the nonaggregated imidazoles can act as catalysts. The probability of a bifunctional catalysis therefore seems extremely low.

Conclusion

Some of our results can help to clarify several aspects of imidazole catalysis as well as of polymer behavior. The following features deserve attention.

(1) A compact conformation of polymer maintained by hydrophobic forces of apolar groups gives rise to rate enhancement. We attribute this effect mainly to an increase in concentration of the substrate in the polymer domain. However, our results show that a tightly coiled conformation does not favor imidazole catalysis. The position on the polymer preferred by different catalytic species as determined by their polar character should be kept in mind. The implication for imidazole is that we are confronting two factors working in opposite directions. This effect therefore sets a limit to our capability to attain a higher acceleration of the hydrolysis of neutral esters.

(2) Hydrophobic binding is getting continual attention because of its supposed crucial role in enzymatic reactions. However, it has been shown above that the enzymelike pathway does not necessarily cause a more efficient catalysis.

(3) Modifications of remaining amino groups in the PEI do not raise the catalytic activity of imidazole. This effect has been already analyzed above. On the other hand, it seems quite possible that an introduction of polar or apolar groups would produce in the environment of the polymer conditions favorable to a higher rate, provided that the catalytic species would not be attracted into the hydrophobic part of the polymer. The modification chosen would depend on the kind of reaction being studied and on the character of its transition state.

(4) We would like to stress the necessity of having a low imidazole concentration on the polymer. The strikingly high activity of PEI-containing imidazole suggests that modified polymers rather than imidazole polymers should be used in the future.

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Registry No. *p*-Nitrophenyl caproate, 956-75-2.

Functionalized (C_s)-C_{17}-Heptaquinane Derivatives. Chemical Transformations along the Fluted Perimeter of a Topologically Spherical Molecule

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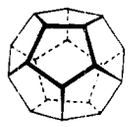
The previously described hexacyclic enedione **2** is shown to be capable of conversion to the functionalized C_{17}-heptaquinane derivative **4** by reaction with ethyl formate and potassium *tert*-butoxide. The hydroxyl group in **4** can be readily functionalized, but a variety of basic reagents induce ready loss of these groups by E_2 elimination. The conversion of **4** to dienedione **9** is smoothly achieved in two steps (tosylation, treatment with tertiary amine), despite the obvious strain associated with its twisted α,β-unsaturated carbonyl moiety. The conjugated double bond in **9** is a good Michael acceptor. Indeed, diethyl sodiomalonate adds with high stereospecificity to give **12**. **12** was subjected to phenylselenation and oxidative elimination of the selenium substituent to orient the malonate group into an endo position. Subsequent catalytic hydrogenation proceeded with delivery of hydrogen from the exterior surface of the molecule to give **15**. The role that the latter compound might play in the ultimate construction of the pentagonal dodecahedrane molecule is discussed.

As the most elaborate of the Platonic solids, the dodecahedron has held a preeminent position in solid geometry for centuries. In recent years, the many rapid advances in synthetic methodology have prompted organic chemists to attempt the construction of **1** from carbon and



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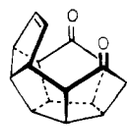

2

hydrogen. Although the bond angles in this highly symmetric array of 12 five-membered rings approximate ideality,[1-3] access to this topologically unique hydrocarbon remains a significant challenge. Nonetheless, imaginatively different approaches are being reported with increasing frequency.[4-8] One major obstacle is the need to control

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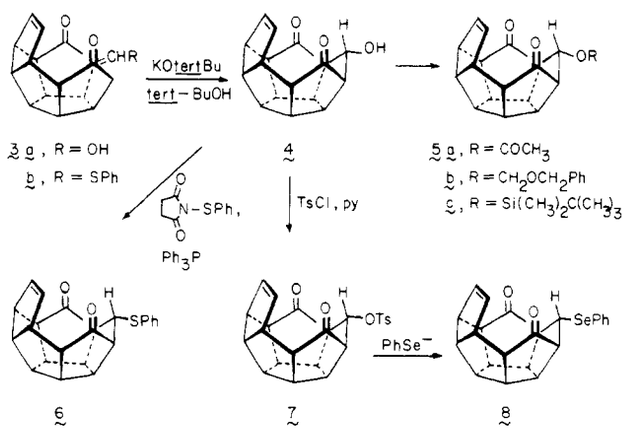
stereochemistry at each and every framework carbon atom with requisite introduction of substituents in a contrathermodynamic sense, i.e., into the interior of the cavity, at every turn. Of possibly greater concern is the presence in **1** of a solvation-free interior which provides greater kinetic inducement to unwanted transannular bonding than to the construction of perimeter bonds.[9] Clearly, the development of effective solutions to such complications is of interest not only because the elaboration of dodecahedrane is intimately associated with them but also because some current gaps in synthetic methodology would be obviated.

Recently, we described a highly efficient route to the hexacyclic enedione **2** in six laboratory steps from cyclopentadienide anion.[8i] This C_{16} structural assembly possesses the requisite all-cis geometry at its ten relevant methine centers and would appear to be adequately functionalized for ultimate transformation to **1**. One of our strategies is founded upon the controlled introduction of an additional carbon between the pair of enolizable centers at an oxidation level suitable for further chemical manipulation, including the proper positioning of the final three carbon atoms. This report deals specifically with this functionalization problem and gives particular attention to the extraordinary facility of α,β-unsaturated ketone formation along the fluted perimeter of the C_{17}-heptaquinane framework, despite the resultant twisted pπ overlap.

Results

Direct construction of the C_{17}-heptaquinane ring system was accomplished by treatment of **2** with ethyl formate and potassium *tert*-butoxide in *tert*-butyl alcohol solution under carefully controlled conditions.[10] At its optimum efficiency, this procedure afforded the desired carbinol **4** in 35% yield, admixed with a comparable amount of the uncyclized hydroxymethylene derivative **3a**. Fortunately, these isomeric substances could be separated by simple trituration with dichloromethane and **3a** could be converted with good efficiency to **4** when again exposed to the original alkaline conditions. The stereochemical homogeneity of **4** follows from its nine-line ^{13}C NMR spectrum which further reveals its inherent C_s symmetry. The marked insolubility of this alcohol required the use of pyridine-d_5 or dimethyl-d_6 sulfoxide as NMR solvent, and in both instances the α-hydroxyl proton was not clearly

Scheme I



evident due to overlapping signals. However, functionalization of **4** to give the more soluble derivatives **5a–5c** established that the hydroxyl group was oriented, as expected from thermodynamic considerations, to the less sterically encumbered exo surface. Each of the three compounds exhibited a low-field (δ 5.5–4.6) singlet for their <CHOR proton, as required for the small coupling constant which should be generated as a consequence of the existing 110° dihedral angle with the pair of flanking hydrogens.[11] An epimeric arrangement would have produced an approximate 10° relationship with the two neighbors and given rise to substantial spin–spin interaction.

At this point, we proceeded to examine the feasibility of functionalization reactions at the carbonyl groups in **5a–5c** (for example, condensation with phosphonate carbanions) and were immediately alerted to serious complications. When several reactions which had previously been tested successfully on **2** were attempted on **5a–5c**, polymerization resulted. Since the nucleophilic reagents examined were not likely to be involved in direct attack at the (*tert*-butyldimethylsilyl)oxy and (benzyloxy)methoxy sites, the possibility of β elimination of these groups was considered. While we are unaware of any detailed study of the susceptibility of variously substituted hydroxyl groups to β elimination, we continued to view this hypothesis with some early suspicion because molecular models revealed the resultant double bond to be strained and twisted away from totally effective pπ overlap. This electronic phenomenon has previously been recognized to be distinctly unfavorable in less complex diquinanes.[12,13]

Two closely related mechanistic inquiries were next pursued almost simultaneously (Scheme I). In the first, **4** was treated with *N*-(phenylthio)succinimide and triphenylphosphine in tetrahydrofuran solution under argon.[14] Although small amounts of a byproduct considered to be **3b** were obtained, the major product proved to be the phenyl sulfide **6** where substitution with retention of stereochemistry had occurred. As before, the exo configuration was clearly evident from the singlet nature of the proton signal at δ 4.46 and retention of the plane of symmetry followed from appropriate simplification of the ^{13}C NMR spectrum. The second observation was made by using the nicely crystalline tosylate **7** as substrate. When added to an absolute ethanol solution containing excess phenylselenide anion, **7** was efficiently converted (88%)

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(9) This subject will be discussed separately elsewhere.
(10) The actual procedure was a closely adapted modification of that developed by Eaton and co-workers.[6b]

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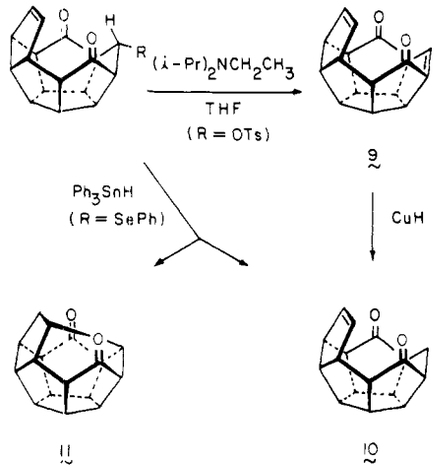
Scheme II



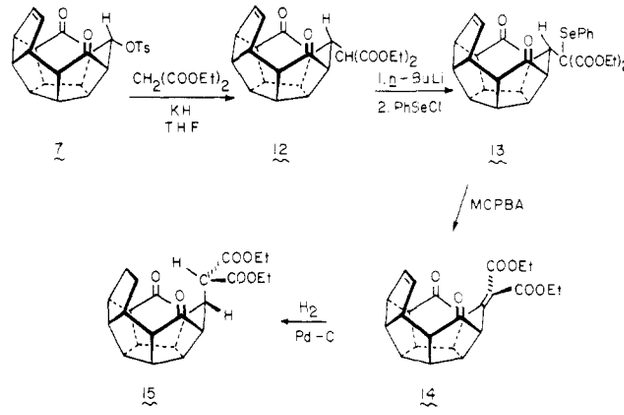
to the selenide **8** with retention of configuration. Since these interconversions are most simply explained by an elimination–conjugate addition sequence, we were led to attempt the direct isolation of the proposed dienedione intermediate and discovered that this could be achieved with little difficulty.

Simple heating of **7** with an approximately equivalent weight of diisopropylethylamine in dry tetrahydrofuran for 4 h delivers **9** in 63% yield after chromatography (Scheme II). Characterized by a broad infrared carbonyl absorption centered at 1725 cm^{-1} and an ultraviolet maximum at 255 nm (ϵ 5500), this strained molecule proved to be prone to polymerization and could only be stored for several days when kept under an inert atmosphere below 0 °C. That the geometric constraints of the spherical topology prohibit full pπ overlap is further evident in its C–C double-bond stretch (ν 1610 cm^{-1}) which is significantly weakened relative to that observed in model unstrained α,β-unsaturated ketones (ν ~1650 cm^{-1}).[15]

Notwithstanding the loss of effective enone conjugation, **9** enters readily into Michael reactions. An interesting example is the 1,4-addition of copper hydride to give **10** in good yield. The return of mirror-plane symmetry to this colorless crystalline solid is confirmed by the ^{13}C NMR spectrum which consists of only 10 signals. In accord with the obvious reduction of ground-state strain, **10** has proven to be indefinitely shelf stable. The ready availability of this C_{17}-heptaquinane by this route contrasts with the complications encountered when phenyl selenide **8** was reduced with triphenyltin hydride. Although a small quantity of **10** could be laboriously obtained in this manner, the product was found to be a two-component mixture consisting predominantly of **11**. Evidently, the free-radical intermediate finds transannular capture by the remote π bond to be a kinetically, if not also a thermodynamically, acceptable way to enter into the product manifold.

The versatility of tosylate **7** in synthesis is particularly noteworthy when carbon nucleophiles are involved. For example, stirring **7** with 3 equiv each of diethyl malonate and sodium hydride in tetrahydrofuran at room temperature for 2 h gave **12** in 94% purified yield (Scheme III). We believe the mechanistic criteria discussed previously to be applicable here also. The exo stereochemistry of **12** follows from direct NMR evidence, previous analogy, and the anticipated steric bias for the less hindered outer region of the fluted rim. Use was next made of the well-established kinetic acidity of the malonate proton. When **12** was treated sequentially with *n*-butyllithium and phenylselenyl chloride in tetrahydrofuran at −78 °C, selenation occurred to produce **13**. This diketo diester was not extensively characterized but oxidized directly with 1 equiv of *m*-chloroperbenzoic acid. As expected, a new center of unsaturation was thereby introduced as indicated in **14**. This structural assignment is fully consistent with the available analytical and spectroscopic data. When **14** was catalytically hydrogenated over 5% palladium-on-carbon, the malonate unit was necessarily projected into the interior of the molecular cavity as a result of the necessary delivery of hydrogen from the exterior surface.[8a,b] The endo orientation of the malonate group in **15** was established unambiguously by comparable hydrogenation of **12**. The spectral dissimilarity of the hydrogenated products was obvious (see Experimental Section), although both clearly possess a mirror plane of symmetry. In particular, the signal for the C_7 proton in dihydro-**12** is seen to be weakly coupled to the neighboring protons (θ ~ 110°), while that in **15** interacts strongly (J = 9 Hz, θ ~ 10°).

Scheme III



Although **15** does contain as many as 13 cis-related methine centers in addition to the 20 requisite carbon atoms, the molecule is somewhat sterically disadvantaged as a precursor to **1**. Thus, rotation about the C_7, α-malonate bond is without doubt seriously impeded because of the bulky ester groups. These rotomers in which one or the other of these functionalities is projected toward the interior of the cavity are decidedly disfavored. This being the case, it can be expected that proper positioning of the carboethoxy carbons relative to the ketone carbonyls located on the fluted rim will prove difficult. The conformations adopted by *meso*- and *dl*-bivalane, as determined by X-ray analysis, serve as closely related prototypes.[16] Nonetheless, we anticipate that steric complications of this type can be overcome and hope to describe methodologies to deal with this problem at a future date.

Experimental Section

Proton magnetic resonance spectra were obtained with Varian A-60A, Varian EM-360, and Bruker HX-90 spectrometers; apparent splittings are given in all cases. Carbon spectra were recorded with the Bruker unit. Infrared spectra were determined on a Perkin-Elmer Model 467 instrument. Mass spectra were recorded on an AEI-MS9 spectrometer at an ionization potential of 70 eV. Elemental analyses were performed by the Scandinavian Microanalytical Laboratory, Herlev, Denmark.

8-(Hydroxymethylene)hexacyclo[8.5.1.$0^{2,6}$.$0^{3,14}$.$0^{7,16}$.$0^{11,15}$]-hexadec-12-ene-4,9-dione (3a) and 17-hydroxyheptacyclo-[8.51.$1^{5,8}$.$0^{2,6}$.$0^{3,14}$.$0^{7,16}$.$0^{11,15}$]heptadec-12-ene-4,9-dione (4). Diketone **2** (390 mg, 1.6 mmol) was added under argon to a solution

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of potassium *tert*-butoxide (1.2 g, 10.7 mmol) in *tert*-butyl alcohol (8 mL, distilled from calcium hydride) and stirred at room temperature for 1.5 h. Ethyl formate (20 mL, freshly distilled from P_2O_5) was introduced dropwise and this mixture was stirred overnight before being poured into water and diluted to a total volume of 60 mL. This solution was in turn stirred for 8 h with periodical addition of 1 N sodium hydroxide as needed to maintain the pH at 7.5–8.0. After the addition of potassium dihydrogen phosphate, the mixture was filtered and the filtrate was extracted with dichloromethane (2 × 15 mL, 2 × 10 mL). The combined organic layers were dried, filtered, and evaporated to give 316 mg of pale yellow solid. This material was triturated with dichloromethane to leave 158 mg (36%) of **4** as a white solid, which decomposes >260 °C: ν_{max}^{KBr} 3460, 2980, 1730, 1210, 1030, 920 cm^{-1}; ^1H NMR (δ, pyridine-d_5) 5.90 (s, 2 H), 5.22 (s, 1 H), 5.4–4.6 (br m, 1 H), 4.0–2.3 (series of m, 12 H); ^{13}C NMR (ppm, pyridine-d_5) 217.9, 130.4, 83.8, 67.1, 60.6, 59.7, 56.1, 55.0, 54.7; *m/e* calcd 268.1099, obsd 268.1106.

The dichloromethane triturates were evaporated to give 158 mg (36%) of **3a**, which could independently be cyclized to **4**: $\nu_{max}^{CHCl_3}$ 2960, 1730, 1660, 1590, 1180, 910 cm^{-1}; *m/e* calcd 268.1099, obsd 268.1106.

17-Hydroxyheptacyclo[8.5.1.1^{5,8}.0^{2,6}.0^{3,14}.0^{7,16}.0^{11,15}]heptadec-12-ene-4,9-dione Acetate (5a). A 226-mg sample of **4** was dissolved in 2 mL of pyridine containing 1 mL of acetic anhydride and this solution was stirred at room temperature for 1.5 days. The reaction mixture was poured into water (20 mL) and extracted three times with dichloromethane. The combined organic layers were washed with 2% hydrochloric acid (3×) and brine, dried, and evaporated. The residue was chromatographed on silica gel using gradient elution techniques (hexane–ethyl acetate) to give 238 mg (91%) of **5a** which was recrystallized from ethyl acetate: mp >200 °C; ^1H NMR (δ, $CDCl_3$) 5.73 (s, 2 H), 5.48 (s, 1 H), 4.0–2.6 (series of m, 12 H), 1.93, (s, 3 H); ^{13}C NMR (ppm, $CDCl_3$) 215.5, 169.5, 129.9, 85.0, 62.8, 60.2, 59.6, 59.1, 55.6, 54.9., 53.7, 21.1; *m/e* calcd 310.1212, obsd 310.1205.

Anal. Calcd for $C_{19}H_{18}O_4$: C, 73.53; H, 5.85. Found: C, 73.47; H, 5.99.

17-[(Benzyloxy)methoxy]heptacyclo[8.5.1.1^{5,8}.0^{2,6}.0^{3,14}.0^{7,16}.0^{11,15}]heptadec-12-ene-4,9-dione (5b). To a magnetically stirred slurry of **4** (163 mg) in dichloromethane (2 mL) was added 150 μL of diisopropylethylamine followed by 100 mL of chloromethyl benzyl ether and the mixture was stirred at room temperature for 2.5 h. Because analytical TLC showed **4** to be still present, another 150 μL of diisopropylethylamine and 100 μL of chloromethyl benzyl ether were added. Within 10 min, all of the solid had dissolved; after a total elapsed time of 20 min, the reaction mixture was quenched with water. The organic phase was twice washed with water and sodium dihydrogen phosphate solution, dried, and evaporated. The residue was purified by preparative TLC on silica gel (elution with 1:1 ethyl acetate–hexane) to give 106 mg (43%) of **5b**: mp 126–127.5 °C (from ethyl acetate); $\nu_{max}^{CHCl_3}$ 2960, 1730, 1030 cm^{-1}; ^1H NMR (δ, $CDCl_3$) 7.32 (s, 5 H), 5.79 (s, 2 H), 4.78 (s, 2 H), 4.65 (s, 1 H), 4.60 (s, 2 H), 4.0–2.6 (series of m, 12 H); ^{13}C NMR (ppm, $CDCl_3$) 217.1, 130.1, 128.5, 127.9, 127.7, 93.8, 88.7, 70.0, 63.8, 60.3, 59.7, 59.4, 55.9, 54.9, 54.0; *m/e* calcd 388.1682, obsd 388.1674.

Anal. Calcd for $C_{25}H_{24}O_4$: C, 77.30; H, 6.23. Found: C, 76.91, H, 6.17.

17-[(*tert*-Butyldimethylsilyl)oxy]heptacyclo[8.5.1.1^{5,8}.0^{2,6}.0^{3,14}.0^{7,16}.0^{11,15}]heptadec-12-ene-4,9-dione (5c). A solution of **4** (260 mg, 0.93 mmol), *tert*-butyldimethylchlorosilane (260 mg, 1.73 mmol), and imidazole (130 mg, 1.94 mmol) in dimethylformamide (2 mL) was heated at 50 °C overnight. The reaction mixture was cooled, dichloromethane was added, and the organic solution was washed in turn with saturated potassium dihydrogen phosphate solution (2×) and water (2×) prior to drying. The solvent was evaporated and the residue was chromatographed on silica gel to give 200 mg (56%) of **5c**: mp 203–213 °C (from ethyl acetate); ν_{max}^{KBr} 2940, 1720, 1040, 840 cm^{-1}; ^1H NMR (δ, $CDCl_3$) 5.78 (s, 2 H), 4.71 (s, 1 H), 4.0–2.6 (series of m, 12 H), 0.85 (s, 9 H), 0.10 (s, 6 H); ^{13}C NMR (ppm, $CDCl_3$), 217.38, 129.99, 84.23, 66.69, 60.26, 59.41, 55.77, 54.80, 53.95, 25.91, 18.02, −4.79.

Anal. Calcd for $C_{23}H_{30}O_3Si$: C, 72.21; H, 7.90. Found: C, 72.28; H, 7.93.

17-(Phenylthio)heptacyclo[8.5.1.1^{5,8}.0^{2,6}.0^{3,14}.0^{7,16}.0^{11,15}]heptadec-12-ene-4,9-dione (6). *N*-(Phenylthio)succinimide (283 mg, 1.37 mmol) was added to a solution of tri-*n*-butylphosphine (300 μL) in tetrahydrofuran (2.5 mL) under argon. The purple solution was stirred 5 min, at which point 200 mg (0.83 mmol) of **4** was added. The solution, which immediately turned brown, was stirred for 1 h prior to the addition of brine and dichloromethane. The organic layer was separated, washed with potassium dihydrogen phosphate and sodium bicarbonate solutions, and dried. The residue was purified by preparative TLC on silica gel (elution with 1:1 ethyl acetate–hexane) to give 88 mg (30%) of **6** along with 30 mg of a second product tentatively identified as **3b**. Recrystallization of **6** from ethyl acetate gave colorless crystals: mp 189–191 °C; ν_{max}^{KBr} 2970, 1730, 1485, 1200, 1165 cm^{-1}; ^1H NMR (δ, $CDCl_3$) 7.6–7.0 (m, 5 H), 5.80 (s, 2 H), 4.46 (s, 1 H), 4.0–2.6 (series of m, 12 H); ^{13}C NMR (ppm, $CDCl_3$) 217.4, 129.9, 129.7, 129.1, 126.6, 62.3, 60.3, 59.7, 58.9, 55.7, 55.3, 55.0, 53.9; *m/e* calcd 360.1190, obsd 360.1184.

Anal. Calcd for $C_{23}H_{20}O_2S$: C, 76.64; H, 5.59; S, 8.89. Found: C, 76.50; H, 5.61; S, 9.09.

17-Hydroxyheptacyclo[8.5.1.1^{5,8}.0^{2,6}.0^{3,14}.0^{7,16}.0^{11,15}]heptadec-12-ene-4,9-dione *p*-Toluenesulfonate (7). *p*-Toluenesulfonyl chloride (397 mg, 2.1 mmol) was added to a solution of **4** (263 mg, 1 mmol) in pyridine (3 mL) at 0 °C. The reaction mixture was allowed to come to room temperature and stirred overnight. Dichloromethane was added; the mixture was cooled to 0 °C, washed with 5% hydrochloric acid solution (4×), water, and saturated sodium bicarbonate solution, and dried. The solvent was evaporated to give 356 mg of solid which was filtered through a short plug of silica gel (dichloromethane elution) to give 331 mg (80%) of **7**. Recrystallization from ethyl acetate afforded a colorless solid which decomposes above 150 °C: $\nu_{max}^{CHCl_3}$ 1740, 1370, 1180, 940, 900 cm^{-1}; ^1H NMR (δ, $CDCl_3$) 7.81 (d, J = 8.5 Hz, 2 H), 7.34 (d, J = 8.4 Hz, 2 H), 5.73 (s, 2 H), 5.16 (s, 1 H), 4.0–2.75 (m, 12 H), 2.43 (s, 3 H); ^{13}C NMR (ppm, $CDCl_3$) 214.2, 145.1, 133.4, 130.1, 129.8, 128.0, 91.3, 63.2, 60.1, 59.4, 59.0, 55.6, 54.6, 53.3, 21.7.

Anal. Calcd for $C_{24}H_{23}O_5S$: C, 68.23; H, 5.25. Found: C, 67.88; H, 5.25.

17-(Phenylseleno)heptacyclo[8.5.1.1^{5,8}.0^{2,6}.0^{3,14}.0^{7,16}.0^{11,15}]heptadec-12-ene-4,9-dione (8). Sodium borohydride (49 mg, 1.3 mmol) was added portionwise to diphenyl diselenide (231 mg, 0.74 mmol) dissolved in absolute ethanol (5 mL). This solution was stirred for 30 min, at which point 140 mg (0.33 mmol) of **7** was added. After 3 h, the reaction mixture was diluted with saturated ammonium chloride solution and extracted with dichloromethane. The combined organic layers were dried and evaporated to leave a residue which was purified by preparative TLC on silica gel (elution with hexane–ethyl acetate, 3:1). There was obtained 119 mg (88%) of **8** as a colorless solid: mp 178–180 °C (from ethyl acetate); $\nu_{max}^{CHCl_3}$ 2960, 1730, 1240, 1165 cm^{-1}; ^1H NMR (δ, $CDCl_3$) 7.7–7.0 (m, 5 H), 5.82 (s, 2 H), 4.55 (s, 1 H), 3.9–2.5 (m, 12 H); ^{13}C NMR (ppm, $CDCl_3$) 217.3, 133.2, 130.2, 129.9, 129.3, 127.5, 63.2, 60.2, 59.7, 58.9, 55.1, 55.0, 54.0, 49.1; *m/e* calcd 408.0628, obsd 408.0633.

Anal. Calcd for $C_{23}H_{20}O_2Se$: C, 67.81; H, 4.95. Found: C, 67.61; H, 4.97.

Tri-*n*-butyltin Hydride Reduction of 8. Octacyclo[8.5.1.1^{5,8}.0^{2,6}.0^{3,14}.0^{7,16}.0^{11,15}.0^{13,14}]heptadecane-4,9-dione (11). A solution of **8** (60 mg), hydroquinone (52 mg), and triphenyltin hydride (150 mg) in 2 mL of toluene was refluxed overnight under nitrogen, diluted with dichloromethane, washed with saturated sodium bicarbonate solution, and dried. After solvent removal under reduced pressure, the residue was subjected to preparative TLC (elution with ethyl acetate–hexane, 2:1) and subsequently high-pressure liquid chromatography (same elution) on silica gel. There was isolated 19 mg (51%) of **11** as a colorless solid: mp 298 °C dec; $\nu_{max}^{CHCl_3}$ 2960, 1730, 1390, 910 cm^{-1}; ^1H NMR (δ, $CDCl_3$) 3.61–1.90 (series of m); ^{13}C NMR (ppm, $CDCl_3$) 65.2, 63.3, 63.2, 62.9, 60.6, 55.7, 54.8, 54.4, 53.9, 53.4, 36.3, 35.4, 29.7; *m/e* calcd 252.1150, obsd 252.1152.

Heptacyclo[8.5.1.1^{5,8}.0^{2,6}.0^{3,14}.0^{7,16}.0^{11,15}]heptadeca-5(17),12-diene-4,9-dione (9). A solution of **7** (320 mg, 0.76 mmol) and diisopropylethylamine (300 mg, 2.3 mmol) in 10 mL of tetrahydrofuran was refluxed under a nitrogen atmosphere for 8 h. The solvent was evaporated and the residue was triturated with

dichloromethane. The resulting solution was washed with saturated potassium dihydrogen phosphate solution, dried, and concentrated. The residue was purified by preparative TLC on silica gel (elution with ethyl acetate–hexane, 3:1) to give 120 mg (63%) of **9** as an air-sensitive colorless solid: $\nu_{max}^{CHCl_3}$ 2960, 1710, 1610, 1160, 1025 cm^{-1}; ^{1}H NMR (δ, $CDCl_3$) 5.6–5.2 (m, 3 H) 4.0–2.5 (series of m, 11 H); m/e calcd 250.0994, obsd 250.1000.

Heptacyclo[8.5.1.1^{5,8}.0^{2,6}.0^{3,14}.0^{7,16}.0^{11,15}]heptadec-12-ene-4,9-dione (10). Vitride (1 mL) was added to a slurry of cuprous bromide (744 mg) and tetrahydrofuran (5 mL) at 0 °C. The resulting brownish black suspension was stirred at 0 °C for 30 min and then cooled to −78 C. 2-Butanol (0.6 mL) was added followed by 75 mg of **9** and 0.25 mL of acetone in a total of 6 mL of tetrahydrofuran (three 2-mL aliquots were needed to completely dissolve **9**). The reaction mixture was allowed to warm to 20 °C and was maintained at this temperature for 2 h before the addition of saturated ammonium chloride solution. This mixture was partitioned between water (60 mL) and dichloromethane (20 mL) and filtered through Celite. The aqueous phase was thrice extracted with dichloromethane and the combined organic layers were dried and evaporated. Purification of the residue by preparative TLC on silica gel (elution with ethyl acetate–hexane, 2:1) gave 47 mg (66%) of **10**: mp >340 °C; (δ, $CDCl_3$) 5.7 (s, 2 H), 4.0–1.6 (series of m, 14 H); ^{13}C NMR (ppm, $CDCl_3$) 221.4, 130.0, 60.4, 60.0, 59.3, 56.6, 55.6, 55.2 (2 C), 37.1; m/e calcd 252.1150, obsd 252.1155.

Anal. Calcd for $C_{17}H_{16}O_2$: C, 80.95; H, 6.35. Found: C, 80.67; H, 6.35.

Diethyl 4,9-Dioxoheptacyclo[8.5.1.1^{5,8}.0^{2,6}.0^{3,14}.0^{7,16}.0^{11,15}]heptadec-12-ene-*exo*-7-malonate (12). To a suspension of 50% sodium hydride oil dispersion (18 mg, 50%) in dry tetrahydrofuran (1.5 mL) cooled to 0 °C under nitrogen was added 86 μL (0.54 mmol) of diethyl malonate. Upon completion of gas evolution, the resultant clear solution was stirred for an additional hour at 0 °C. Tosylate **7** (82 mg, 0.19 mmol) was introduced in one portion and the mixture was allowed to come to room temperature. After 2 h, saturated ammonium chloride solution (5 mL) was added and the product was extracted into dichloromethane. The combined organic layers were dried, filtered, and concentrated to leave a light brown oil which was chromatographed on silica gel (elution with 50% ethyl acetate in hexane). Trituration with ether gave crystalline **12** (74 mg, 94%): mp 152–153 °C; $\nu_{max}^{CHCl_3}$ 2960, 1730, 1260, 1100, 1020 cm^{-1}; ^{1}H NMR (δ, $CDCl_3$) 5.75 (s, 2 H), 4.18 (q, J = 7.1 Hz, 4 H), 3.40 (s, 1 H), 3.80–2.30 (series of m, 13 H), 1.24 (t, J = 7.1 Hz, 6 H); ^{13}C NMR (ppm, $CDCl_3$) 219.2, 168.2, 130.2, 61.6, 60.5, 60.1, 59.4, 56.2, 55.8, 55.3 (2 C), 55.0, 51.0, 14.1; m/e calcd 410.1729, obsd 410.1736.

Anal. Calcd for $C_{24}H_{26}O_6$: C, 70.24; H, 6.34. Found: C, 69.98; H, 6.44.

Catalytic Hydrogenation of 12. A solution of **12** (200 mg, 0.49 mmol) in ethyl acetate (5 mL) containing 50 mg of 5% palladium-on-carbon was hydrogenated at 50 psig in a Parr apparatus (30 h, 25 °C). The reaction mixture was filtered, concentrated, and chromatographed on silica gel. Elution with 50% ethyl acetate in hexane furnished 154 mg (77%) of the saturated exo malonate derivative: mp 129–132 °C; $\nu_{max}^{CHCl_3}$ 2960, 1735, 1452, 1300, 1155, 1030 cm^{-1}; ^{1}H NMR (δ, $CDCl_3$) 4.11 (q, J = 7.2 Hz, 4 H), 3.50 (s, 1 H), 3.79–3.20 (series of m, 9 H), 2.82 (br s, 6 H), 1.77 (br s, 2 H), 1.25 (t, J = 7.2 Hz, 6 H); m/e calcd 412.1886, obsd 412.1842.

Anal. Calcd for $C_{24}H_{28}O_6$: C, 69.90, H, 6.80. Found: C, 69.53; H, 6.82.

Diethyl 4,9-Dioxoheptacyclo[8.5.1.1^{5,8}.0^{2,6}.0^{3,14}.0^{7,16}.0^{11,15}]heptadec-1-ene-Δ$^{17\alpha}$-malonate (14). A solution of **12** (130 mg, 0.32 mmol) in dry tetrahydrofuran (2 mL) cooled to 78 °C under argon was treated with *n*-butyllithium in hexane (0.24 mL of 1.6 M, 0.38 mmol). The resulting pale yellow solution was stirred at −78 °C for 30 min before phenylselenyl chloride (80 mg, 0.42 mmol) in 1.5 mL of tetrahydrofuran was introduced. After 3 h at 78 °C, the reaction mixture was allowed to come to 5 °C and treated with saturated ammonium chloride solution (5 mL). The product was extracted into dichloromethane and the combined organic layers were washed with water, dried, and evaporated. Silica gel thin-layer chromatography (50% ethyl acetate in hexane elution) of the residue gave partially purified selenide **13** which was directly oxidized.

A 40-mg sample of impure **13** was dissolved in dichloromethane (2 mL), cooled to −78 °C, and treated with a solution of *m*-chloroperbenzoic acid (13 mg, 85% purity, 0.06 mmol) in dichloromethane (2 mL). The reaction mixture was stirred at −78 °C for 2 h, warmed to room temperature, treated with 25 μL of triethylamine, and carefully transferred to 3 mL of refluxing hexane. After 2 h, the mixture was cooled and poured into 30 mL of dichloromethane. The organic phase was washed with saturated sodium bicarbonate solution, dried, filtered, and concentrated. Chromatography of the residue on silica gel (elution with 50% ethyl acetate in hexane) afforded 15 mg (21%) of **14**: $\delta_{max}^{CHCl_3}$ 2965, 1735, 1375, 1268, 1160 cm^{-1}; ^{1}H NMR (δ, $CDCl_3$) 5.70 (s, 2 H), 4.17 (q, J = 7.1 Hz, 4 H), 3.80–3.00 (series of m, 12 H), 1.22 (t, J = 7.1 Hz, 6 H); ^{13}C NMR (ppm, $CDCl_3$) 130.2, 61.1, 60.8, 56.0, 55.2, 52.7, 29.7, 14.1 (not including carbonyl and quaternary carbons); m/e calcd 408.1573, obsd 408.1578.

Diethyl 4,9-Dioxoheptacyclo[8.5.1.1^{5,8}.0^{2,6}.0^{3,14}.0^{7,16}.0^{11,15}]heptadecane-*endo*-7-malonate (15). A solution of **14** (10 mg, 0.025 mmol) in ethyl acetate (5 mL) was hydrogenated in the predescribed fashion to give **15** which was purified by thin-layer chromatography on silica gel (elution with 50% ethyl acetate in hexane): 5 mg (50%); $\nu_{max}^{CHCl_3}$ 2960, 1735, 1450, 1360, 1250 cm^{-1}; ^{1}H NMR (δ, $CDCl_3$) 4.28 (q, J = 7.1 Hz, 4 H), 3.62 (m, 6 H), 3.50–3.00 (m, 4 H), 2.90 (m, 6 H), 1.60 (br s 2 H), 1.23 (t, J = 7.1 Hz, 6 H); ^{13}C NMR (ppm, $CDCl_3$) 62.2, 61.3, 61.2, 58.5, 56.4, 56.1, 53.5, 50.4, 34.5, 30.8, 29.7, 14.0 (not including carbonyl carbons); m/e calcd 412.1886, obsd 412. 1892.

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