Topologically Spherical Molecules. Transannular and Other Rearrangement Reactions of Dihomodioxatrisecododecahedranes

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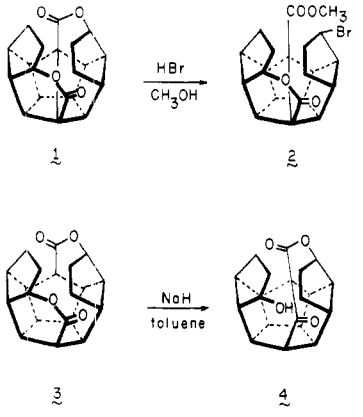
With the availability of 4a,8a-dimethyloctadecahydro-3,7-dioxadicyclopenta[*cd*,*c'd'*]pentaleno[2,1,6-*hia*:5,4,3-*h'i'a'*]diindene-4,8-dione (**5**), it has been possible to determine the relative ordering of three reactions experienced by potential dodecahedrane precursors of this general type. Direct ring opening of the lactone rings in **5** with Meerwein's reagent proceeds only at more elevated temperatures and only with subsequent prototropic shift. In contrast, the derived dilactol **9** and hemiacetal **10** are particularly prone to transannular hydride shifting and neighboring-group involvement of the ether oxygen. The proposed mechanism was confirmed by a suitable deuterium-labeling experiment. Further indications of the factors controlling ring opening were obtained from ether lactone **11**, from which the C_2 symmetric dihomodioxatrisecododecahedrane **23** could be prepared as well. The collective results indicate the chemical reactivity of these compounds to be controlled in large part by energetic and stereoelectronic factors recognized to be operative in simpler systems. Quite apparent is a substantial kinetic inducement for bond making within the solvent-free cavities of these highly spherical molecules.

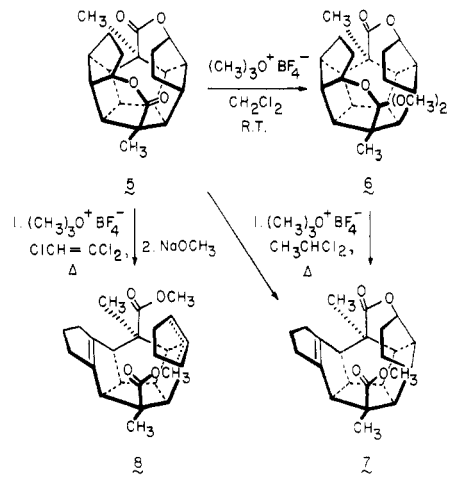
In previous papers, we have described an efficient "domino Diels–Alder" route[2-4] to the "closed" dilactone **1** and detailed its conversion to "open" dilactone **3** by simple reductive cleavage.[5] Both topologically interesting compounds[6] are axially symmetric and have their 20 carbon atoms correctly linked together for ultimate elaboration of the pentagonal dodecahedrane ($C_{20}H_{20}$).[7] Significantly, all 12 methine carbons within **1** are cis locked with the hydrogens oriented to the outside of the developing sphere, as they must be if the target molecule is to be attained. In **3**, the methine count reaches 14, leaving only six centers to connect together in the proper fashion.

While both **1** and **3** are obviously attractive intermediates, each has its own penchant for kinetically preferred bond making and bond breaking which contradicts the reaction schemes initially planned for them. In the case of **1**, this special reactivity takes the form of an allosteric effect.[8] Cleavage of one lactone ring to give, for example, **2** proceeds quite readily as expected. However, with but



one exception to date,[5] the second lactone ring is not opened, even under forcing conditions. This phenomenon materializes presumably because of structural distortions within **2**, driven by a desire on the part of the two central methylene groups to avoid each other (not possible in **1**).

Scheme I



As a consequence of its essentially solvent-free interior, lactone **3** has proven to be highly sensitive to unwanted transannular cyclization under both alkaline and acidic conditions. Unsymmetrical products typified by **4** are produced. Although novel in their own right, such structural entities serve no utilitarian purpose in the present context.

Because of the sensitivity of **3** to intramolecular condensation, no assessment of potentially useful transformations along its fluted perimeter[9,10] has been possible. Through examination of molecular models, we had convinced ourselves that the appreciably altered topology of **3** relative to **1**, as well as its somewhat higher degree of conformational flexibility, would be a source of yet uncovered chemical transformations. In order to pursue investigation of this question, it became necessary to devoid the α-carbonyl carbons of **3** of enolizable protons. To this end, the dimethyl homologue **5** was prepared[5] and its chemical reactivity scrutinized in some detail.

(1) Presidential Fellow, 1979–1980.
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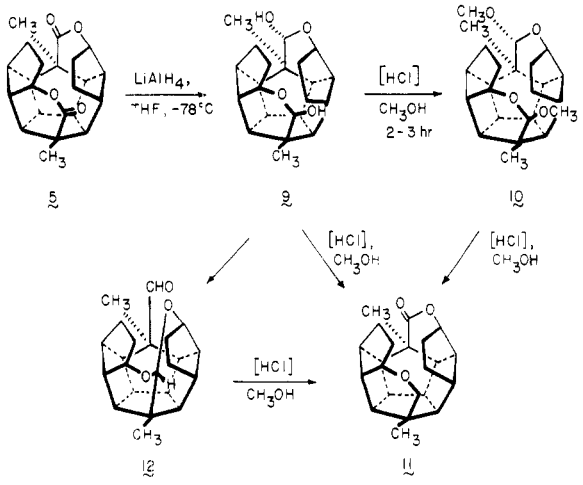
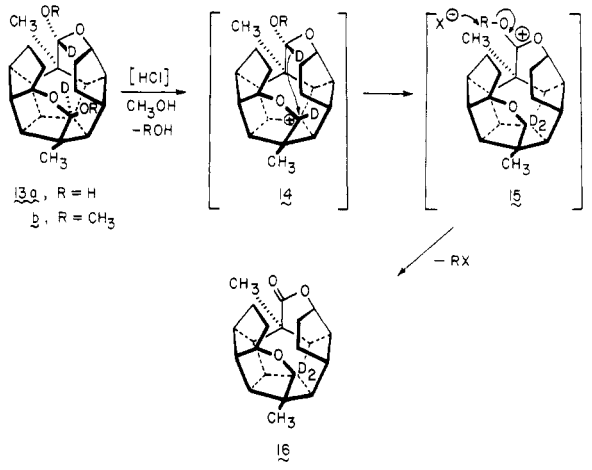
Scheme II



Scheme III



Results

Little imagination is required to see that retrograde Baeyer–Villiger ring contraction of the lactone functions in **5** to cyclopentanone rings would deliver an attractive trisecododecahedranedione derivative with retention of C_2 symmetry in common with its precursors. Since we had previously established that standard acid-promoted elimination and intramolecular acylation go astray in this instance,[5] recourse was herein made to the milder trimethyloxonium tetrafluoroborate reagent. Exposure of **5** to a fivefold excess of the oxonium salt in dichloromethane at room temperature for 16 h, followed by direct treatment with a solution of sodium methoxide in methanol, resulted in high-yield formation of monoortholactone **6** (Scheme I). Evidently, methylation of the first carbonyl generates a carbocation intermediate whose charge deters subsequent electrophilic attack at the second, transannularly positioned carbonyl group because of incipient high levels of charge–charge repulsion. Since **6** is no longer symmetric, it becomes difficult to rule out on the basis of spectroscopic data alone that more deep-seated structural change had not occurred. That such was not the case was substantiated by mild acid hydrolysis of **6** to return **5**.

When heated with excess trimethyloxonium fluoroborate in 1,1-dichloroethane, both **5** and **6** were converted to ester lactone **7**. The ^{1}H NMR spectrum of this obviously nonsymmetric compound exhibited no vinyl proton absorptions, a fact which suggested that the double bond which is introduced upon initial ring opening becomes translocated to a more highly substituted site by ensuing prototropic migration. This finding was disappointing, since it meant that the pivotal carbon which was originally bonded to the lactone oxygen was no longer functionalized. Whereas both lactone rings in **5** were eventually cleaved by making recourse to ethylene trichloride as solvent, the resultant diene diester, tentatively assigned structure **8**, was similarly beset with this complication.

An alternative to the direct dilactone approach to a C_2-symmetric trisecododecahedranedione comprises initial reduction to the dilactol level and appropriate utilization of the masked aldehyde groups. Experimentally, we found that **5** could be efficiently reduced to **9** with lithium aluminum hydride in tetrahydrofuran at −78 °C (Scheme II). As is customary in these circumstances,[5,11] **9** is the product of thermodynamic control and results from equilibration of the kinetically favored endo,endo isomer during workup and/or isolation. The assignment of stereochemistry is based upon appearance of the pair of hemiacetal protons as a singlet at δ 4.80 (in pyridine-d_5), which is not appreciably altered upon conversion to the more highly soluble methyl acetal **10** (δ 4.52, s, 2 H, $CDCl_3$). The latter substance was accessible by *short-term* treatment of **9** with methanolic hydrogen chloride. Capture of methanol by the oxonium ion intermediates can realistically occur only from the convex molecular surface. As before, retention of symmetry in both cases was substantiated by ^{13}C NMR.

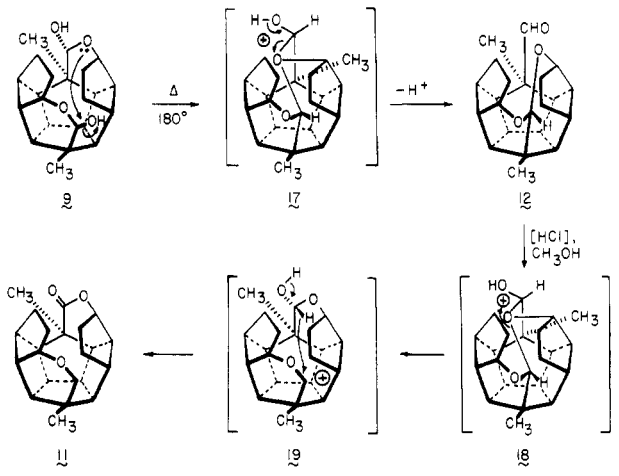
When either **9** or **10** was allowed to stand in methanolic hydrogen chloride solution for 3 days, internal oxidation–reduction took place with formation of ether lactone **11**. The identical transformation was observed upon admixture of **10** with titanium trichloride in $CDCl_3$ solution (NMR-tube experiment). That the product carried a δ-lactone carbonyl group was apparent from the IR (1710 cm^{-1}) and ^{13}C NMR spectra (176.91 ppm). In addition, the ^{1}H NMR spectrum showed a widely spaced AB absorption at δ 3.86 (d, J = 12 Hz) and 2.98 (d, J = 12 Hz) which is very typical of an ether methylene group fixed in a rigid spherical framework.[11]

The simplest rationalization of this interesting reaction requires transannular hydride migration through the molecular cavity from one lactol carbon atom to the second which has become cationic as a result of proton-induced loss of water or methanol. This explanation was bolstered by lithium aluminum deuteride reduction of **5** to the doubly deuterated dilactol **13a**. Brief acid-catalyzed methanolysis of **13a** gave **13b**. When solutions of either substance in methanolic hydrogen chloride were allowed to stand at room temperature for 3 days, a single product identified as **16** was obtained in high yield. Like its undeuterated counterpart (**11**), **16** showed an intense infrared carbonyl absorption at 1710 cm^{-1}. Its ^{1}H NMR spectrum was identical with that of **11**, except for the notable absence of the pair of doublets due to the CH_2O moiety. Thus, whereas the two deuterium atoms are introduced on opposite sides of the spherically shaped **13a** and **13b**, they become geminally positioned in **16**. The direct involvement of **14** and **15** (Scheme III) would thereby appear to be vindicated.

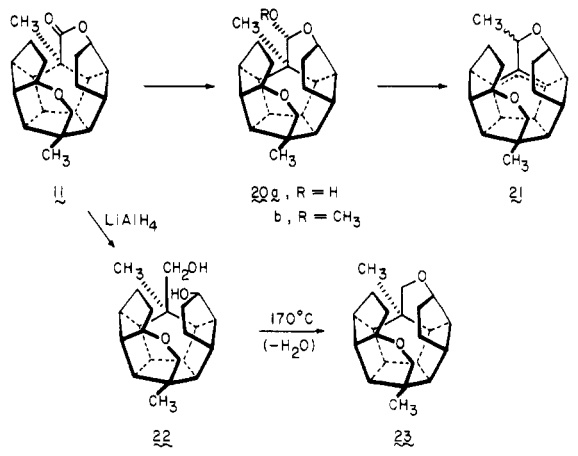
A further indication of the extraordinary facility for transannular reaction within **9** was obtained serendipitously when it was noted that melting of the dilactol (180 °C) caused tiny gas bubbles (H_2O) to be evolved. Isolation and characterization of the thermolysis product showed it to be the aldehydo acetal **12**. The infrared spectrum of **12** is characterized by a strong carbonyl absorption at 1715

(11) Balogh, D.; Begley, W. J.; Bremner, D.; Wyvratt, M. J.; Paquette, L. A. *J. Am. Chem. Soc.* **1979**, *101*, 749. Paquette, L. A.; Begley, W. J.; Balogh, D.; Wyvratt, M. J.; Bremner, D. *J. Org. Chem.* **1979**, *44*, 3630.

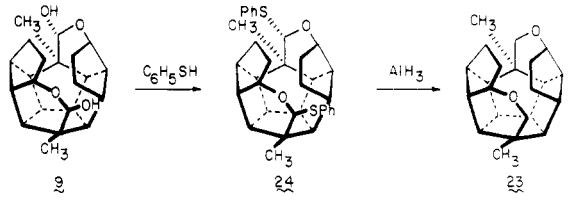
Scheme IV



Scheme V



Scheme VI



cm^{-1}, appropriate for a saturated carboxaldehyde. The ^1H NMR spectrum in $CDCl_3$ features an uncoupled aldehydo proton at δ 9.85 (s, 1 H), a distinctive acetal proton at δ 4.86 (s, 1 H), and two different methyl groups at δ 1.18 and 1.09. Particularly diagnostic is the ^{13}C NMR spectrum where the four most downfield shifted peaks seen at 204.15, 95.64, 76.95, and 71.67 ppm can be confidently assigned to the aldehyde carbonyl carbon, acetal carbon, and unsymmetrical ether-substituted carbons of **12**.

At the mechanistic level, this process is viewed to be the result of transannular attack by the lactol ether oxygen with displacement of "hydroxide ion", in a process presumably facilitated by catalytic agents present on the glassware surface (Scheme IV). If this hypothesis is correct, then it should in principle be possible to induce an analogous chemical change under milder conditions with a suitable electrophilic reagent. An aprotic medium is required since the presence of such a solvent might redirect the chemistry in the direction previously observed (Scheme III). Lead tetraacetate in cyclohexane buffered with solid calcium carbonate was the first reagent tried. Indeed, efficient conversion to **12** was realized at the reflux temperature of the solvent.

Also examined was the effect of dilute hydrochloric acid in catalytic quantities on dilactol **9** in tetrahydrofuran solution. After the solution stood at room temperature for 2 days, conversion to a mixture of **12** (60%), **11** (25%), and an unidentified substance (15%) was observed.

Intriguingly, aldehydo acetal **12** was also found to undergo isomerization to **11** when allowed to stand in methanolic hydrogen chloride. It appears, therefore, that the acetal oxygen proximate to the protonated carboxaldehyde center is adequately nucleophilic to attack the carbocation and produce **18** in a formal microscopic reverse of the formation of **12** (Scheme IV). Fragmentation of this species can give rise to **19** which can proceed to product by transannular hydride shift in a manner paralleling that seen earlier with **14**.

With ether lactone **11** in hand, we sought to determine if ring opening of the lactone group could be achieved under relatively mild conditions. For this purpose, lactol **20a** and methyl acetal **20b** were prepared (Scheme V). When heated in benzene containing a quantity of *p*-toluenesulfonic acid under conditions where methanol was continuously removed, **20b** was transformed into a product (**21**, 60%) which had experienced a 1,2 Wagner–Meerwein methyl shift. Although an isomerically pure substance was formed, it has not proven conveniently possible to distinguish between the two possible double bond isomers. What is clear is that the unique double bond is tetrasubstituted and that one of the methyl groups is now bonded to a secondary carbon (d, J = 7 Hz). Therefore, cleavage of the heterocyclic ring is again not kinetically preferred, at least under these reaction conditions.

The action of lithium aluminum hydride on **11** afforded diol **22**, heating of which to 170 °C led to cyclizative dehydration and formation of the C_2 symmetric dihomodioxatrisecododecahedrane **23** in low yield.[12,13] In terms of convenience and reaction efficiency, the route involving admixture of dilactol **9** with thiophenol in tetrahydrofuran solvent to give **24** and subsequent alane reduction is much preferred (Scheme VI).

Discussion

The collective results suggest the chemical reactivity of dihomodioxatrisecododecahedranes to be dictated to a large extent by familiar energetic and stereoelectronic factors. Although thermochemical data for the various derivatives is not available, analogy to simpler, more well-studied model systems is considered reasonable. This assumed parallelism forms the basis of the present discussion.

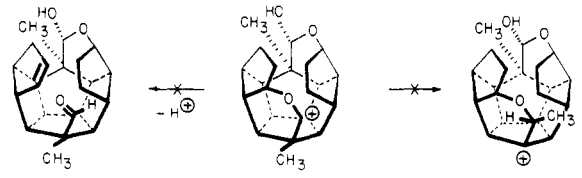
The transannular hydride (deuteride) shifts which operate in **14** and **19** are, first of all, dependent upon the endo stereochemistry of the migrating group. Beyond this, the facility of the process can be interpreted to be a consequence of the large stabilization which results from the conversion of an oxonium ion (e.g., **14**) to a dioxonium ion (e.g., **15**) where two divalent oxygens now directly assist in delocalization of the positive charge. Additional driving force could come from incipient formation of the lactone carbonyl group at the rate-determining transition state, although this is probably not a pivotal factor.

The preceding analysis is helpful in understanding why certain other chemical changes are not observed. For example, **19** is in principle capable of ring cleavage to produce

(12) The successful synthesis of the lower homologous (C_2)-dioxa-C_{20}-octaquinane has been reported earlier (ref 11).

(13) The corresponding dimethyl (C_2)-dioxa-C_{20}-octaquinane has been prepared (Balogh, D., unpublished results) and its topology established by X-ray analysis (Engel, P., private communication).

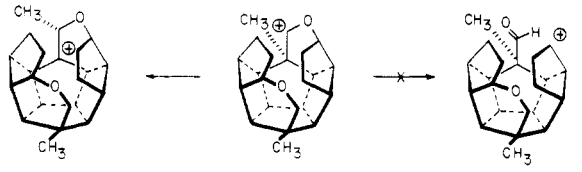
25. Although this unsaturated aldehyde was not seen, we



25 19 26

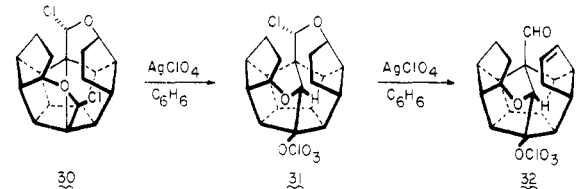
cannot strictly rule out the possibility that it was formed but rapidly recyclized to **19** under the reaction conditions. Although a carbonyl group is formed in this process, other indications are available (see below) to permit the conclusion to be made that ring opening in this manner is likely to be too slow to compete with the transannular hydride shift. Certainly, a Wagner–Meerwein methyl shift leading to **26** is energetically less accessible since the cationic center is geometrically inhibited from becoming completely planar[14,15] and must therefore be less stabilized than the average tertiary carbocation.

The preceding conclusions derive their justification largely from the following observations. Firstly, it is readily apparent that transannular hydride shifts within cation **27**, as produced from **20** under acidic conditions, would be degenerate if actually operative and not determinative per se of product structure. Experimentally, **27** is seen to be transformed into **28** without indication of ring opening.



28 27 29

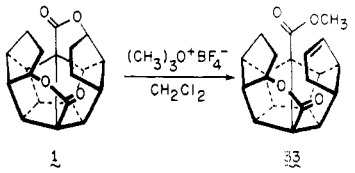
While this new cation should be as destabilized as **26**, its formation is not now contravened by a faster transannular process. The possible operation of the **19** → **25** reaction is accordingly made suspect. Some light is shed on the priority ordering of these processes by the behavior of **30** which was elucidated earlier in this laboratory.[11] Thus, exposure of **30** to silver perchlorate in benzene was found to lead by Wagner–Meerwein 1,2 carbon shift to the unusual tertiary perchlorate **31** which only subsequently experienced ring opening to ene aldehyde **32**. This overall



30 31 32

reaction, which has proven to be general, suggests that the stereorelationship of the oxonium ion center to the β exo hydrogen cannot attain a proper level of antiperiplanarity suitable for facile fragmentation *as long as the molecular framework is spherical in the dodecahedrane sense.* Only when gross structural distortions materialize as they do in **31** does the ring fragmentation to deliver ene aldehyde become kinetically competitive. Molecular models provide ample support for this conclusion. As concerns **27**, this would mean that ring cleavage would not be concerted and therefore require the intervention of secondary cation **29**. An understandably formidable energy barrier is thereby introduced.

In the presence of Meerwein's reagent, **1** is converted to **33** at room temperature. Because Wagner–Meerwein



1 33

shifting of the central bond in the intermediate dioxonium ion would be very energy inefficient in this instance, such is not observed.[5] However, comparison of the facility of the **1** → **33** transformation to the more difficult opening of **5** to **7** or **8** suggests that the stereoelectronic factors relating to E_2 elimination are improved somewhat when the internal σ bond is in place.

Lastly, it should be noted that the ability of the lactol oxygen in **9** to enter into transannular bonding schemes is unprecedented. This finding points up once again the constant need in such topologically elaborate molecules to deter the substantial kinetic inducement for bridging the solvent-free interior in favor of perimeter bond construction, if dodecahedrane is to be synthesized.

Experimental Section

Melting points are uncorrected. Proton magnetic resonance spectra were obtained with Varian EM-360 and T-60 spectrometers; apparent splittings are given in all cases. Carbon spectra were recorded with a Bruker HX-90 spectrometer. 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.

Octadecahydro-8,8-dimethoxy-4a,8a-dimethyl-3,7-dioxadicyclopenta[*cd*,*c'd'*]pentaleno[2,1,6-*hia*:5,4,3-*h'i'a'*]diinden-4(1*H*)-one (6). To a magnetically stirred solution of **5** (50 mg, 0.14 mmol) in dry dichloromethane (4 mL) which was maintained under a nitrogen atmosphere was added 100 mg (0.68 mmol) of trimethyloxonium tetrafluoroborate. After 16 h at room temperature, a solution of sodium methoxide in methanol was added and a color change from red to pale yellow was noted. The mixture was poured into water and extracted three times with dichloromethane. The combined organic layers were washed twice with water, shaken with brine, and dried. Upon removal of solvent, a yellow crystalline residue remained. Preparative thin-layer chromatographic (TLC) purification on silica gel (elution with 10% ether in hexane) gave 40 mg (73%) of **6** as colorless crystals: mp 154–157 °C; ^{1}H NMR ($CDCl_3$) δ 4.6–4.1 (m, 2 H), 4.0–0.8 (series of m, 18 H), 3.64 (s, 3 H), 3.23 (s, 3 H), 1.38 (s, 3 H), 1.06 (s, 3 H); *m/e* calcd 400.2250, obsd 400.2256.

Hydrolysis of 6. A solution of **6** (40 mg, 0.1 mmol) was dissolved in 6 mL of aqueous tetrahydrofuran (50%) and treated with three drops of 5% hydrochloric acid. The mixture was stirred at room temperature for 24 h and the product was extracted into dichloromethane. After the solution was dried and the solvent was evaporated, dilactone **5** was recovered whose spectra were identical with those of the authentic sample.

Methyl 2,2a,4,4a,4b,5,6,7,7b,8,8a,8b,8c,8d,8e,8f-Hexadecahydro-4a,8-dimethyl-4-oxo-1*H*-3-oxacyclopenta[*cd*]pentaleno[1',2',3':3,4]pentaleno[2,1,6-*hia*]indene-8-carboxylate (7). A. Cleavage of 5. Dilactone **5** (50 mg, 0.14 mmol) was dissolved in dry 1,1-dichloroethane (5 mL) with stirring under nitrogen. Trimethyloxonium fluoroborate (200 mg, 1.35 mmol) was added and the mixture was heated at reflux for 18 h. After the solution was cooled, a solution of sodium methoxide in methanol was added and a color change from orange to milky white was noted. Workup as described above afforded 50 mg of a clear oil. Preparative TLC purification on silica gel (ether elution) furnished 35 mg (68%) of **7** as a colorless crystalline solid: mp 135–138 °C; IR (KBr) 2940,

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(15) Bosse, D.; de Meijere, A. *Angew. Chem.* **1976**, *88*, 610; *Angew. Chem., Int. Ed. Engl.* **1976**, *15*, 557. Bischof, P. *Angew. Chem.* **1976**, *88*, 609; *Angew. Chem., Int. Ed. Engl.* **1976**, *15*, 556.

1730, 1272, 1133, 1118, 996 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.00–4.7 (m, 1 H), 4.0–3.3 (m, 2 H), 3.67 (s, 3 H), 3.3–1.0 (series of m, 16 H), and 1.36 (s, 6 H); ^{13}C NMR ($CDCl_3$) 206.71, 176.14, 149.14, 148.46, 84.67, 78.65, 75.45, 63.31, 60.69, 58.26, 56.80, 54.57, 52.04, 51.75, 50.98, 49.42, 46.12, 39.03, 32.92, 30.88, 28.35, 28.06, 25.92 ppm; *m/e* calcd 368.1987, obsd 368.1994.

Anal. Calcd for $C_{23}H_{28}O_4$: C, 74.97; H, 7.66. Found: C, 75.01; H, 7.79.

B. Cleavage of 6. A mixture containing 30 mg (0.08 mmol) of **6**, 20 mg (0.056 mmol) of **5**, and 5 mL of dry 1,1-dichloroethane was heated at reflux with magnetic stirring for 18 h. The usual workup afforded 34 mg (68%) of **7** as a colorless solid, mp 135–138 °C.

Double Lactone Cleavage in 5. A solution of **5** (50 mg, 0.14 mmol) and trimethyloxonium tetrafluoroborate (150 mg, 1.0 mmol) in ethylene trichloride (10 mL) was heated at the reflux temperature under nitrogen for 24 h. The orange-colored solution was cooled, treated with methanolic sodium methoxide, and poured into water. The product was extracted into dichloromethane and the combined organic layers were processed as before to give 40 mg of a clear oil. Preparative TLC purification on silica gel (elution with ether–hexane (1:1)) afforded 15 mg (28%) of **8**: ^{1}H NMR ($CDCl_3$) δ 3.61 (s, 6 H), 3.8–0.8 (series of m, 18 H), 1.15 (s, 6 H); ^{13}C NMR ($CDCl_3$) 178.22, 167.12, 66.52, 57.98, 55.90, 53.05, 51.82, 51.35, 49.26, 47.36, 41.20, 41.01, 38.31, 25.70, 23.90 ppm; *m/e* calcd 382.2144, obsd 328.2150.

Anal. Calcd for $C_{24}H_{30}O_4$: C, 75.36; H, 7.91. Found: C, 75.32; H, 7.89.

Eicosahydro-4a,8a-dimethyl-3,7-dioxadicyclopenta[*cd*,*c'd'*]pentaleno[2,1,6-*hia*:5,4,3-*h'i'a'*]diindene-4,8-diol (9). A solution of **5** (400 mg, 1.13 mmol) in dry tetrahydrofuran (45 mL) was cooled to −78 °C and lithium aluminum hydride (120 mg, 3.16 mmol) was added with stirring. After 4 h at this temperature, the progress of reaction was arrested by addition of water. The mixture was allowed to warm to 25 °C whereupon it was added to 400 mL of dichloromethane. The resulting solution was washed with 50 mL of water containing a small amount of hydrochloric acid, water (2×), and brine before drying. Removal of solvent left 410 mg of a colorless oil which crystallized upon the addition of dichloromethane. The solid was filtered, washed with additional dichloromethane, and dried to give 390 mg (97%) of **9** as a colorless solid: mp 171–173 °C dec (loss of H_2O); IR (KBr) 3390, 2920, 1118, 1050, 750 cm^{-1}; ^{1}H NMR (pyridine-d_5) δ 8.3–6.0 (m, 2 H), 4.80 (m, 2 H), 4.3–1.0 (series of m, 20 H), 1.30 (s, 6 H); ^{13}C NMR ($CDCl_3$) 100.45, 78.45, 64.30, 57.09, 54.93, 51.63, 50.12, 49.20, 38.33, 36.27, 30.95 ppm; *m/e* ($M^+ - H_2O$) calcd 340.2038, obsd 320.2043.

Eicosahydro-4,8-dimethoxy-4a,8a-dimethyl-3,7-dioxadicyclopenta[*cd*,*c'd'*]pentaleno[2,1,6-*hia*:5,4,3-*h'i'a'*]diindene (10). To a stirred solution of **9** (100 mg, 0.8 mmol) in dry methanol (30 mL) maintained under a nitrogen atmosphere was added 1–2 drops of a saturated methanolic hydrogen chloride solution. After 10 min, a white precipitate appeared. Stirring was continued for 3 h, whereupon the reaction mixture was concentrated and the colorless solid filtered off to give 108 mg (98%) of pure **10**: mp 184–186 °C (from acetone); IR (KBr) 2940, 1170, 1108, 1045, 950 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.52 (s, 2 H), 4.0–3.4 (m, 2 H), 3.28 (s, 6 H), 3.2–0.9 (series of m, 18 H), 0.98 (s, 6 H); ^{13}C NMR ($CDCl_3$) 100.98, 67.05, 64.23, 60.78, 55.05, 50.30, 49.57, 49.33, 46.61, 37.82, 35.00, 27.28 ppm; *m/e* 386 (1%), 371 ($M^+ - CH_3$), calcd 371.2222, obsd 371.2228.

Anal. Calcd for $C_{24}H_{34}O_6$: C, 74.58; H, 8.87. Found: C, 74.45; H, 8.85.

Octadecahydro-4a,8a-dimethyl-3,7-dioxadicyclopenta[*cd*,*c'd'*]pentaleno[2,1,6-*hia*:5,4,3-*h'i'a'*]diinden-4(1*H*)-one (11).

A. Isomerization of 9. A solution of **9** (100 mg, 0.28 mmol) in dry methanol (25 mL) was treated with a small amount of hydrogen chloride under nitrogen and the reaction mixture was stirred at room temperature for 3 days. Concentration of the resulting solution gave a semisolid which was purified by preparative TLC on silica gel (ether elution). There was isolated 82 mg (82%) of **11** as colorless crystals: mp 186–188 °C (from ethyl acetate); IR (KBr) 2920, 2850, 1710, 1450, 1095 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.9–4.65 (m, 1 H), 4.2–3.4 (m, 3 H), 3.86 (d, J = 12 Hz, 1 H), 3.4–1.1 (series of m, 16 H), 2.98 (d, J = 12 Hz, 1 H), 1.43 (s, 3 H), 0.95 (s, 3 H); ^{13}C NMR ($CDCl_3$) 176.91, 83.16, 76.32, 71.27, 65.49, 63.70 (2 C), 59.76, 54.33, 52.38, 50.35, 50.25, 49.76, 48.55, 47.24, 42.38, 39.81, 38.16, 38.01, 35.83, 28.11, 27.14 ppm; *m/e* calcd 340.2038, obsd 340.2043.

Anal. Calcd for $C_{22}H_{28}O_3$: C, 77.61; H, 8.29. Found: C, 77.43; H, 8.25.

B. Rearrangement of 10 in Acidic Methanol. A solution of **10** (50 mg, 0.13 mmol) in dry methanol (10 mL) was treated with 1 drop of 2 N methanolic hydrogen chloride and stirred under nitrogen for 3 days. Removal of the solvent in vacuo left 50 mg of crude **11**. Preparative TLC on silica gel furnished 45 mg (90%) of colorless crystals, mp 186–188 °C.

C. Titanium Trichloride Promoted Isomerization of 10. A solution of **10** (10 mg) in 0.5 mL of $CDCl_3$ was placed in an NMR tube. To this tube was added 8 mg of titanium trichloride. After 1 h, a spectrum showed a mixture of **10**, **11**, and **12** to be present. After 2.5 h, only **11** and **12** were present. After 7 h, the tube contained essentially pure **11**.

Eicosahydro-4a,8a-dimethyl-3,7-dioxadicyclopenta[*cd*,*c'd'*]pentaleno[2,1,6-*hia*:5,4,3-*h'i'a'*]diindene-4,8-d_2-4,8-diol (13a). A 100-mg (0.28 mmol) sample of **5** dissolved in **10** mL of dry tetrahydrofuran was cooled to −78 °C and while stirred was treated with 33 mg (0.79 mmol) of lithium aluminum deuteride as described earlier. There was obtained 100 mg (98%) of **13a** as a colorless solid: mp 171–173 °C dec (loss of H_2O); IR (KBr) 3420, 2920, 1175, 1120, 1055 cm^{-1}; *m/e*, M^+ not observed, 342 ($M^+ - H_2O$).

Eicosahydro-4,8-dimethoxy-4a,8a-dimethyl-3,7-dioxadicyclopenta[*cd*,*c'd'*]pentaleno[2,1,6-*hia*:5,4,3-*h'i'a'*]diindene-4,8-d_2 (13b). Dilactol **13a** (70 mg, 0.194 mmol) was dissolved in dry methanol (30 mL) and treated while being stirred under nitrogen with 1 drop of methanolic hydrogen chloride. After 2 h, the precipitated solid was filtered to give 50 mg (68%) of **13b** as colorless crystals: mp 188–190 °C; IR (KBr) 2925, 1173, 1115, 1065, 1045, 908 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.81 (m, 2 H), 3.35 (s, 6 H), 3.3–1.2 (m, 18 H), 1.02 (s, 6 H); *m/e*, M^+ (388) not observed, 373 ($M^+ - CH_3$).

Octadecahydro-4a,8a-dimethyl-3,7-dioxadicyclopenta-[*cd*,*c'd'*]pentaleno[2,1,6-*hia*:5,4,3-*h'i'a'*]diinden-8,8-d_2-4-(1*H*)-one (16). An approximate 1:1 mixture of **13a** and **13b** (70 mg) dissolved in methanol (30 mL) containing 1 drop of methanolic hydrogen chloride was stirred at room temperature for a period of 3 days. The solvent was removed in vacuo and the resulting solid was purified by preparative TLC on silica gel (ether elution). There was obtained 60 mg of **16**: mp 187–189 °C; IR (KBr) 2930, 1710, 1160, 1130, 1088 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.9–4.65 (m, 1 H), 4.2–3.4 (m, 4 H), 3.4–1.1 (series of m, 16 H), 1.43 (s, 3 H), 0.95 (s, 3 H); ^{13}C NMR ($CDCl_3$) 176.91, 83.16, 76.22, 70.44, 65.50, 63.65 (2 C), 59.76, 54.33, 52.38, 50.35, 50.25, 49.76, 48.56, 47.19, 42.19, 39.81, 38.16, 38.01, 35.78, 28.11, 27.14 ppm; *m/e* calcd 342.2164, obsd 342.2170.

Octadecahydro-4a,8-dimethyl-4,7-epoxy-1*H*-3-oxacyclopenta[*cd*]pentaleno[1′,2′,3′:3,4]pentaleno[2,1,6-*hia*]indene-8-carboxaldehyde (12).

A. Thermal Dehydration of 9. A 100-mg (0.28 mmol) sample of **9** was heated under nitrogen at 175 °C for 4 min. The evolution of water, as noted by the formation of tiny gas bubbles in the melt, had stopped at the end of this time. The residue, which solidified upon cooling, was purified by preparative TLC on silica gel (elution with 50% ether in hexane) to give 50 mg (53%) of **12** as colorless crystals, mp 144–146 °C (from ether). A second band of lower R_f (0.45 vs. 0.2) proved to be ether lactone **11** (15 mg). For **12**: IR (KBr) 2931, 2700, 1715, 1454, 1092, 1050 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 9.85 (s, 1 H), 4.86 (s, 1 H), 4.5–0.9 (series of m, 20 H), 1.18 (s, 3 H), 1.09 (s, 3 H); ^{13}C NMR ($CDCl_3$) 204.15, 95.64, 76.95, 71.67, 61.90, 61.54, 60.99, 59.59, 58.50, 56.13, 55.34, 52.98, 51.58, 51.04, 47.34, 45.51, 40.84, 35.56, 31.68 (2 C), 28.58, 23.79 ppm; *m/e* calcd 340.2038, obsd 340.2044.

Anal. Calcd for $C_{22}H_{28}O_3$: C, 77.61; H, 8.29. Found: C, 77.38; H, 8.27.

B. Reaction of 12 with Lead Tetraacetate. A mixture of lead tetraacetate (155 mg, 0.35 mmol), calcium carbonate (140 mg, 1.4 mmol), and cyclohexane (5 mL) was stirred at reflux for 10 min. Dilactol **12** (50 mg, 0.14 mmol) and iodine (142 mg, 0.56 mmol) were added and heating was continued with concomitant irradiation from a 150-W sunlamp. After 1.5 h, the dark mixture was cooled and the inorganic solids were filtered off. The filtrate was diluted with ether (30 mL) and the organic phase was washed

with sodium thiosulfate solution, water, and brine prior to drying. Removal of solvent gave 40 mg of an oil whose ^{1}H NMR spectrum showed it to be essentially pure **12**.

C. Rearrangement of 9 with Hydrochloric Acid in Tetrahydrofuran. A solution of **9** (50 mg, 0.14 mmol) in dry tetrahydrofuran (5 mL) was treated with 1 drop of dilute hydrochloric acid and stirred under nitrogen for 2 days. The solvent was removed in vacuo to give 50 mg of an amorphous solid. ^{1}H NMR analysis of this material showed it to consist of **12** (60%), **11** (25%), and an unidentified substance (~15%).

Acid-Catalyzed Isomerization of 12. A solution of **12** (50 mg, 0.15 mmol) was dissolved in methanol (10 mL) under a nitrogen atmosphere. One drop of 1% methanolic hydrogen chloride was added, and the reaction mixture was stirred at room temperature for 48 h. The solvent was removed in vacuo and the residue was purified by preparative TLC on silica gel (ether elution). There was obtained 40 mg (80%) of ether lactone **12**.

Eicosahydro-4a,8a-dimethyl-3,7-dioxadicyclopenta[*cd*,*c'd'*]pentaleno[2,1,6-*hia*:5,4,3-*h'i'a'*]diinden-4-ol (20a). A stirred solution of **11** (100 mg, 0.29 mmol) in dry tetrahydrofuran (5 mL) was cooled to −78 °C and treated under nitrogen with 0.313 mmol of 1 M diisobutylaluminum hydride dissolved in hexane. After 3 h at this temperature, water was introduced, a small amount of dilute hydrochloric acid was added to dissolve the aluminum salts, and the mixture was extracted with dichloromethane. The combined organic extracts were washed with water (2×) and brine before drying. Removal of solvent left 100 mg of crude **20a** which was utilized without further purification.

Eicosahydro-4-methoxy-4a,8a-dimethyl-3,7-dioxadicyclopenta[*cd*,*c'd'*]pentaleno[2,1,6-*hia*:5,4,3-*h'i'a'*]diindene (20b). The crude lactol prepared above was dissolved in methanol (10 mL) and treated with 1 drop of 2 N methanolic hydrogen chloride. The solution was stirred at 25 °C for 10 h and evaporated. Preparative TLC purification of the resulting clear oil (elution with 50% ether in hexane) afforded 60 mg (92% overall) of **20b** as colorless crystals, mp 157–160 °C (from acetone). In addition, 30 mg of **11** was recovered. For **20b**: IR (KBr) 2930, 1455, 1170, 1095, 1042, 975 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.65 (s, 1 H), 4.3–3.3 (m, 4 H), 3.96 (d, J = 13 Hz, 1 H), 3.35 (s, 3 H), 3.3–0.9 (m, 16 H), 2.97 (d, J = 13 Hz, 1 H), 1.02 (s, 3 H), 0.92 (s, 3 H); m/e calcd 356.2351, obsd 356.2358.

Anal. Calcd for $C_{23}H_{32}O_3$: C, 77.49; H, 9.05. Found: C, 77.06; H, 8.92.

Acid-Promoted Rearrangement of 20b. A solution of **20b** (100 mg, 0.28 mmol) and *p*-toluenesulfonic acid monohydrate (5 mg) in benzene (30 mL) was heated to reflux for 40 h, during which time methanol was slowly removed through a modified Dean–Stark trap. The darkened reaction mixture was added to water and extracted with ether. The combined organic layers were washed with water, dried, and evaporated to furnish a yellow oil (100 mg) which was purified by preparative TLC on silica gel (elution with 20% ether in hexane). There was obtained 60 mg (66%) of **21** as colorless crystals: mp 116–118 °C (from ethyl acetate); IR (KBr) 2930, 1450, 1175, 1090, 992 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.0–4.0 (m, 3 H), 4.0 (d, J = 12 Hz, 1 H), 4.0–1.0 (series of m, 17 H), 3.05 (d, J = 12 Hz, 1 H), 1.22 (d, J = 7 Hz, 3 H), 1.0 (s, 3 H); ^{13}C NMR ($CDCl_3$) 142.78, 132.93, 76.76, 75.30, 73.94, 68.21, 65.78, 62.77, 54.96, 53.99 (2 C), 52.68, 50.05, 49.47, 42.92, 40.78, 37.82, 35.78, 35.49, 30.05, 23.25, 22.38 ppm; m/e calcd 324.2089, obsd 324.2094.

Anal. Calcd for $C_{22}H_{28}O_2$: C, 81.44; H, 8.70. Found: C, 81.44; H, 8.78.

Octadecahydro-7-hydroxy-4a,8-dimethyl-1*H*-3-oxacyclopenta[*cd*]pentaleno[1′,2′,3′:3,4]pentaleno[2,1,6-*hia*]indene-8-methanol (22). A 200-mg (0.59 mmol) sample of **11** was reduced with lithium aluminum hydride (40 mg, 1 mmol) in tetrahydrofuran (10 mL) at −78 °C for 3 h. The usual workup afforded 180 mg (90%) of **22** as a white solid: mp 145–147 °C (from ethyl acetate); IR (KBr) 3375, 2910, 1450, 1178, 1100, 1045 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.40 (d, J = 6.2 Hz, 1 H), 4.3–0.8 (series of m, 20 H), 3.88 (d, J = 12 Hz, 1 H), 3.20 (d, J = 6.2 Hz, 1 H), 2.93 (d, J = 12 Hz, 1 H), 1.14 (s, 3 H), 0.90 (s, 3 H).

Thermal Cyclization of 22. A 10-mg sample of **22** was placed in an NMR tube and heated at 170 °C for 5 min under a nitrogen atmosphere. Gas evolution was noted as melting occurred. The tube was cooled and $CDCl_3$ (0.5 mL) was added. The bisether **23** was seen to be produced in 70% yield based upon appropriate integration of the ^{1}H NMR spectrum. The other 30% was not identified.

Eicosahydro-4a,8a-dimethyl-4,8-bis(phenylthio)-3,7-dioxadicyclopenta[*cd*,*c'd'*]pentaleno[2,1,6-*hia*:5,4,3-*h'i'a'*]diindene (24). To a solution of **9** (100 mg, 0.28 mmol) in dry tetrahydrofuran (1 mL) was added 700 mg (6.4 mmol) of thiophenol. After 1 h at 25 °C, the formation of a white precipitate was noted. The mixture was stirred for an additional 4 h, poured into dichloromethane (125 mL), and washed with 10% sodium hydroxide solution (2×), water, and brine prior to drying. Removal of the solvent furnished 130 mg (86%) of **24** as a colorless crystalline solid: mp 227–232 °C (sealed tube, gradual decomposition above 200 °C; from dichloromethane); IR (KBr) 2925, 1564, 1479, 1437, 1068, 900, 730 cm^{-1}; ^{1}H NMR ($CCCl_3$) δ 7.7–7.0 (m, 10 H), 5.83 (s, 2 H), 4.5–4.2 (m, 2 H), 4.2–3.3 (m, 2 H), 3.3–0.9 (series of m, 14 H), 1.17 (s, 6 H); ^{13}C NMR ($CDCl_3$) 136.73, 129.99, 128.72, 125.86, 87.69, 68.27, 64.21, 62.93, 50.37 (2 C), 49.52, 47.15, 37.69, 37.26, 27.19 ppm.

Anal. Calcd for $C_{34}H_{38}O_2S_2$: C, 75.23; H, 7.06. Found: C, 74.83; H, 7.17.

Eicosahydro-4a,8a-dimethyl-3,7-dioxadicyclopenta[*cd*,*c'd'*]pentaleno[2,1,6-*hia*:5,4,3-*h'i'a'*]diindene (23). Aluminum chloride (147 mg, 1.1 mmol) was cooled to 0 °C and 4 mL of dry tetrahydrofuran followed by lithium aluminum hydride (10.4 mg, 0.28 mmol) were added with stirring under nitrogen. After 15 min, **24** (100 mg, 0.18 mmol) was added as a slurry in ether to the alane. The reaction mixture was heated at reflux for 24 h, cooled, quenched with water, and added to ether. The customary workup including preparative TLC purification on silica gel (elution with 10% ether in hexane) gave 55 mg (90%) of **23** as colorless crystals: mp 104–106 °C (from hexane); ^{1}H NMR ($CDCl_3$) δ 4.2–3.3 (m, 2 H), 4.0 (d, J = 12.5 Hz, 2 H), 3.3–1.0 (series of m, 18 H), 2.95 (d, J = 12.5 Hz, 2 H), and 0.92 (s, 6 H); ^{13}C NMR ($CDCl_3$) 76.27 (d), 71.12 (t), 64.86 (d), 60.10 (d), 52.77 (d), 50.97 (d), 49.91 (d), 42.72 (s), 38.63 (t), 36.46 (q), 26.80 (t) ppm; m/e calcd 326.2246, obsd 326.2252.

Anal. Calcd for $C_{22}H_{30}O_2$: C, 80.94; H, 9.26. Found: C, 81.06; H, 9.21.

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