{max} 256 nm (ϵ 5100); ^1H NMR δ 5.94 (1 H, t, $J \simeq 2$ Hz, HC-4), 3.99 (1 H, d of t, J = 9.3, 7.6, 2.6 Hz, HC-13), 3.82 (1 H, m, HC-5), 3.64 (1 H, q, J = 9 Hz), 3.5–3.2 (3 H, m), 3.00 (1 H, t, J = 9.3 Hz, HC-1), 2.9–2.7 (2 H, m), 2.3–2.1 (2 H, m, H(exo)C-8,15), 1.97 (1 H, d, J = 14 Hz, H(endo)C-15), 1.22 (1 H, d of t, J = 14.4, 10.0 Hz, H(endo)C-8); ^{13}C NMR δ 217.5 (C-2), 205.5 (C-6), 150.1 (s, C-3), 132.5 (d, J = 170 Hz, C-4), 66.1, 62.5, 58.2, 58.1, 54.7, 53.6, 50.8, 50.7, 47.0, 41.1, 40.6; m/e 226.0994 ($C_{15}H_{14}O_2$ requires 226.0994).

Diels–Alder Adducts (10, 11) to Enone 8. Enone **8** (15.6 mg) was dissolved in furan (5 mL) and the solution kept at room temperature under nitrogen for 3 h. TLC analysis on silica gel with 1:4 ethyl acetate–methylene chloride showed that the enone (R_f 0.58) was nearly gone after this period. Two products, R_f 0.51 (major) and 0.36 (minor), were formed. The furan was removed in vacuo; the products were separated and isolated as crystalline materials by chromatography on an Altex 10 × 240 mm, 5-μm silica gel high-pressure LC column eluted with 1:4 ethyl acetate–methylene chloride. The major adduct was **10** (11.7 mg, 58%): mp 163–164 °C; IR ν 1725 cm^{-1}; ^1H NMR δ 6.62 (1 H, d of d, J = 5.8, 1.6 Hz), 6.44 (1 H, d of d, J = 5.8, 1.7 Hz), 4.76 (1 H, s, OCH), 4.59 (1 H, s, OCH), 3.82 (1 H, q, J = 10.5 Hz), 3.6–3.4 (3 H, m), 3.25 (1 H, q, $J \sim 10$ Hz), 2.90 (1 H, d of t, J = 11.2, 1.9 Hz), 2.78 (2 H, m), 2.64 (2 H, m), 2.1–1.9 (3 H, m), 1.08 (1 H, d of t, J = 14.8, 9.5 Hz); m/e 294.1253 ($C_{19}H_{18}O_3$ requires 294.1255). The minor isomer was **11** (3.9 mg, 19%): mp 166–167 °C; IR ν 1725 cm^{-1}; ^1H NMR δ 6.59 (1 H, d of d, J = 5.8, 1.4 Hz), 6.52 (1 H, d of d, J = 5.8, 1.4 Hz), 5.04 (1 H, d, J = 4.9 Hz, OCH), 4.89 (1 H, s, OCH), 3.6–3.2 (4 H, m), 3.14 (1 H, q, J = 9 Hz), 2.97 (1 H, t, J = 10 Hz), 2.82 (1 H, q?, J = 10 Hz), 2.8–2.6 (2 H, m), 2.47 (1 H, br d, $J \sim 11$ Hz), 2.3–2.1 (2 H, overlapping m), 1.99 (1 H, m), 1.13 (1 H, d of t, J = 14.9, 10.5 Hz); m/e 294.1268 ($C_{19}H_{18}O_3$ requires 294.1255).

Dimethyl 2,6-Dioxohexacyclo[7.5.1.$0^{3,13}$.$0^{5,12}$.$0^{7,11}$.$0^{10,14}$]pentadecane-*exo*-4-malonate (14). Dimethyl malonate (462 mg, 3.5 mmol) was added to a magnetically stirred solution of sodium methoxide (75 mg, 1.4 mmol) in dry methanol (10 mL) under nitrogen. After 30 min, peristylanedione acetate **4** (200 mg, 0.70 mmol) was added as a solid in one portion. It dissolved rapidly, but in a few minutes a new fluffy white solid formed. After 1 h, 1 M HCl (30 mL) was added, and the mixture was extracted with methylene chloride (4 × 25 mL). The combined organic extract was dried over sodium sulfate, filtered, and concentrated in vacuo. The remaining dimethyl malonate was removed by pumping at 1 mm overnight. The light yellow, crystalline residue was crystallized from ethyl acetate giving 180 mg (72%) of colorless **14**, mp 141–142 °C. A further 50 mg of **14** was obtained by chromatography of the mother liquors on silica gel with 1:9 ethyl acetate–methylene chloride for a total yield of 92%: IR ν 1740 cm^{-1}; ^1H NMR δ 3.77 (6 H, s, OCH_3), 3.7–3.5 (3 H, m), 3.58 (1 H, d, J = 5.8 Hz, $HC(CO_2CH_3)_2$), 3.50 (1 H, br d, J = 5.8 Hz, HC-4), 3.37 (2 H, q of m, J = 10 Hz, HC-11,14), 2.9–2.6 (5 H, m), 2.12 (2 H, d of t, J = 14, 10 Hz, H(exo)C-8,15), 1.74 (2 H, d of t, J = 14, 4 Hz, H(endo)C-8,15); ^{13}C NMR δ 208.1 (C=O), 168.2 (OC=O), 63.6 (1), 59.6 (2), 55.8 (1), 55.3 (2), 54.7 (2), 52.3 (CH_3OC=O?), 51.5 (3?), 46.9 (1), 37.8 (2); m/e 358.1406 ($C_{20}H_{22}O_6$ requires 358.1415). Anal. Calcd for $C_{20}H_{22}O_6$: C, 67.02; H, 6.19. Found: C, 66.98; H, 6.28.

4-(Dimethylmalonylidene)hexacyclo-[7.5.1.$0^{3,13}$.$0^{5,12}$.$0^{7,11}$.$0^{10,14}$]pentadecane-2,6-dione (20). A. Preparation of Selenide 18. *n*-Butyllithium in hexane (1.6 M, 0.51 mL, 0.81 mmol) was added dropwise over 5 min to an ice-cooled, magnetically stirred solution of *exo*-malonate **14** (281 mg, 0.81 mmol) in dry benzene under nitrogen. After 10 min, purified phenylselenenyl chloride (163 mg, 0.85 mmol) was added as a solid. The solution was allowed to warm to room temperature and stirred for 30 min. Aqueous HCl (1 M, 10 mL) was added, and the layers were separated. The aqueous layer was extracted with methylene chloride (2 × 10 mL), and the combined organic solution was dried (Na_2SO_4), filtered, and concentrated in vacuo to give yellow, crystalline material which was usually carried on without purification. An analytical sample was prepared by crystallization from ethyl acetate to give **18** as colorless crystals: mp 189–190 °C; ^1H NMR δ 7.83 (2 H, br d, PhH_o), 7.39 (3 H, $PhH_{m,p}$), 3.72 (1 H, br s, HC-4), 3.62 (6 H, s, OCH_3), 3.6–3.1 (7 H, multiplets), 2.72 (3 H, m), 2.09 (2 H, d of t, J = 14, 9 Hz, H(exo)C-8,15), 1.74 (2 H, d of t, J = 14, 4 Hz, H(endo)C-8,15). Anal. Calcd for $C_{26}H_{26}O_6Se$: C, 60.82; H, 5.10. Found: C, 60.65; H, 5.11.

B. Oxidation of 18 to Selenoxide 19. Formation of 20. The crude preparation of **18** as above was dissolved in ethyl acetate and THF (15 mL each) and stirred for 3 h with 30% aqueous hydrogen peroxide (0.28 mL, 2.5 mmol). Saturated aqueous sodium carbonate solution (15 mL) was added, and the mixture was extracted thoroughly with methylene chloride. Evaporation of the extract in vacuo left a yellow crystalline crude that on crystallization from ethyl acetate gave 140 mg of the olefin **20**. Chromatography of the mother liquor on silica gel with ethyl acetate–methylene chloride gave an additional 65 mg (total yield 71%) of **20**: mp 177–178 °C; IR ν 1740, 1635 cm^{-1}; ^1H NMR δ 4.44 (2 H, d of m, J = 10 Hz, HC-3,5), 3.82 (6 H, s, OCH_3), 3.73

(2 H, m), 3.60 (1 H, q, J = 9.5 Hz, HC-10), 3.40 (2 H, q of m, $J \simeq 10$ Hz), 2.86 (2 H, t of d, $J \sim 10$, 6 Hz, HC-1,7), 2.70 (1 H, m, HC-9), 2.05 (2 H, d of d of d, J = 8.4, 9.7, 14.6 Hz, H(exo)C-8,15), 1.55 (2 H, d of t, J = 14.5, 5.3 Hz, H(endo)C-8,15).

Dimethyl 2,6-Dioxohexacyclo[7.5.1.0^{3,13}.0^{5,12}.0^{7,11}.0^{10,14}]pentadecane-*endo*-4-malonate (21). A solution of the malonylidene **20** (215 mg, 0.60 mmol) in ethyl acetate (25 mL) and neutralized[1g] 10% Pd/C (150 mg) were agitated together vigorously for 18 h under hydrogen at atmospheric pressure. The reduction was slow; good stirring was essential. The catalyst was removed by filtration through Celite, and the product was isolated by crystallization from ethyl acetate. Three crops were taken to give 176 mg of **21** as fine, colorless needles: mp 210–215 °C (dec); IR ν 1750 cm^{-1}; ^{1}H NMR δ 4.66 (1 H, d J = 12.2 Hz, HC(CO$_2$CH$_3$)$_2$), 3.77 (6 H, s, OCH$_3$), 3.7–3.5 (3 H, m), 3.36 (2 H, q of m, $J \simeq 10$ Hz), 3.26 (1 H, d of t, J = 12.2, 9.1 Hz, HC-4), 3.06 (2 H, t of m, $J \simeq 10$ Hz, HC-1,7), 2.8–2.6 (3 H, m), 2.11 (2 H, d of d of d, J = 14.4, 10.8, 9.5 Hz, H(exo)C-8,15), 1.77 (2 H, d of t, J = 14.4, 3.9 Hz, H(endo)C-8,15); ^{13}C NMR δ 223.1 (C=O), 169.4 (OC=O), 64.0 (1), 56.1 (2), 54.7 (2), 53.3 (2), 52.3 (CH$_3$OC=O?), 51.7 (2), 47.7 (1), 47.1 (1), 46.9 (1), 38.0 (2); m/e 358.1408 (C$_{20}$H$_{22}$O$_6$ requires 358.1415).

6,10-Dibromohexacyclo[6.6.0.0^{2,6}.0^{3,13}.0^{4,12}.0^{10,14}]tetradecane-5,11-dione (23).[22] Norperistylane-5,11-dione **22** (32 mg, 0.15 mmol) was dissolved in methylene chloride (2 mL, freshly distilled from P_2O_5). The solution was stirred shielded from light at room temperature under nitrogen as bromine (16 μL, 49 mg, 0.31 mmol) was added. Stirring was continued for 1 h at room temperature, and then the orange solution was rinsed with methylene chloride through a short column of basic alumina. Solvent was removed in vacuo from the very light yellow eluate leaving 48 mg (89%) of off-white crystals of reasonable purity. Crystallization from ethyl acetate gave a pure sample of **23** as colorless crystals: decomposition above 210 °C; ^{1}H NMR δ 3.97 (1 H, q, J = 10.5 Hz, HC-1), 3.73 (2 H, m), 3.65 (2 H, m), 3.56 (2 H, m), 3.16 (1 H, q of t, J = 10.5, 3 Hz, HC-8), 2.72 (2 H, d of d, J = 15, 10.5 Hz, H(exo)C-7,9), 2.57 (2 H, d of d, J = 15, 3 Hz, H(endo)C-7,9); m/e 373.9184, 371.9212, 369.9238 (C$_{14}$H$_{12}$Br$_2$O$_2$ requires 373.9165, 371.9184, 369.9204).

6,10-Bis(phenylselenenyl)hexacyclo[6.6.0.0^{2,6}.0^{3,13}.0^{4,12}.0^{10,14}]tetradecane-5,11-dione (27). Norperistylane-5,11-dione (386 mg, 1.80 mmol) and phenylselenenyl chloride (772 mg, 4.0 mmol) were dissolved together in ethyl acetate (10 mL). The deep reddish brown solution was stirred at 50 °C under nitrogen. After 5 min, much of the initial color had faded, and a precipitate had formed. Heating was continued for 1 h, after which the solvent was removed in vacuo. The orange solid residue was triturated with 1:1 hexane–ether (4 × 5 mL) to remove color and residual reactants. The residue consisted of almost colorless fine needles of **27** (851 mg, 90%) and was sufficiently pure for use in the next steps. A small amount was crystallized from benzene to give sharp melting, colorless needles: mp 220–220.5 °C; IR (KBr) ν 1725 cm^{-1}; ^{1}H NMR δ 7.51 (4 H, d, J = 7 Hz, PhH$_o$), 7.37 (2 H, t, J = 7 Hz, PhH$_p$), 7.25 (4 H, t, J = 7 Hz, PhH$_m$), 3.83 (1 H, q, J = 10 Hz, HC-1), 3.43 (2 H, m), 3.12 (2 H, m), 3.04 (1 H, q of t, J = 10, 2 Hz, HC-8), 2.87 (2 H, m), 2.44 (2 H, d of d, J = 15, 10 Hz, H(exo)C-7,9, 2.29 (2 H, d of d, J = 15, 2 Hz, H(endo)C-7,9); ^{13}C NMR δ 215.0 (C=O), 137.0 (4), 129.4 (2), 129.0 (4), 127.5 (2), 64.4 (2), 63.8 (1), 62.6 (2), 47.7 (2), 46.4 (1), 45.4 (2), 43.5 (2); m/e 525.9904 (C$_{26}$H$_{22}$O$_2$^{80}Se$_2$ requires 525.9949).

***exo,exo*-7,9-Diacetoxyhexacyclo[6.6.0.0^{2,6}.0^{3,13}.0^{4,12}.0^{10,14}]tetradecane-5,11-dione (31).** A stream of ozone in oxygen was bubbled into a dry ice–acetone cooled solution of bis(selenide) **27** (300 mg, 0.57 mmol) in methylene chloride (25 mL) until the solution turned bright blue. The solution was allowed to stand at −72 °C for 30 min, and then excess ozone was removed in a nitrogen purging stream until moistened starch–iodide paper held at the gas outlet no longer colored. Vinyl acetate (3 mL) was added to the cold solution. The mixture was poured into a well-stirred solution of potassium acetate (7 g) in acetic acid (70 mL) at room temperature, and the whole was left to stir for 17 h under nitrogen. Most of the volatiles were then removed at room temperature at 1 mm on the rotary evaporator. The solid residue was dissolved in water (75 mL) and extracted with methylene chloride (4 × 75 mL). The extract was washed with water and saturated sodium bicarbonate solution, dried (Na_2SO_4), filtered, and concentrated to give 510 mg of a mixture of light yellow, oily crystals of **31** and selenium-containing reaction byproducts. The desired material could be isolated pure by chromatography on silica gel with 3:7 ethyl acetate–methylene chloride. A simpler procedure, which gave only slightly less pure material, was usually used instead. The crude was dissolved in the minimum amount of methylene chloride; slow addition of hexane caused fine needles of **31** (141 mg) to precipitate. The mother liquors were concentrated, and the process was repeated to give additional crystals (38 mg). The combined product was recrystallized in the same way to give slightly yellow needles (179 mg, 95%), mp 175–178 °C. An analytical sample was obtained chromatographically: mp 178.5–179.5 °C; IR (KBr) ν 1740, 1240, 1030 cm^{-1}; ^{1}H NMR δ 5.37 (2 H, s, HC-7,9), 4.10 (1 H, q, J = 10 Hz, HC-1), 3.71 (2 H, m), 3.47 (2 H, m), 3.37 (2 H, m), 2.97 (2 H, d, J = 10 Hz, HC-6,10), 2.76 (1 H, d, J = 10 Hz, HC-8), 2.03 (6 H, s, OCOCH$_3$); ^{13}C NMR δ 216.4 (C-5, C-11), 169.4 (OC=O), 86.5 (2), 63.9 (1), 63.1 (2), 62.6 (1), 53.2 (2), 46.7 (2), 45.2 (2), 21.1 (2); m/e 330.1063 (C$_{18}$H$_{18}$O$_6$ requires 330.1103).

Chromatography on silica gel of the mother liquors left from the preparation above gave (2,2-diacetoxyethyl)phenyl selenide in 80% yield as a colorless oil: IR ν 1760 cm^{-1}; ^{1}H NMR δ 7.57 (2 H, m, PhH$_o$), 7.27 (3 H, m, PhH$_{m,p}$), 6.92 (1 H, t, J = 5 Hz, CH(OAc)$_2$), 3.18 (2 H, d, J = 5 Hz, CH$_2$Se), 1.99 (6 H, s, OAc).

***exo*-7-Acetoxyhexacyclo[6.6.0.0^{2,6}.0^{3,13}.0^{4,12}.0^{10,14}]tetradec-6-ene-5,11-dione (30).** A solution of diacetate **31** (10 mg) in chloroform (1 mL, ethanol free) under nitrogen was stirred with finely powdered, anhydrous potassium carbonate at room temperature for 15 h. The solution was then diluted with chloroform (10 mL) and filtered. The filtrate was washed with brine (5 mL) and concentrated in vacuo. The solid residue (8.5 mg) was triturated with ether and then crystallized from acetone (slow evaporation) to give pure acetoxy enedione **30** (7.0 mg, 85%): decomposition at 184–187 °C; IR ν 1740, 1610, 1250 cm^{-1}; UV (THF) λ_{max} 240 nm (ϵ 3400); ^{1}NMR δ 5.87 (1 H, br s), 5.53 (1 H, s), 3.92 (1 H, m), 3.82 (1 H, m), 3.73 (1 H, m), 3.61 (1 H, m), 3.42 (2 H, m), 3.16 (2 H, m), 2.83 (1 H, d, J = 9 Hz), 2.08 (3 H, s); m/e 270.0893 (C$_{16}$H$_{14}$O$_4$ requires 270.0892).

***exo,exo*-7,9-Dihydroxyhexacyclo[6.6.0.0^{2,6}.0^{3,13}.0^{4,12}.0^{10,14}]tetradecane-5,11-dione (32).** A mixture of diacetate **31** (50 mg), 10% aqueous hydrochloric acid (1 mL), and THF (1 mL) was stirred at 45 °C for 7 h and then at room temperature overnight. In the morning, the volatiles were removed in vacuo leaving a colorless solid. This was washed twice with ether and then dried under vacuum to give 36 mg (97%) of diol **32** as a colorless powder of low organic solubility: mp >260 °C; IR (Nujol) ν 3300, 1720 cm^{-1}; ^{1}H NMR (D$_2$O) δ 4.33 (2 H, s, H(endo)C-7,9), 4.10 (1 H, q, J = 10 Hz, HC-8), 3.77 (2 H, m), 3.46 (4 H, br s), 2.96 (2 H, d, J = 11 Hz, HC-6,10), 2.66 (1 H, J = 10 Hz, HC-8); m/e 246.0865 (C$_{14}$H$_{14}$O$_4$ requires 246.0892).

Hexacyclo[6.6.0.0^{2,6}.0^{3,13}.0^{4,12}.0^{10,14}]tetradecane-5,7,9,11-tetrone (33). A solution of the diol–dione **32** (15 mg, 0.061 mmol) in water (0.5 mL) and acetone (3 mL) was stirred at 0 °C while standard Jones' reagent (chromium trioxide in aqueous sulfuric acid, 2.67 M, 100 μL, 0.27 mmol) was added dropwise over 10 min. The mixture was allowed to warm to room temperature and stirred there for 13 h. The excess oxidant was destroyed with 200 μL of 6% sulfurous acid. Most of the acetone was removed in vacuo on the rotary evaporator. Water (3 mL) was added. The precipitate was taken up in methylene chloride (100 mL) and the solution filtered, first through Celite and then through silica gel. Evaporation left 15 mg of colorless microcrystals. These were washed with small amounts of ether, methylene chloride, and acetone and then dried leaving 14 mg (95%) of tetrone **33**: mp >260 °C; IR (KBr) 1770, 1720 cm^{-1}; ^{1}H NMR (CD$_3$CN) δ 4.02 (1 H, q, $J \simeq 10$ Hz, HC-1), 3.88 (2 H, m), 3.60 (2 H, m), 3.49 (2 H, m), 3.40 (2 H, d, $J \simeq 10$ Hz, HC-6,10), 3.38 (1 H, $J \simeq 10$ Hz, HC-8); m/e 242.0581 (C$_{14}$H$_{10}$O$_4$ requires 242.0578).

Furan Adducts (34, 35) to Enone 30. The norperistylenone **30** (3 mg) was dissolved in freshly distilled furan (1 mL). The solution was kept at room temperature under nitrogen for 15 h. Excess furan was removed in vacuo. Mass spectral analysis of

(22) First prepared here by Dr. Ronald Roth.

the white, solid residue indicated only 1:1 addition of furan to **30**: *m/e* 388.1120 ($C_{20}H_{18}O_5$ requires 338.1153). ^1H NMR analysis showed that two such adducts were formed in the ratio of roughly 3:1. Small samples of each were obtained by preparative TLC on silica gel eluting with ethyl acetate. Distinguishing features in the low-field region of the ^1H NMR spectra were as follows. Major isomer (**34**): δ 6.46 (2 H, s, HC=CH), 5.47 (1 H, **H**COAc), 4.78 (1 H, s, HCO), 4.53 (1 H, s, HCO). Minor adduct (**35**): δ 6.62 (2 H, s), 5.52 (1 H, s), 5.05 (1 H, d, $J \simeq 5$ Hz), 4.78 (1 H, s).

***exo,exo*-7,9-Bis(acetylacetonyl)hexacyclo[6.6.0.0^{2,6}.0^{3,13}.0^{4,12}.0^{10,14}]tetradecane-5,11-dione (36).** Diacetate **31** (50 mg, 0.151 mmol) was added to a suspension of potassium carbonate (150 mg, 1.1 mmol) in 2,2,2-trifluoroethanol (2 mL) and acetylacetone (2 mL, 20 mmol). The mixture was stirred at 60 °C under nitrogen for 1 h. The solution was concentrated on the rotary evaporator. Water (4 mL) and methylene chloride (2 mL) were added, and the whole was acidified carefully with 10% aqueous sulfuric acid and then extracted thoroughly with methylene chloride. The extract was washed with brine and dried over sodium sulfate. Evaporation gave 68 mg of a yellow solid of reasonable purity. Pure material (50 mg, 80%) was obtained by crystallization from methylene chloride–ether as colorless needles: mp 178–180 °C (dec); IR (KBr) ν 1730, 1695 cm^{-1}; ^1H NMR δ 3.90 (1 H, q, J = 10 Hz, HC-1), 3.79 (2 H, d, J = 8 Hz, **H**C(Ac)$_2$), 3.68 (2 H, m), 3.40 (4 H, m), 3.07 (2 H, d, J = 8 Hz, HC-7,9), 2.41 (2 H, d, J = 10 Hz, HC-6,10), 2.31 (6 H, s, $COCH_3$), 2.19 (6 H, s, $COCH_3$), 1.97 (1 H, d of t, J = 10, 2 Hz, HC-8); ^{13}C NMR 220.8 (O=C-5,11), 204.3 (CH_3C=O), 204.1 (CH_3C=O), 73.3 (2, **C**H(Ac)$_2$), 64.0 (1), 60.0 (2), 59.6 (1), 55.3 (2), 54.4 (2), 46.4 (2), 45.0 (2), 30.6 (CH_3C=O), 29.0 (CH_3C=O); *m/e* 367.1558 ($C_{24}H_{26}O_6 \cdot C_2H_3O$ requires 367.1544).

In another run, **36** was prepared by reaction of **31** (30 mg, 0.091 mmol), potassium carbonate (90 mg, 0.65 mmol), and neat acetylacetone (5 mL, 50 mmol) at 60 °C for 24 h. The excess acetylacetone was removed in vacuo. Workup as above and purification by preparative TLC on silica gel eluted with 1:1 benzene–ethyl acetate gave **36** in excellent yield (36 mg, 97%).

***exo,exo*-7,9-Dicarbomethoxyhexacyclo[6.6.0.0^{2,6}.0^{3,13}.0^{4,12}.0^{10,14}]tetradecane-5,11-dione (37).** A solution of bis(acetylacetone) adduct **36** (10 mg, 0.0244 mmol) in acetone (0.4 mL), water (0.2 mL), and acetic acid (0.1 mL) was stirred at 0 °C while standard Jones' reagent (2.67 mol/L, 350 μL, 0.93 mmol) was added over 10 min. The oxidation was quite slow. The solution was allowed to come to room temperature and stirred there for 24 h. Another portion of the same size of Jones' reagent was added, and the solution was stirred for an additional 24 h. The excess oxidant was destroyed with 6% sulfurous acid. The solution was concentrated in vacuo to one-fourth volume, saturated with ammonium sulfate, and extracted thoroughly with methylene chloride (continuous extraction would have been better). The extract was dried over Na_2SO_4, and the solvent was removed leaving the crude diacid as a colorless solid. This crude was dissolved in 1:1 methanol–methylene chloride (5 mL). The solution was cooled in an ice bath; ethereal diazomethane was added, and the mixture was stirred for 10 min. The solvent and excess diazomethane were removed in vacuo. The residue was purified by preparative TLC on silica gel plates eluting with 1:1 ethyl acetate–benzene giving the pure dimethyl ester **37** (6.5 mg, 81%) as colorless crystals: decomposition at 156–160 °C; IR ν 1735 cm^{-1}; ^1H NMR δ 3.96 (1 H, q, J = 10.5 Hz, HC-1), 3.71 (6 H, s, $COOCH_3$), 3.63 (2 H, m), 3.3–3.5 (5 H, m), 3.28 (2 H, s, HC-7,9), 3.14 (2 H, d, J = 11 Hz, HC-6,10); *m/e* 330.1074 ($C_{18}H_{18}O_6$ requires 330.1103).

7,9-Bis(nitromethyl)hexacyclo[6.6.0.0^{2,6}.0^{3,13}.0^{4,12}.0^{10,14}]tetradecane-5,11-dione (39). A solution of diacetate **31** (50 mg, 0.151 mmol) and methyl nitroacetate[21] (100 mg, 0.84 mmol) in 2,2,2-trifluoroethanol (2.5 mL) containing suspended potassium carbonate (125 mg, 0.91 mmol) was stirred at 60 °C under nitrogen for 40 min. The solvent was removed in vacuo. The solids remaining were taken up in methylene chloride (2 mL) and water (1 mL); 5% hydrochloric acid was added slowly with stirring until the aqueous layer was acidic to pH paper. At this point, concentration under vacuum and TLC purification gave a mixture of the three diastereomers of **38** as a glassy solid: IR (KBr) ν 1745, 1560, 1365 cm^{-1}; ^1H NMR δ 5.30–5.19 (2 H, four closely spaced doublets, $J \simeq 6$–8 Hz, C**H**(NO$_2$)COO), 3.90–3.87 (6 H, four closely spaced singlets, $COOCH_3$). Hydrolysis and decarboxylation were effected by stirring the crude nitro esters with methanol (15 mL) and 20% aqueous potassium carbonate (20 mL) at 60 °C for 15 h.[21] The solution was then concentrated to one-fourth volume, acidified with 5% sulfuric acid, saturated with sodium chloride, and extracted thoroughly with methylene chloride. The extract was washed with brine and dried (Na_2SO_4). Removal of the solvent left 54 mg of slightly brown crystals. Preparative TLC on silica gel with 1:1 benzene–ethyl acetate gave the pure bis(nitromethyl) compound **39** (36 mg, 79% overall from **31**): decomposition at 165–170 °C; IR (KBr) ν 1730, 1550, 1380 cm^{-1}; ^1H NMR δ 4.39 (4 H, d, J = 7 Hz, CH_2NO_2), 3.96 (1 H, q, J = 10 Hz, HC-1), 3.61 (2 H, m), 3.47 (2 H, m), 3.41 (2 H, m), 3.16 (2 H, m), 2.69 (2 H, d, J = 10 Hz, HC-6,10), 2.61 (1 H, d of t, J = 10, 2 Hz, HC-8); ^{13}C NMR (CD_3CN) δ 220.8 (C=O), 80.9 (2, CH_2NO_2), 63.8 (1), 60.6 (2), 57.0 (1), 54.8 (2), 54.6 (2), 47.1 (2), 46.4 (2); *m/e* 332.1014 ($C_{16}H_{16}N_2O_6$ requires 332.1006).

***exo*-4-Acetoxy-1,7-bis(phenylselenenyl)hexacyclo[7.5.1.0^{3,13}.0^{5,12}.0^{7,11}.0^{10,14}]pentadecane-2,6-dione (40).** A stirred solution of peristylanedione acetate **4** (504 mg, 1.76 mmol) in ethyl acetate (30 mL) was heated under nitrogen to 50 °C. Phenylselenenyl chloride (742 mg, 3.87 mmol) was added in one portion. Heating and stirring were continued. A copious light yellow precipitate formed. After 1 h, the mixture was cooled in an ice bath, and the precipitate (680 mg) was isolated by filtration. Crystallization from ethyl acetate gave 527 mg of pale yellow, microcrystalline material, mp 211–214 °C. Chromatography of the combined mother liquors on silica gel eluting with 5:95 ethyl acetate–methylene chloride gave an additional 200 mg of **40**: total yield 69%; IR ν 1740 cm^{-1}; ^1H NMR δ 7.48 (4 H, d, J = 7 Hz, PhH_o), 7.33 (2 H, t, J = 7 Hz, PhH_p), 7.26 (4 H, t, J = 7 Hz, PhH_m), 5.71 (1 H, s, HC-4), 3.83 (1 H, q, J = 11 Hz), 3.47 (2 H, m), 3.4–3.1 (4 H, m), 2.98 (1 H, m), 2.31 (2 H, d of d, J = 15, 10.6 Hz, H(exo)C-8,15), 2.00 (3 H, s, $OCOCH_3$), 1.98 (2 H, d of d, J = 15, 2.5 Hz, H(endo)C-8,15).

***exo,exo*-4,15-Diacetoxyhexacyclo[7.5.1.0^{3,13}.0^{5,12}.0^{7,11}.0^{10,14}]pentadec-7-ene-2,6-dione (42).** Bis(selenide) **40** (35.7 mg) in methylene chloride (10 mL) was oxidized with ozone at dry ice–acetone temperature as described for **27** → **28**. After removal of excess ozone, vinyl acetate (0.1 mL) was added, and the mixture was poured into a solution of potassium acetate (3 g) in acetic acid (15 mL). This was stirred at room temperature for 20 h, after which it was added slowly to an ice-cooled solution of potassium carbonate (25 g) in water (100 mL). The aqueous layer was extracted with methylene chloride (3 × 30 mL). The combined organic phase was dried (Na_2SO_4), filtered, and concentrated to give a colorless oil. This showed two mobile spots (R_f 0.46, 0.65) on silica gel TLC with ethyl acetate, but considerable material was immobile and remained at the base line. After a preliminary filtration of the crude through silica gel with ethyl acetate, chromatography on an Altex, 10 × 250 mm, 5-μm silica gel high-pressure LC column gave (2,2-diacetoxyethyl)phenyl selenide (17.3 mg, 47%) and the ene diacetate **42** (6.0 mg, 30%) as a low-melting, unstable solid: ^1H NMR δ 5.69 (1 H, s), 5.62 (1 H, s), 5.50 (1 H, s), 3.9–3.6 (6 H, m), 3.1–2.9 (3 H, m), 2.07 (3 H, s), 2.04 (3 H, s); *m/e* 342.1151 ($C_{19}H_{18}O_6$ requires 342.1103).

***exo,exo,exo*-4,8,15-Tris(diethylamino)hexacyclo[7.5.1.0^{3,13}.0^{5,12}.0^{7,11}.0^{10,14}]pentadecane-2,6-dione (45).** Bis(selenide) **40** (104 mg, 0.174 mmol) was dissolved in methylene chloride (30 mL) and ozonized at −72 °C. After removal of excess ozone, diethylamine (1.5 mL, freshly distilled from KOH) was added with stirring, and the solution was allowed to warm to room temperature under nitrogen. The next morning, the solvent and excess amine were removed in vacuo, and the residue was dissolved in methylene chloride (10 mL). This was extracted with 2 M HCl (10 mL), and the extract was washed twice with methylene chloride. The aqueous layer was made basic with potassium carbonate and extracted with methylene chloride (3 × 10 mL). This methylene chloride extract was dried (Na_2SO_4) and concentrated to give 61 mg of a brownish oil. NMR analysis showed that about half of the sample was the olefin diamine **44** (δ 5.61 for the olefinic hydrogen). The material was dissolved in diethylamine (5 mL), and the solution was heated at reflux for 15 min. The solvent was removed in vacuo to give 67 mg of a brownish oil containing many needle-shaped crystals, characterized

without further purification: ^{1}H NMR δ 4.09 (1 H, s, HC-4), 3.7–3.3 (7 H, m), 2.75 (5 H, m), 2.5–2.2 (12 H, m, CH_3CH_2N), 1.33 (6 H, t, J = 7 Hz, CH_3CH_2NC-4), 1.07 (12 H, t, J = 7 Hz, CH_3CH_2NC-8,15); m/e 441.3325 ($C_{27}H_{43}N_3O_2$ requires 441.3355).

***exo,exo,exo*-4,8,15-Tris(2,2,2-trifluoroethoxy)hexacyclo[7.5.1.0^{3,13}.0^{5,12}.0^{7,11}.0^{10,14}]pentadecane-2,6-dione (46).** A solution of selenide **40** (105 mg, 0.18 mmol) in methylene chloride (30 mL) was ozonized as described earlier. After excess ozone was removed, ethyl vinyl ether (1 mL) and a solution of potassium carbonate (150 mg) in trifluoroethanol (20 mL) were added to the cold solution. The mixture was then allowed to warm to room temperature with stirring over 4 h. The colorless solution was poured into water (50 mL), and the mixture was extracted with methylene chloride (5 × 50 mL). The extract was dried, filtered, and concentrated to leave a light yellow oil (148 mg). The desired product was obtained from this mixture by chromatography on an Altex, 90 × 250 mm, 5-μm silica gel column eluted with 2:1 chloroform–cyclohexane as a low-melting, crystalline material (40 mg, 43%): IR ν 1735 cm^{-1}; ^{1}H NMR δ 4.47 (1 H, s, HC-4), 4.0–3.6 (11 H, m), 3.64 (2 H, q of m, $J \simeq$ 10 Hz), 3.02 (2 H, d, J = 10 Hz), 2.94 (2 H, d, J = 11 Hz), 2.82 (1 H, d, J = 10 Hz, HC-9); m/e 522.1014 ($C_{21}H_{19}F_9O_5$ requires 522.1086).

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Registry No. **4**, 36269-21-3; **5**, 70179-06-5; **6**, 70179-07-6; **8**, 70179-08-7; **10**, 70179-09-8; **11**, 70223-46-0; **14**, 70179-10-1; **18**, 70179-11-2; **20**, 70179-12-3; **21**, 70223-47-1; **22**, 36269-18-8; **23**, 70179-13-4; **27**, 70179-14-5; **30**, 70179-15-6; **31**, 70179-16-7; **32**, 70179-17-8; **33**, 70179-18-9; **34**, 70179-19-0; **35**, 70223-48-2; **36**, 70179-20-3; **37**, 70179-21-4; **38** isomer 1, 70179-22-5; **38** isomer 2, 70223-49-3; **38** isomer 3, 70223-50-6; **39**, 70179-23-6; **40**, 70179-24-7; **42**, 70179-25-8; **45**, 70179-26-9; **46**, 70179-27-0; diethylamine, 109-89-7; 2,2,2-trifluoroethanol, 75-89-8; furan, 110-00-9; dimethyl malonate, 108-59-8; phenylselenenyl chloride, 5707-04-0; potassium acetate, 127-08-2; (2,2-diacetoxyethyl)phenyl selenide, 70209-07-3; acetylacetone, 123-54-6; methyl nitroacetate, 2483-57-0.

Stereoselectivity in Formation of Spiro[5.5]undecanes by Cationic π Cyclization

Kenn E. Harding,* James L. Cooper, and Paul M. Puckett

Department of Chemistry, Texas A&M University, College Station, Texas 77843

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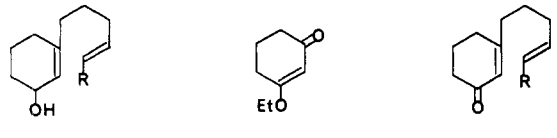
Cationic π cyclization of cyclohexenols **1a–c** leads to spiro[5.5]undecane derivatives in high yield and stereoselectivity. The stereoselectivity of the cyclization is higher with the disubstituted alkenyl side chain (**1b** and **1c**). A rationale for the stereoselectivity of these cyclizations and related heteroatom-substituted analogues is presented.

Biogenetically patterned cationic π cyclizations have been used for synthesis of several spirocyclic sesquiterpenoid systems.[1,2] As part of our continuing study[3] on the general synthetic utility of cationic π cyclization, we have investigated the synthesis of spiro[5.5]undecane derivatives through cyclohexenyl cation initiated π cyclization.[4] The cyclizations of cyclohexenols **1a–c** proceeded in high yield and with a high degree of stereoselectivity.[5] These results provide the basis for development of new stereorational syntheses of a variety of spirocyclic systems via π cyclization.



1a, R = H
1b, R = CH_3
1c, R = Bu

3

2a, R = H
2b, R = CH_3
2c, R = Bu

The cyclohexenones **2a–c** were prepared in good yield by addition of the appropriate unsaturated Grignard reagent or organolithium reagent to 3-ethoxy-2-cyclohexenone (**3**), followed by acid hydrolysis.[8] Reduction of the enones with lithium aluminum hydride in ether at 0 °C gave the allylic alcohols **1a–c** in excellent yield. Treatment of alcohol **1a** with anhydrous formic acid at room temperature for 30 min gave, after normal workup, a mixture of cyclic formates in 80% yield. Cleavage of the formate ester functionality by treatment with lithium aluminum hydride gave a mixture of alcohols **4** and **5**. Although this mixture is not readily separable by VPC (one peak on SE-30 and Carbowax), the presence of two isomers in a ratio of ~4:1 is evidenced by the ^{13}C NMR spectrum. The stereoisomeric relationship of **4** and **5** was proven by catalytic hydrogenation of the mixture to give the known

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