the cyclopropane group, the presence of which we have argued to be an essential ingredient for the occurrence of homoaromaticity.[22,32-34]

Registry No. 1, 32731-02-5; 2, 11070-36-3; 3, 71328-62-6; 4, 71328-61-5; 5, 71328-60-4; 6, 71328-63-7; 7, 61103-50-2; 9, 71276-90-9; 11, 26811-28-9; 13, 42295-07-8; 14, 31886-99-4.

Supplementary Material Available: Figures 1, 2, 8–13, and 15 (5 pages). Ordering information is given on any current masthead page. Reprints including this material may be obtained from the author.

Topologically Spherical Molecules. Synthesis of a Pair of C_2-Symmetric Hexaquinane Dilactones and Insights into Their Chemical Reactivity. An Efficient π-Mediated 1,6-Dicarbonyl Reduction

Leo A. Paquette,* Matthew J. Wyvratt,[1a] Otto Schallner,[1b] Jean L. Muthard,[1c] William J. Begley,[1d] Robert M. Blankenship, and Douglas Balogh

Evans Chemical Laboratories, The Ohio State University, Columbus, Ohio 43210

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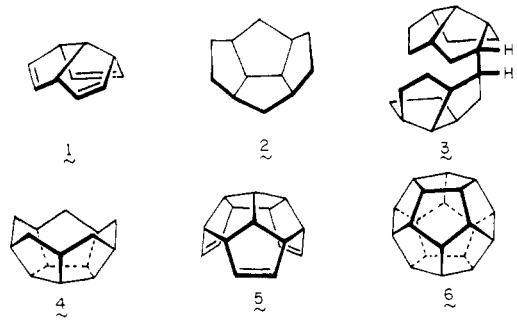
Details of the efficient conversion of dimethyl 3,3a,3b,4,6a,7a-hexahydro-3,4,7-metheno-7*H*-cyclopenta[*a*]-pentalene-7,8-dicarboxylate (**9a**), a product of the domino Diels–Alder addition of dimethyl acetylenedicarboxylate and 9,10-dihydrofulvalene, to a pair of C_2-symmetric hexaquinane dilactones are presented. The initial phase of the strategy, which was to retain minimal C_2 symmetry in all intermediates, required exclusive "cross-corner" oxygenation of the double bonds in **9a**. This objective was realized by sequential iodolactonization of the derived dicarboxylic acid, methoxide-promoted opening of the dilactone at room temperature, oxidation, and reductive deiodination. Cyclopentenone annulation of the resulting dimethyl decahydro-1,5-dioxo-3,4,7-metheno-7*H*-cyclopenta[*a*]pentalene-7,8-dicarboxylate **13** involved condensation with diphenylsulfonium cyclopropylide and Baeyer–Villiger oxidation or alkylation with (trimethylsilyl)allyl anion and oxidative cyclization, followed by acid-promoted rearrangement. Catalytic hydrogenation of **18** provided **22** whose borohydride reduction delivered the "closed" dilactone tetradecahydro-5*H*,6*H*-1,5b,12:5a,10,11-dimethenodicyclopenta[*e*,*e*']benzo[2,1-*c*:3,4-*c*']-dipyran-5,6-dione (**7**). Results of alkali metal reduction of both **7** and **18** are given. In the first instance, the "open" dilactone **8** was formed stereoselectively as a consequence of exclusive protonation from the convex surface. The behavior of **18** comprises the first example of a π-mediated 1,6-dicarbonyl reduction. The chemical behavior of dilactones **7** and **8** is described; indications of the effects of their highly spherical topology, conformational character, and essentially solvent-free cavity on the differing product-forming steps are pointed out and discussed.

The unusual topological features of triquinacene (**1**), noted first by Woodward[2] and Jacobson,[3] have more recently been incorporated into structures of greater complexity. Tetracyclo[7.2.1.$0^{4,11}$.$0^{6,10}$]dodecane (**2**),[4,5] *dl*-bivalvane (**3**),[6] peristylane (**4**),[7] and C_{16}-hexaquinacene (**5**)[8] are especially notable examples. The all-cis,syn stereochemistry of these frameworks has assumed central importance because of their obvious model relationship to the still unknown pentagonal dodecahedrane structure **6**. The carbon skeletons of **2**–**5**, like that of **1**, are rigid, bowl-shaped, relatively strain free,[9] and in certain cases rather highly symmetric.[10]



1 **2** **3** **4** **5** **6**

There is associated with **6** a particular fascination because this $(CH)_{20}$ hydrocarbon possesses the highest known point-group symmetry (I_h, icosahedral), encloses a cavity incapable of solvation, and appeals to one's scientific curiosity and imagination. As a result, the molecule has recently become the focal point of intense synthetic[2,3,6-8,11-15] and theoretical research.[9,16-18]

In principle, a variety of methods are available for the tactical elaboration of **6**. Although all are necessarily complex, we have had particular interest in schemes which would capitalize on the inherent symmetry of the target molecule. In this way, the number of individual laboratory steps should be appreciably reduced. An additional ad-

(1) (a) National Science Foundation Graduate Fellow, 1972–1975. (b) Postdoctoral Fellow of the Deutsche Akademische Austauschdienst (NATO), 1974–1975. (c) Dissertation Fellow, 1977–1978. (d) Postdoctoral Fellow of the Science Research Council, 1975–1977.

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(11) Paquette, L. A.; Farnham, W. B.; Ley, S. V. *J. Am. Chem. Soc.* **1975**, *97*, 7273.

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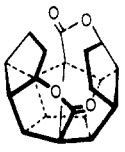
vantage is seen in the routine application of ^{13}C NMR spectroscopy which, at a glance, would reveal whether the symmetry of an intermediate had been retained in any particular chemical transformation. Because of the large number of saturated methine protons which must be contended with, particularly at the more advanced stages, ^1H NMR would understandably not have comparable analytic capability in these circumstances.

We wish to report herein the details of one such synthetic scheme. The ready elaboration of dilactones **7** and **8** is described, as is the rather special reactivity of these



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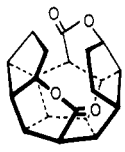


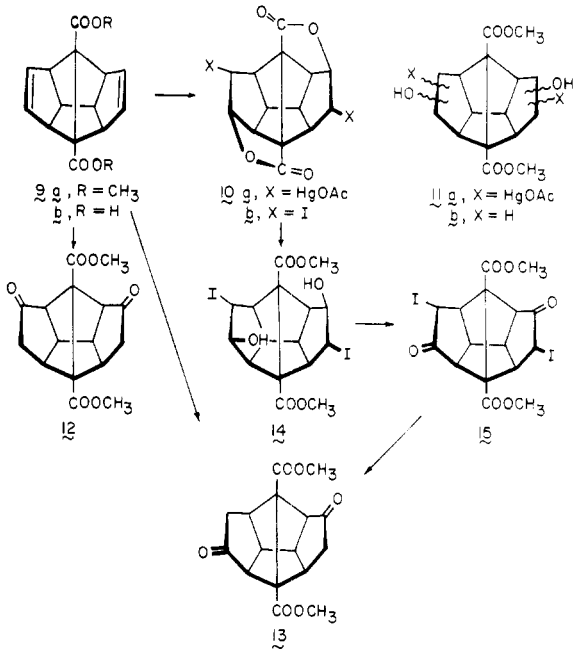
8

systems.[19] Also documented is the first example known to us of a π-mediated 1,6-dicarbonyl reduction.

"Cross-Corner" Oxygenation of 9. The present strategy capitalizes on the ready availability of diester **9a**[5a,13,14] which already possesses four cis-fused cyclopentanoid rings and C_{2v} symmetry. Considering the well-established capability of ester groups for neighboring-group participation in electrophilic reactions, the direct oxymercuration or hydroboration of **9a** was initially envisioned. As concerns oxymercuration, the earlier results of Factor and Traylor with simpler norbornene derivatives served as our guide.[20] However, treatment of **9a** with mercuric acetate under a variety of conditions did not give **10a**. Instead, electrophilic addition proceeded without apparent ester involvement to produce the mixture **11a**, reduction of which with alkaline sodium borohydride or 2% sodium amalgam furnished **11b** admixed with several byproducts.[21] Such complications could not be alleviated.

In the second attack on the problem, **9a** was hydroborated with disiamylborane and sequentially oxidized with alkaline hydrogen peroxide and Jones' reagent. High-pressure liquid chromatography separated the resulting mixture of diketo diesters **12** and **13** (79% total isolated) in which the unwanted C_s isomer **12** predominated (relative percentage 62%). The identity of **12** follows from its elemental composition, the presence of two quite distinct methyl ester signals in its ^1H NMR spectrum, and the ^{13}C NMR spectrum which is characterized by 11 lines. In accord with the C_2 symmetry of **13**, its spectra exhibit a single methyl ester proton absorption and eight carbon signals.

To circumvent the above complications and achieve efficient "cross-corner" functionalization, we subjected diacid **9b** (available in 98% yield from alkaline hydrolysis of **9a**) to standard iodolactonization conditions.[22] The highly crystalline product **10b**, isolated in 96% yield, shows proton resonances comparable to those of simpler analogues.[23] Exposure of **10b** to a catalytic quantity of sodium methoxide in methanol *at room temperature* efficiently transformed the bis(iodo lactone) to bis(iodo hydrin) **14**. Due to the steric stress prevailing at the carbonyl groups



in **10b**, base-promoted ring opening can be achieved under such mild conditions. This enables the iodohydrin functional groups to survive and precludes ensuing intramolecular S_N2 displacement of iodide by the transient alkoxide ions. Epoxide formation is also deterred by the molecular superstructure which maintains these groups in a geometric relationship approaching 120°.[19] Jones' oxidation of **14** produced bis(iodo ketone) **15** which when reduced with zinc–copper couple in methanol[24] afforded pure **13** in 68% overall yield from **9a**. This efficient procedure can be performed on large scale quantities (>100 g) without diminution in yield.

Cyclopentenone Annulation. Given the availability of **13**, we next sought to accomplish the simultaneous elaboration of its two keto groups into fused cyclopentenone rings. Although a variety of procedures capable of performing this particular transformation do, in principle, exist,[25-35] those developed by Raphael[28] and Büchi[35] were first attempted because of their relative simplicity. However, these were found not to proceed as desired. Thus, treatment of **13** with the Grignard reagent derived from tetrahydropyranyloxypropyne gave no recognizable 1,2-addition product, while condensation with diethyl succinate in base caused polymer formation. On the basis of these negative results, it was reasoned that true carbanionic reagents should probably by avoided (however, see below), and the applicability of Trost's diphenylsulfonium cyclopropylide[31] was next examined. In the reversible generation of this ylide from its sulfonium

(19) A preliminary report describing certain of these findings has appeared: Paquette, L. A.; Wyvratt, M. J.; Schallner, O.; Schneider, D. F.; Begley, W. J.; Blankenship, R. M. *J. Am. Chem. Soc.* **1976**, *98*, 6744.
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(21) See: Giese, B. *Tetrahedron Lett.* **1974**, 3579. Giese, B.; Gantert, S.; Schulz, A. *Ibid.* **1974**, 3583.
(22) van Tamelen, E. E.; Shamma, M. *J. Am. Chem. Soc.* **1954**, *76*, 2315.
(23) Ramey, K. C.; Lini, D. C.; Moriarty, R. M.; Gopal, G.; Welsh, H. G. *J. Am. Chem. Soc.* **1967**, *89*, 2401.
(24) Noyori, R.; Baba, Y.; Hayakowa, Y. *J. Am. Chem. Soc.* **1974**, *96*, 3336.
(25) Sturtz, G.; Corbel, B.; Paugam, J.-P. *Tetrahedron Lett.* **1975**, 47.
(26) Marino, J. P.; Landich, R. C. *Tetrahedron Lett.* **1975**, 4531.
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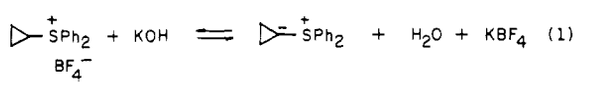
(28) MacAlpine, G. A.; Raphael, R. A.; Shaw, A.; Taylor, A. W.; Wild, H. J. *J. Chem. Soc., Chem. Commun.* **1974**, 834.
(29) Hiyama, T.; Tsukunaka, M.; Nozaki, H. *J. Am. Chem. Soc.* **1974**, *96*, 3713.
(30) Ellison, R. A. *Synthesis* **1973**, 397.
(31) Trost, B. M.; Bogdanowicz, M. J. *J. Am. Chem. Soc.* **1973**, *95*, 5298 and related papers from this group.
(32) Eaton, P. E.; Cooper, G. F.; Johnson, R. C.; Mueller, R. H. *J. Org. Chem.* **1972**, *37*, 1947.
(33) Creger, P. L. *J. Org. Chem.* **1972**, *37*, 1907.
(34) Jacob, T. M.; Vatakencherry, P. A.; Dev, S. *Tetrahedron* **1964**, *20*, 2815.
(35) Biemann, K. Büchi, G.; Walker, B. H. *J. Am. Chem. Soc.* **1957**, *79*, 5558.

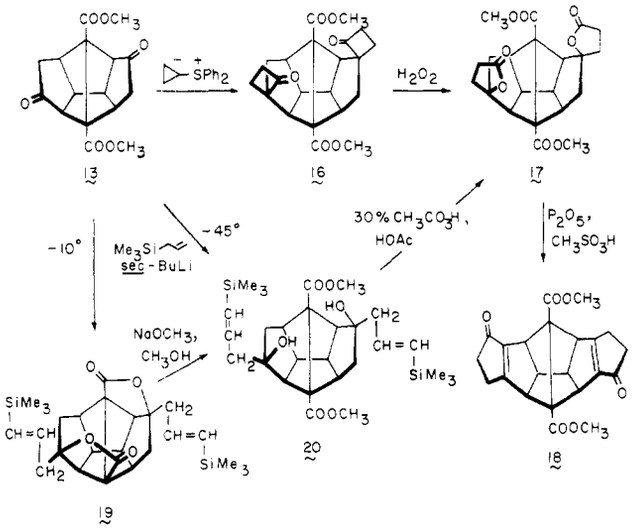
precursor (eq 1), the equilibrium can of course be shifted



to the right by increasing the concentration either of the sulfonium salt or of the base. However, **13** was found to experience hydrolysis under the alkaline reaction conditions developed earlier, and the utilization of a large excess of potassium hydroxide was therefore precluded. Attempts to substitute sodium methoxide for KOH led to very complex reaction mixtures. Accordingly, recourse was made to increasing the amount of sulfonium salt to the fivefold molar equivalent level in the presence of only a slight excess of potassium hydroxide. This modification, coupled with acid-catalyzed rearrangement of the initially formed oxaspiropentanes, provided **16** in quite respectable yield (77%). No monocondensation product was found, and the excess sulfonium salt could be recovered chromatographically with 88% efficiency. The bis(spirocyclobutanone) produced in this fashion is not stereochemically homogeneous, although one symmetrical isomer, assigned the indicated endo,endo stereochemistry by analogy to the 2-norbornanone example,[31] does predominate heavily.

Baeyer–Villiger oxidation of **16** with 30% hydrogen peroxide afforded dilactone **17** in quantitative yield. At this stage, fractional recrystallization resulted in convenient purification of the major stereoisomer. From the simplified display in its ^{13}C NMR spectrum (11 lines) and the chemical shifts of key proton and carbon resonances, it is clear that twofold axial symmetry has been maintained and that ring expansion has occurred via migration of the more highly substituted carbons.

Despite the successful conversion of **13** to **17**, the high cost of diphenylsulfonium cyclopropylide (which requires stoichiometric amounts of silver salt for its preparation) taxed our ability to prepare this intermediate on a large scale. As a result, we were attracted to the recent report



of Magnus et al.,[36] which suggested that the (trimethylsilyl)allyl anion might serve as a substitute reagent for the ylide. Under the conditions described earlier (−10 °C), **13** was converted to **19**. Although **19** underwent lactone ring opening in the presence of methanolic sodium methoxide to provide the desired **20**, it was subsequently discovered that more suitable temperature control (−45 °C) during addition of the allyllithium reagent to **13** gave rise directly to **20** in fair yield. This hydroxy ester could be efficiently transformed to **17** upon treatment with peracetic acid in acetic acid. Upon reaction with 8% phosphorus pentoxide in methanesulfonic acid at 50 °C for 36.5 h,[37] **17** cleanly underwent intramolecular Friedel–Crafts acylation to give the desired bis(cyclopentenone) **18** in 83% yield. This process of transforming spirofunctionality to laterally fused rings results in 1,2-translocation of the carbonyl groups. Since this rearrangement occurs on two opposed faces in the present example, C_2 symmetry is maintained in **18** (^{13}C NMR analysis; see Experimental Section).

Elaboration of Dilactones 7 and 8. At this point, explicit recognition should be made of the fact that bis(spirocyclobutanone) **16** already contains all 20 carbon atoms (the ester methyl groups are not included for reasons to become apparent) necessary to elaborate the pentagonal dodecahedrane **6**. As a consequence of its C_2 symmetry, the synthetic problem is reduced to one of manipulating only *two* different types of carbonyl groups *without introducing additional carbon-containing substituents or functional groups*. The two-step conversion of **16** to **18** falls within these guidelines. Further, **16** and its precursors are seen to contain an unnecessary central bond. While its cleavage can be achieved satisfactorily at several points, this bond has been retained to maintain norbornene character in the two structural halves and thereby guarantee excellent stereochemical control in the immediately ensuing transformations.

Although the alkaline peroxidation of **18** leading to **21** exemplifies this thinking, the key transformation is the catalytic hydrogenation of **18** in ethyl acetate over standardized 10% palladium on charcoal. Under these conditions, diketo diester **22** is formed stereospecifically in quantitative yield. Thus, delivery of hydrogen from the sterically unencumbered convex surface of the enone operates exclusively as expected, with the result that the two cyclopentanone rings are projected to the inner regions of the developing sphere.

Our stereochemical assignment to epoxy ketone **21** is based upon a similar assessment of steric factors and suitable analogy.[38] That **22** has adopted a highly folded nature can be shown simply by its sodium borohydride or sodium cyanoborohydride reduction, which eventuates in the formation of **7**. At the experimental level, careful quenching of the excess hydride with aqueous 2 N acetic acid produced predominantly the monolactone **23** whose subsequent conversion to **7** was effected with *p*-toluenesulfonic acid in refluxing benzene. Alternatively, the borohydride mixture could be quenched with excess 2 N hydrochloric acid to effect the more direct formation of **7**. The relatively simple ^1H and ^{13}C NMR spectra of **7** clearly revealed the continued maintenance of a molecular C_2 axis. The sphericality of this dilactone appears from various molecular models to be adequate to seriously impede the entry of solvent into its cavity. This phenomenon had a decided impact on the ensuing synthetic plan, since further molecular manipulation of this system was now considered to require little additional attention to stereochemical detail. Stated differently, all reagents were presumed to be relegated hereafter to convex approach.

This feature was first used to advantage in the reductive cleavage of the internal bond in **7**. In the presence of sodium and trimethylsilyl chloride in refluxing toluene,[39,40]

(36) Ayalon-Chass, D.; Ehlinger, E.; Magnus, P. *J. Chem. Soc., Chem. Commun.* **1977**, 772. Magnus, P., private communication.

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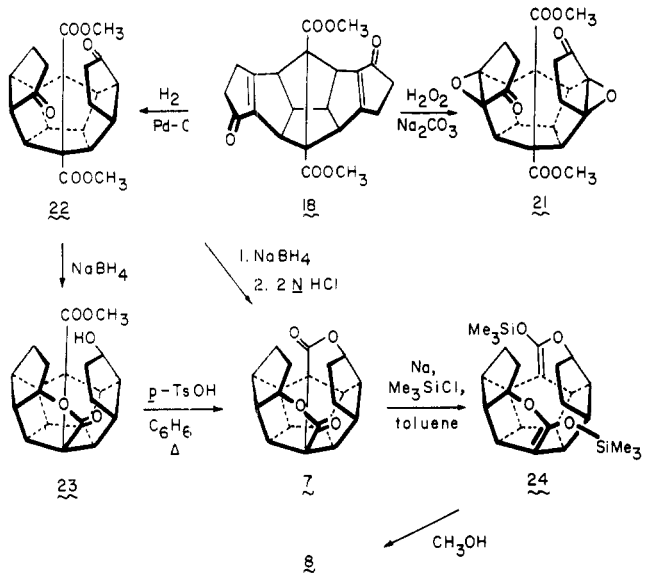
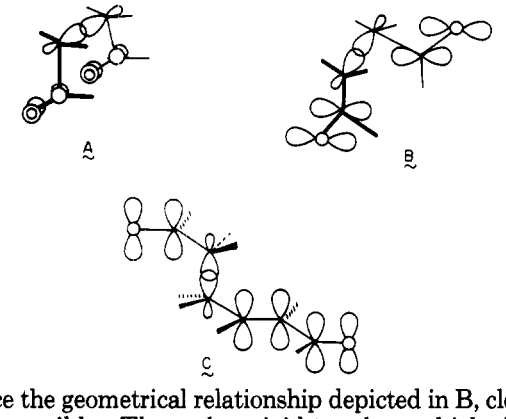


there was produced the bis(trimethylsilyl enol ester) **24**, hydrolysis of which in methanol furnished **8**. Confirmation of this structural assignment and elaboration of the key molecular dimensions of **8** have been accomplished through X-ray crystal structure analysis (Figure 1).[41] It is of particular interest that the molecular dimensions agree closely with those which have been calculated for the pentagonal dodecahedrane **6**.[16,17]

π-Mediated 1,6-Dicarbonyl Reduction. Our knowledge of 1,4-dicarbonyl reductions has advanced to the stage where the stereoelectronic requirements for cleavage of the C_2–C_3 bond are now realistically appreciated. Briefly stated, only when the σ bond to be broken is aligned with the planes defined by the carbonyl groups as in A is through-bond interaction maximized and the transition state for reduction accessible.[8,42,43] If structural factors



enforce the geometrical relationship depicted in B, cleavage is not possible. The rather rigid topology which characterizes **7** causes this molecule to be stereoelectronically aligned as in A.

When consideration is given to 1,6-dicarbonyl reduction, which should be rendered possible through application of the principle of vinylogy, the benefits of orbital overlap are of course no different. As denoted in C, a given system

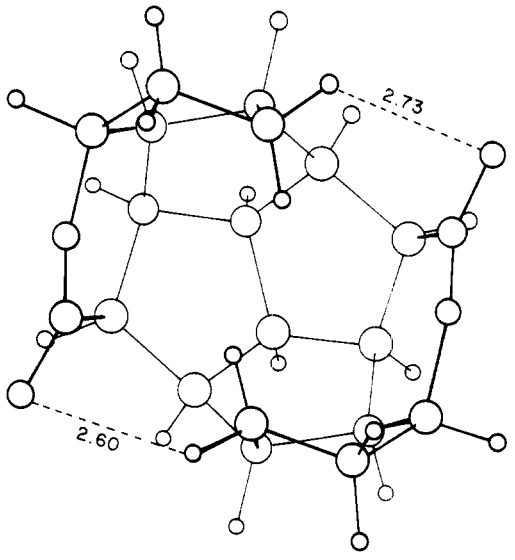
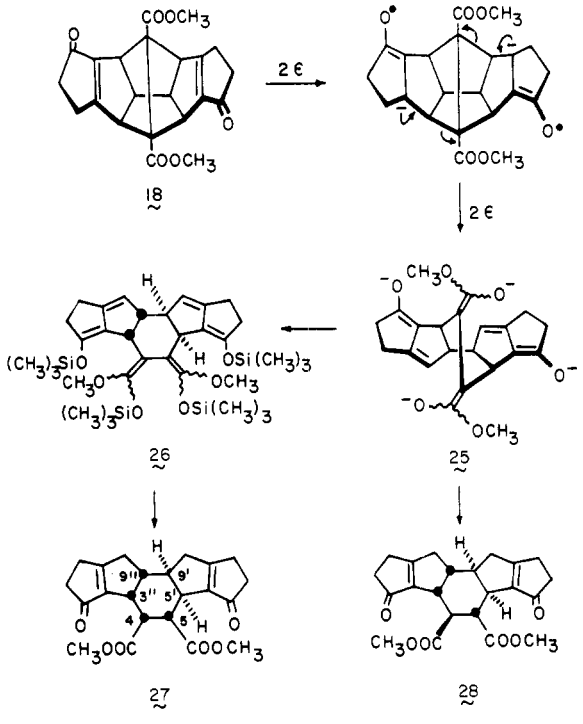


Figure 1. X-ray crystal structure of dilactone **8** (courtesy of Professor W. Nowacki and Dr. P. Engel[41]).

Scheme I



must be capable of attaining the indicated arrangement in order that acceptance of a pair of electrons by the carbonyl groups can lead to severance of the carbon–carbon single bond.

In the specific case of **18**, one quickly recognizes that the carbon framework which incorporates the α,β-unsaturated carbonyl moieties is quite inflexible and, in particular, not conducive to rotation in the ketone carbonyl subunits. On the other hand, the ester groups are expected to be capable of conformational rotation much as was observed previously with **9a**,[5a,b] notwithstanding the obvious steric compression they experience. Since an inspection of molecular models corroborated this analysis, we became intrigued with the possibility of converting **18** to a symmetrical tetrahydro derivative.

Since the reduction potentials of cyclopentenones are generally lower and more accessible than those of saturated carboxylic esters, the actual transfer of electrons was expected to occur at the ketone carbonyl groups (see

(39) Bloomfield, J. J.; Owsley, D. C.; Nelke, J. M. *Org. React.* **1976**, *23*, 259. Bloomfield, J. J.; Martin, R. A.; Nelke, J. M. *J. Chem. Soc., Chem. Commun.* **1972**, 96.

(40) An alternative procedure which makes use of liquid ammonia as solvent [Gassman, P. G.; Creary, X. *J. Chem. Soc., Chem. Commun.* **1972**, 96] was not successful in this particular instance.

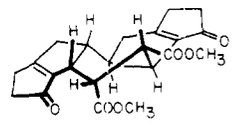
(41) Nowacki, W.; Engel, P., private communication. Engel, P.; Nowacki, W. *Z. Kristallogr., Kristallgeom., Kristallphys., Kristallchem.* **1977**, 4.

(42) Grimshaw, J.; Haslett, R. J. *J. Chem. Soc., Chem. Commun.* **1974**, 174.

(43) Wenkert, E.; Yoder, J. E. *J. Org. Chem.* **1970**, *35*, 2986.

Scheme I). Competitive 1,4 reduction of the dicarbomethoxy part structure (compare the behavior of **9a**[5]) was not anticipated in this instance. In the event, exposure of a toluene solution of **18** to dispersed sodium metal in the presence of chlorotrimethylsilane resulted in smooth fragmentation of its polycondensed ring system to deliver silylated tetraenolate **26**. This intermediate was not characterized but was in turn subjected directly to methanolysis under conditions of kinetic protonation. Such treatment led to the isolation of **27**. From two strong bands at 1740 and 1695 cm^{-1} and a medium-intensity absorption at 1645 cm^{-1} in the infrared spectrum, the continued presence of cyclopentenone and saturated ester carbonyl groups could be inferred. Since the ^1H NMR spectrum of **27** exhibits two different methyl ester singlets, a lack of symmetry is evident. This conclusion was supported by the ^{13}C NMR spectrum which is characterized by individual signals for each of the 22 carbon atoms. The structural assignment indicated for **27** is based further on the observation that one α-carbomethoxy proton is substantially more deshielded than its counterpart, as would be expected if proton delivery to these adjacent sites (C_4 and C_5) occurred in cis fashion for reasons of steric accessibility. Since the origins of **27** require that the stereochemistry existent at carbons 3″, 5′, 9′, and 9″ be cis-anti-cis (Scheme I), it follows that protonolysis of **26** under kinetically controlled conditions should deliver **27**. The stereochemical assignments are further reinforced by chemical interconversions to be described subsequently.

Given the large size of the substituents about the six-membered ring in **27** and their relative stereochemical relationship, we consider it likely that the cyclohexane ring adopts a skew-boat conformation[44] as shown in D. This



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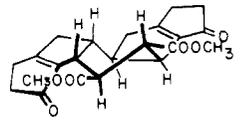
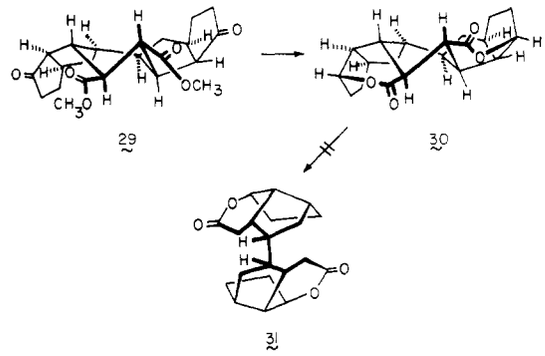


E

arrangement permits both bicyclic enone subunits to be disposed equatorially or, perhaps more accurately, to be projected in pseudoequatorial planes away from the central core. Additionally, H_5 is situated in an axial environment and protrudes into the deshielding region of the C_5''–C_8' double bond, while H_4 finds itself oriented equatorially, in agreement with the ^1H NMR spectrum.

When reduced with sodium in liquid ammonia, **18** was transformed into the highly symmetric diketo diester **28**, the identical substance into which **27** is epimerized under suitable alkaline conditions. The simplified ^1H NMR spectrum exhibited a sharp six-proton singlet for the methoxyl groups and a relatively low-field narrow multiplet of area 2 for the α-carbomethoxy protons. The ^{13}C NMR spectrum showed 11 signals. We see, therefore, that **28** has retained the C_2 symmetry of its precursor and that its ester groups exist as equatorial substituents (see E). Given the conditions of its formation, **28** can be logically considered to arise as the result of thermodynamic-control factors.

In an assessment of the catalytic reduction of **28**, extensive experimental study revealed that maximum selectivity in catalyst approach to the less hindered faces of this molecule could best be realized in ethyl acetate solution at −23 °C with acetic acid washed 10% palladium on carbon. An appreciation of the level of stereochemical control can best be gained by the fact that recrystallized pure **29** could be routinely isolated in 83–84% yield under these conditions. The nuclear magnetic resonance spectra



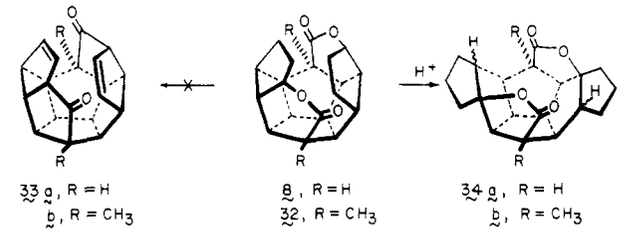
29 30 31

of **29** provide convincing testimony to its C_2 symmetry (see Experimental Section). Notwithstanding, chemical proof of the coiled configuration of this molecule was available by sodium borohydride reduction under standard conditions. The folded nature of the bicyclo[3.3.0]octanone part structures in **29** forces convex delivery of hydride and projection of the developing alkoxide anions to the inner surfaces of the molecular framework where facile lactonization can occur. Because of structural constraints, this additional ring construction is restricted to proceed with maintenance of twofold axial symmetry and to deliver **30** exclusively. Indeed, this dilactone exhibited only 10 lines as expected.

Dilactone **30** is a functionalized dimeric triquinane which possesses a nonfragile 1,4-dicarbonyl system because of its highly rigid conformational features which fix the geometry of the two lactone carbonyl groups in the stereoalignment previously given by B. If greater flexibility were to prevail, then ready conversion to the oxygenated *dl*-bivalvane derivative **31** would likely be possible. However, **30** is totally resistant to 1,4 reduction, as anticipated from our earlier considerations.

The Projected "Molecular Knitting" Plan. Returning now to **8**, we see this molecule to be a triseco precursor to **6** having all 20 carbon atoms properly predisposed. To arrive at the pentagonal dodecahedrane, one must develop a dehydrative retro-Baeyer–Villiger sequence and an ultimate threefold C–C bond formation.

The conversion of lactones to cycloalkenones has been carried out frequently in strongly acidic solution[35,37,45] and was, in fact, employed to advantage in the construction of **18**. However, these earlier studies do not comprise good models for the chemical behavior of **8**, since this dilactone was not analogously transformed to the highly desirable **33a**. Rather, stirring **8** in sulfuric acid, polyphosphoric



33a, R = H; b, R = CH_3 8, R = H; 32, R = CH_3 34a, R = H; b, R = CH_3

acid, or 8% phosphorus pentoxide in methanesulfonic acid for several hours at 70–95 °C resulted uniquely in isomerization. The infrared carbonyl stretching frequency

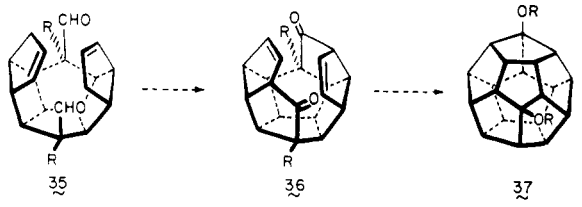
(44) Eliel, E. L. "Stereochemistry of Carbon Compounds"; McGraw-Hill: New York, 1962; pp 206–207.

(45) (a) Rai, C.; Dev, S. *J. Indian Chem. Soc.* **1957**, *34*, 178. (b) Jacob, T. M.; Dev, S. *Ibid.* **1959**, *36*, 429. (b) Metz, G. *Synthesis* **1972**, 612. (c) Jacob, T. M.; Vatakencherry, P. A.; Dev, S. *Tetrahedron* **1964**, *20*, 2815, 2831. (d) Ansell, M. F.; Brown, S. S. *J. Chem. Soc.* **1958**, 2955. (e) Gilmore R. C., Jr. *J. Am. Chem. Soc.* **1951**, *73*, 5879.

(1760 cm^{-1}) of the new substance, coupled with its ^1H NMR spectrum which lacks the downfield absorption characteristic of the >CHOCO– protons, implies the product is the γ-lactone **34a** with ether oxygen attached to a quaternary carbon atom.

The dimethyl dilactone **32**, obtained by reductive bond cleavage of **7** with sodium in liquid ammonia followed by reaction with excess methyl iodide, underwent an identical transformation. In addition to exhibiting spectra fully comparable to those of **34a**, dilactone **34b** retains a C_2 axis of symmetry as revealed by its 11-line carbon spectrum.

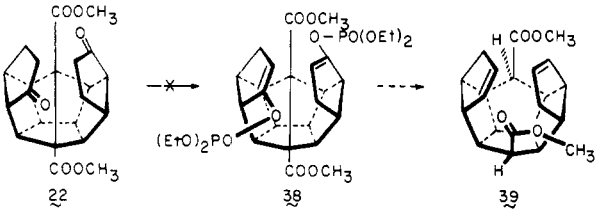
As an alternative to the above, our attention subsequently focused on **35** (R = H, blocking group, or transannular bond). Were such a diene dialdehyde in hand, it might be induced to undergo an intramolecular Prins reaction[46] to give **36**. At this point, the internal bond, if



35 **36** **37**

present, should be capable of cleavage as before. Suitable blocking groups could similarly be reductively removed as a consequence of their location α to the carbonyl groups. In **36**, severe steric crowding has been minimized as a result of the sp^2 character of the six functionalized carbon atoms. Also, it is clear from molecular models that the internal lobes of the p orbitals are exceedingly well disposed for transannular bonding, such that reduction of **36** (e.g., R = H) under pinacolic conditions might result in multiple transannular interaction and "knitting" of the molecular framework to give diol **37** (R = H). Subsequent removal of the hydroxyl groups by one of several methods was expected to be straightforward.

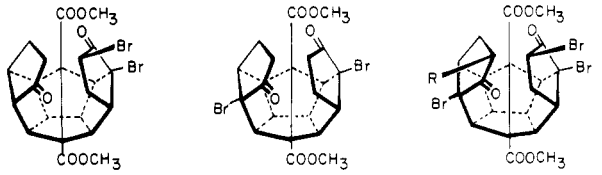
One approach to **35**, delightfully simple if it would have been successful, involved preliminary conversion of **22** to bis(enol phosphate) **38**, followed by dissolving metal reduction[47] under conditions where the central bond would be cleaved simultaneously. Unfortunately, the second step



22 **38** **39**

leading potentially to **39** was never attempted, for the successful preparation of **38** was not realized even under the most suitable kinetic conditions. The major component in the mixtures obtained from various experiments appeared to be the product derived from enolization to the more highly substituted α carbon atoms. Reactions designed to furnish the trimethylsilyl enol ether and enol acetate derivatives gave comparable results.

In line with these findings, keto ester **22** undergoes initial bromination under "neutral" conditions to give the product in which the bromine atom has entered the more highly substituted α position. Thus, treatment of **22** with 2 equiv of *N*-bromosuccinimide led uniquely to dibromide **41**.

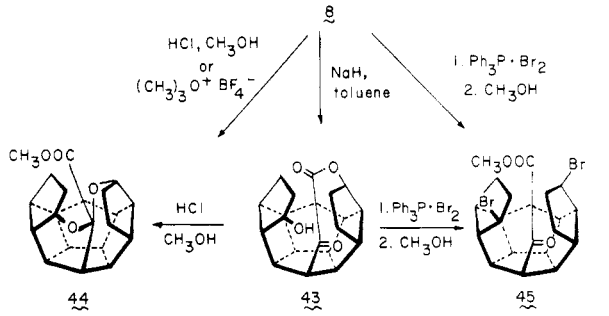


40 **41** **42** a, R = H; b, R = Br

Interestingly, contrasting results were realized when 2,4,4,6-tetrabromocyclohexa-2,5-dienone was utilized under conditions of acid catalysis.[48] In this case, dibromide **40** was isolated. With increasing amounts of the latter reagent, the tribromide **42a** and tetrabromide **42b** could also be obtained in high yield. Structural assignments to these substances were made on the basis of their ^1H NMR spectra and, a fortiori, their elemental analyses. We see, therefore, that α bromination of a ketone can, under appropriate conditions, activate the α′ position to electrophilic attack, perhaps through favorable inductive and/or perconjugative interaction of the bromine atom or the C–Br bond, respectively, with the enol π system in the bromo ketone.

In principle, the direct conversion of open lactones **8** or **32** to **35** would comprise a most efficient route to this pivotal intermediate. For this reason, it was particularly disappointing to recognize that **8** is highly sensitive to unwanted transannular cyclization under both alkaline and acidic conditions. For example, heating **8** with a sodium hydride dispersion in toluene was found to trigger Dieckmann condensation and formation of **43**. In general, the driving force in such reactions is the formation of a stabilized enolate anion of the resulting β-keto ester. This event prevents attack by the generated alkoxide at the ketone carbonyl with conversion back to starting material. In **43**, the production of such a carbanion is not possible due to the absence of an α proton. However, the ketone carbonyl is apparently shielded adequately by the molecular framework to prevent facile attack by the external base. Indeed, keto lactone **43** possesses a potential internal base (the hydroxyl group) capable of returning it to **8**. On the other hand, models indicate that the steric congestion which arises from nonbonded interactions within the molecular cavity in **8** is greatly diminished on proceeding to **43**, and this, together with steric strain release, appears to be the driving force for this reaction.

Conversion to the internal ketal **44** occurred when **8** was exposed to methanolic hydrogen chloride (0 °C) or trimethyloxonium tetrafluoroborate (25 °C). This product was also obtained from **43** under analogous acidic conditions. Absorptions of diagnostic value in the ^1H NMR



44 **43** **45**

spectrum of **44** include a broad singlet (2 H) at δ 4.39–4.09

(46) (a) Johnson, W. S. *Angew. Chem., Int. Ed. Engl.* **1976**, *15*, 9. (b) Piers, E.; Isenring, H.-P. *Synth. Commun.* **1976**, *6*, 221. (c) Cunningham, I. M.; Overton, K. H. *J. Chem. Soc., Perkin Trans. 1* **1975**, 2140. (d) Corey, E. J.; Ensley, H. E.; Suggs, J. W. *J. Org. Chem.* **1976**, *41*, 380. (e) Corey, E. J.; Boger, D. L. *Tetrahedron Lett.* **1978**, 2461 and references and contained therein.

(47) Ireland, R. E.; Muchmore, D. C.; Hentgartner, U. *J. Am. Chem. Soc.* **1972**, *94*, 5098.

(48) Calò, V.; Lopez, L.; Pesce, G.; Todesco, P. E. *Tetrahedron* **1973**, *29*, 1625.

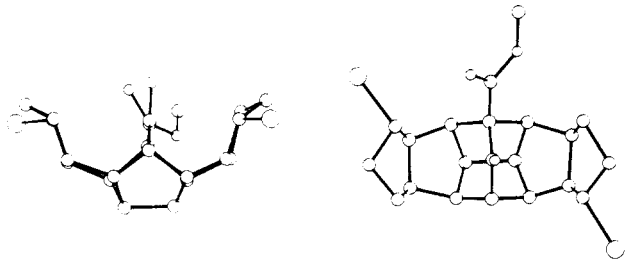


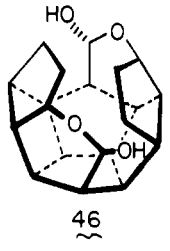
Figure 2. Three-dimensional features of **45** (courtesy of Professor W. Nowacki and Dr. P. Engel[41]).

belonging to the >CHO protons and a sharp singlet of area 3 at δ 3.70 arising from the methyl ester. The off-resonance decoupled ^{13}C NMR spectrum exhibits, inter alia, key signals at 174.62 (C(O)–O), 100.21 (O–C–O), 74.58 and 74.24 (>CHO), and 55.70 ppm (>C–$COOCH_3$). Similarly, reaction of **8** with triphenylphosphine dibromide in refluxing acetonitrile and subsequent methanolysis did not afford the anticipated[49] ring-opened dibromo diester, but **45** instead. The ^1H NMR spectrum of **45** shows a broad multiplet (2 H) at δ 4.74–3.83 due to the hydrogens on carbon bearing bromine and a sharp singlet (3 H) at δ 3.77 assigned to the methyl ester. Its ^{13}C NMR spectrum consists of 19 lines. Further structural evidence was derived by comparable treatment of **43** with triphenylphosphine dibromide and by X-ray crystal structure analysis.[41] Key three-dimensional features of this molecule are given in Figure 2.

These transformations can best be understood at the mechanistic level if the monoenolate or monoenol of the dilactone is the product-determining intermediate. This suggestion receives added support from our observations that dimethyl dilactone **32** is totally inert to the same array of reagents.

Close inspection of Figure 1 reveals that the carbon atoms which enter into transannular bonding are rather distant in the crystal. A scale model of the structure shows the molecule to be somewhat flexible conformationally. However, all conformations are seen to preclude the entry of solvent into the cavity. Given the absence or very low degree of solvation in the interior of this dilactone, it is not surprising that a reactive functional group, once generated, acquires hyperactive intramolecular tendencies under such circumstances. In solution, one has also to contend with solvent pressures, their effect being to bring the transannular centers into reasonable spatial proximity. In a sense, the interior of **8** can be considered to be a miniaturized enzyme cavity.

While **8** could be reduced under carefully controlled conditions to dilactol **46**, this substance proved unsuitable

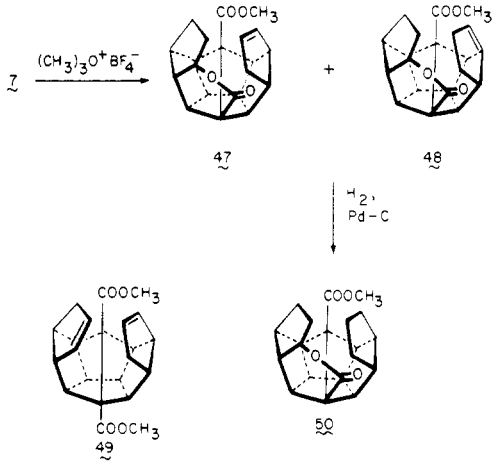


46

for further study because of its marked propensity for transannular bonding with loss of C_2 symmetry in subsequent reactions. On the basis of steric approach control, the initially formed product arising from hydride reduction of **8** should possess endo hydroxyl groups. Rapid handling did permit spectroscopic detection (^1H NMR) of two protons on the carbon bearing two oxygens. However, isomerization to the thermodynamically more favored and far less soluble **46** was very rapid.

At this point, our efforts were directed back to the closed dilactone **7** as a means of circumventing transannular bonding. These studies also proved unrewarding at first, but for a very different and unexpected reason. An example of the complication was initially encountered upon treatment of **7** with 2 equiv of trimethyloxonium fluoroborate followed by a methanolic solution of sodium methoxide. The cleavage of one lactone ring occurred to give a mixture of **47** and **48** rich in the former (84%) but not a doubly cleaved product. Ortho lactone production was not in evidence, ^1H NMR studies revealing that the conversion to **47** and **48** takes place prior to addition of the base. As a result, we could not consider bis(tosylhydrazone) formation and retro-Baeyer–Villiger ring contraction via oxacarbene intermediates.[50]

Even under the most forcing conditions tolerable to **47** (e.g., $Me_3O^+BF_4^-$ in C_6H_5Cl at 65–70 °C for 6 days), no evidence for conversion to **49** could be found. Conversion of **47** to an O-methylated species was indicated by ^1H NMR, but no further reaction of this intermediate took place. Evidently, the substantial conformational change



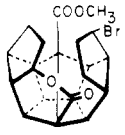
which accompanies the conversion of **7** to **47** and **48** leads to improper stereoalignment about the lactone functionality for facile repetition of the first reaction. In this regard, it is worth pointing out that the heavy preponderance of **47** may equally be attributable to stereoelectronic control.

The separation of **47** from **48** could not be efficiently achieved and for this reason catalytic hydrogenation of the mixture over 10% palladium on charcoal was carried out. The singular dihydro derivative **50** was obtained.

Identical conformational factors become important in the reaction of **7** with methanolic hydrogen bromide which afforded **51** in good yield. Heating **51** with additional HBr in methanol at the reflux temperature for more than 1 week led to no additional chemical change. In contrast, **7** reacted with methanolic hydrogen chloride at room temperature and gave rise to **52** (62%) together with a complex mixture of olefinic products. Consistent with retention of the C_2 axis in this dichloro diester, **52** exhibited a single methyl ester absorption at δ 3.73 and an 11-line ^{13}C NMR spectrum. To this time, we have not found it possible to dehydrochlorinate **52** and gain access to **49** in this manner. For example, treatment of **52** with DBU in

(49) Smissman, E. E.; Alkaysi, H. N.; Creese, M. W. *J. Org. Chem.* **1975**, *40*, 1640

(50) Foster, A. M.; Agosta, W. C. *J. Am. Chem. Soc.* **1972**, *94*, 5777. *Ibid.* **1973**, *95*, 608.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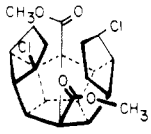
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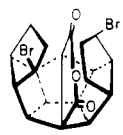
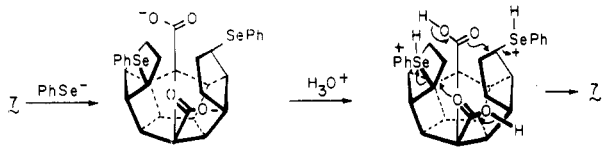

53

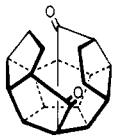
refluxing tetrahydrofuran or silver fluoride in pyridine at room temperature[51] led only to recovery of starting material. Trans elimination of HCl from **52** is not likely because the relevant hydrogen atoms are projected into the spherical cavity. However, elimination via the more difficult E2 mechanism is possible. Unfortunately, when more forcing conditions (KO-*t*-Bu in *t*-BuOH at 80 °C or $LiCl/Li_2CO_3$ in HMPA at 100 °C) were employed, the methyl esters were cleaved to give the corresponding dicarboxylic acid which underwent intramolecular S_N2 displacement of chloride ion to return dilactone **7** as the sole product.

The facility of this reclosure reaction appears universal. As an additional sample, we cite the behavior of **7** toward phenylselenide anion, a reagent recently recognized to be rather unique in its ability to cleave lactones by alkyl–oxygen fission.[52,53] Under the best conditions, $PhSe^-$ was generated by reduction of the diselenide with potassium metal in tetrahydrofuran solution containing dicyclohexyl-18-crown-6 or hexamethylphosphoramide. After a suitable reflux period, the cooled reaction mixture was diluted with water and basified. Dichloromethane extraction of this solution furnished no organic soluble material. Acidification and reextraction returned only lactone **7**, a compound otherwise isolable from dilute alkali solution. These observations suggest that **54** is produced initially but upon acidification rapidly cyclizes as a consequence of protonation at selenium (see **55**).


54 55

A reaction of comparable type was also noted with dibromo anhydride **53**, the product which results in relatively low yield (10–15%) when **7** is heated with triphenylphosphine dibromide in acetonitrile solution. Its attempted esterification with *p*-toluenesulfonic acid or boron trifluoride etherate[54] in methanol did not yield a dibromo diester comparable in structure to **52**. Rather, monolactone **51** was isolated in 65% yield.

Consideration was now given to the possible direct conversion of dichloro diester **52** to the bis(cyclopentanone) **56** through intramolecular cyclization of a derived organometallic. Attempts to generate the double Grignard derivative of **52** by standard methods proved futile. However, treatment with activated magnesium powder according to the procedure of Rieke and Bales[55] did produce the desired Grignard. Disappointingly, this substance could not be induced to cyclize. Instead, the reduction product **57** was obtained in 35% yield after preparative TLC (silica gel) isolation. The failure of the intended conversion to **56** was not especially surprising.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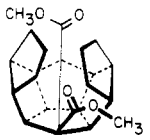
57

We are aware of no examples in the literature of such a reaction, although intramolecular addition of organometallics to ketone carbonyls is adequately precedented.[56] Because of the relative ease with which the central bond is cleaved in these molecules, the range of utilizable methods is restricted rather appreciably.

Free radicals are known to cyclize intramolecularly with carbonyl partners to generate five- or six-membered rings.[57] Reduction of halides with tri-*n*-butyltin hydride is known to proceed via a radical mechanism, and, in certain cases, cyclization unto a carbonyl group has been observed.[57a,c] Nonetheless, treatment of **52** with this reagent under conditions known to effect such cyclization cleanly afforded the reduction product **57**.

It remains, therefore, to uncover other methodology for converting such hexaquinane intermediates into C_2-symmetric octaquinane structures. The ensuing paper[58] constitutes a sequel to the present study.

Experimental Section

Melting points are uncorrected. Proton magnetic resonance spectra were obtained with Varian A-60A, Varian HA-100, 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 Perkin-Elmer Model 137 and 467 instruments. 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.

3,3a,3b,4,6a,7a-Hexahydro-3,4,7-metheno-7*H*-cyclopenta[*a*]pentalene-7,8-dicarboxylic Acid (9b). To a solution of **9a**[13] (21.94 g, 0.08 mol) in 65 mL of methanol was added 15 g of potassium hydroxide (85%, 0.228 mol) in 65 mL of water and the resulting solution was heated at reflux for 1 h under nitrogen. The methanol was removed under reduced pressure until a brownish precipitate appeared. To this mixture was added 120 mL of water, and the solution was heated at reflux for an additional 10.5 h. After acidification with concentrated hydrochloric acid, the diacid was collected. The brown solid was dissolved in 95% ethanol (350 mL), and 2.5 g of charcoal was added. After standing for 12 h, the solution was filtered through a Celite pad and the filtrate concentrated to yield 19.27 g (98%) of **9b**: dec at 240 °C; ν_{max} (KBr) 1695 cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 5.99 (t, J = 1.5 Hz, 4 H), 3.32–3.12 (m, 4 H), 2.35 (m, 2 H).

Anal. Calcd for $C_{14}H_{12}O_4$: C, 68.84; H, 4.95. Found: C, 68.76; H, 5.18.

Decahydro-3,7-*exo*,*exo*-diiodo-1*H*-6,4,5,7b-(epoxyethanylylidyne)cyclopenta[4,5]pentaleno[1,6-*bc*]furan-1,9-dione (10b). To a solution of **9b** (44 g, 0.180 mol) in aqueous sodium bicarbonate solution (90 g in 1 L of water) was added dropwise a solution of sublimed iodine (182 g, 0.718 mol) and potassium iodide (364 g, 2.19 mol) in 600 mL of water over 3 h with protection from light. After an additional 20 h of stirring, an aqueous sodium thiosulfate (150 g) solution was added until no free iodine was evident. The yellow precipitate was collected and washed with an aqueous sodium thiosulfate solution, water (3 × 100 mL), and acetone (2 × 50 mL) before being dried in vacuo [63 °C (0.1 mm)] for 48 h. There was isolated 86 g (96%) of **10b**:

(51) Verheyden, J. P. H.; Moffatt, J. G. *J. Org. Chem.* **1974**, *39*, 3573.
(52) Liotta, D.; Santiesteban, H. *Tetrahedron Lett.* **1977**, 4372.
(53) Scarborough, R. M., Jr.; Smith, A. B., III. *Tetrahedron Lett.* **1977**, 4361.
(54) Marshall, J. L.; Erickson, K. C.; Folsom, T. K. *Tetrahedron Lett.* **1970**, 4011.
(55) Rieke, R. D. Bales, S. E. *J. Am. Chem. Soc.* **1974**, *96*, 1775.
(56) (a) Corey, E. J.; Kuwajima, I. *J. Am. Chem. Soc.* **1970**, *92*, 395. (b) Danishefsky, S.; Dumas, D. *J. Chem. Soc., Chem. Commun.* **1968**, 1287.
(57) (a) Flies, F.; Lalande, R.; Maillard, B. *Tetrahedron Lett.* **1976**, 439. (b) Nikishin, G. I.; Starostin, E. K.; Golovin, B. A.; Kessenikh, A. V.; Ignatenko, A. V. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1971**, 1742. (c) Menapace, L. W.; Kuivila, H. G. *J. Am. Chem. Soc.* **1964**, *86*, 3047.
(58) Paquette, L. A.; Begley, W. J.; Balogh, D.; Wyvratt, M. J.; Bremner, D., following paper in this issue.

dec pt 160 °C (from acetonitrile); ν_{max} (KBr) 1780, 1792 cm^{-1}; ^{1}H NMR (Me_2SO-d_6) δ 5.14 (d, J = 5.2 Hz, 2 H), 4.31 (s, 2 H), 3.69 (d, J = 5.2 Hz, 2 H), 3.27 (m, 2 H), 3.14 (m, 2 H); m/e calcd 495.8672, obsd 495.8679.

Anal. Calcd for $C_{14}H_{10}I_2O_4$: C, 33.90; H, 2.03; I, 51.17. Found: C, 33.62; H, 2.07; I, 50.69.

Dimethyl Decahydro-1,5-*endo*,*endo*-dihydroxy-2,6-*exo*,-*exo*-diiodo-3,4,7-metheno-7*H*-cyclopenta[*a*]pentalene-7,8-dicarboxylate (14). Bis(iodo lactone) **10b** (72.7 g, 0.147 mol) was suspended in 425 mL of dry methanol under nitrogen. A solution of sodium methoxide in methanol was slowly added to the heterogeneous mixture with stirring until a pH of 9–10 was established. A gradual color change from yellow to white occurred within 0.5 h. After 2.5 h, the methanol was removed under reduced pressure, and the residue was treated with 100 mL of water and 800 mL of dichloromethane. After separation of the layers, the aqueous layer was further extracted with dichloromethane (4 × 100 mL). The combined organic layers were washed with brine (2×), dried, filtered through Celite, and concentrated to yield 78.7 g of **14** as a white solid, mp 145 °C dec (from chloroform/ether); ν_{max} (KBr) 3410 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.76 (m, J = 4 Hz, 2 H), 4.30 (d, J = 3.6 Hz, 2 H), 4.08 (d, J = 8.2 Hz, 2 H), 3.79 (s, 6 H), 2.96 (d, J = 1.8 Hz, 4 H), 2.68 (br d, J = 4.2 Hz, 2 H).

Anal. Calcd for $C_{16}H_{18}I_2O_6$: C, 34.31; H, 3.24. Found: C, 34.41; H, 3.31.

Dimethyl Decahydro-1,5-*exo*,*exo*-diiodo-2,6-dioxo-3,4,7-metheno-7*H*-cyclopenta[*a*]pentalene-7,8-dicarboxylate (15). In a 3-L three-necked reaction flask which was equipped with an overhead stirrer, addition funnel, and thermometer was prepared a solution of unpurified **14** (78.7 g, 0.140 mol) in 1.3 L of acetone. With cooling of the solution to 5 °C, 420 mL of a stock solution of chromic acid (prepared from 200 g of sodium dichromate dihydrate, 272 g of concentrated sulfuric acid, and 600 mL of water) was added dropwise at such a rate that the temperature of the reaction mixture did not rise above 5 °C (2 h). After an additional 0.5 h of stirring at room temperature, the acetone was decanted from the precipitate and filtered through a sintered-glass funnel. The chromium salts were dissolved in water and also filtered through the funnel but into a separate filtration flask. The product was washed with water until the washings were clear. The collected product was then permitted to stand with a saturated aqueous sodium bicarbonate solution with occasional stirring. Upon filtration, the product was washed with water (2×) and acetone (2×) (filtered into the filtration flask containing the original reaction mixture). After the product was dried in vacuo, the yield of **15** was 62.3 g.

The aqueous filtrates were extracted with dichloromethane (3 × 200 mL). The acetone filtrates were concentrated under reduced pressure to produce a dark brown aqueous solution which was diluted with 1 L of water and extracted with dichloromethane (5 × 200 mL). The combined organic layers were washed with aqueous sodium bicarbonate solution (2 × 500 mL), aqueous (5%) sodium thiosulfate solution (1 × 300 mL), and brine (1 × 500 mL) prior to drying. Concentration afforded an additional 13.06 g of **15** (92% total based on **14**), dec pt 170 °C (from acetone); ν_{max} (KBr) 1760, 1745, 1730 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.98 (s, 2 H), 3.65 (s, 6 H), 3.33–2.99 (m, 6 H).

Anal. Calcd for $C_{16}H_{14}I_2O_6$: C, 34.56; H, 2.54. Found: C, 34.73; H, 2.66.

Dimethyl Decahydro-1,5-dioxo-3,4,7-metheno-7*H*-cyclopenta[*a*]pentalene-7,8-dicarboxylate (13). In a 3-L three-necked reaction flask, copper(II) acetate monohydrate (4.5 g, 0.0225 mol) was dissolved under nitrogen in 250 mL of glacial acetic acid with heating. Zinc dust (67.5 g, 1.03 g-atom) was added, and with the disappearance of the greenish blue color, the liquid was decanted. The couple was rinsed with glacial acetic acid (2 × 10 mL), ether (8 × 100 mL), and dry methanol (2 × 100 mL). To the suspension of zinc–copper couple in 2.5 L of dry methanol were added 89.0 g (0.16 mol) of **15** and 80 g of ammonium chloride, and the heterogeneous mixture was stirred for 5 h under nitrogen. The methanolic solution was decanted from the couple and concentrated under reduced pressure. The methanolic residue was extracted with 1.5 L of dichloromethane and filtered through Celite. The zinc and copper residues were then extracted with 500 mL of dichloromethane and likewise filtered through Celite. The combined organic layers were washed with aqueous 10% ammonium chloride solution (2×), saturated sodium bicarbonate solution (1×), and brine (1×) before drying. Concentration afforded 45.0 g of **13** which was purified by recrystallization from acetone (38 g, 78%), mp 220–222 °C. This material was identical in all respects with the diketo diester prepared as described below.

Dimethyl Decahydro-1,5-dioxo-3,4,7-metheno-7*H*-cyclopenta[*a*]pentalene-7,8-dicarboxylate (13) and Dimethyl Decahydro-1,6-dioxo-3,4,7-metheno-7*H*-cyclopenta[*a*]pentalene-7,8-dicarboxylate (12). To a heterogeneous mixture of sodium borohydride (5.65 g, 0.149 mol) and 2-methyl-2-butene (27.45 g, 0.391 mol) in 140 mL of dry diglyme was added dropwise 27.43 g (0.193 mol) of freshly distilled boron trifluoride etherate in 20 mL of dry diglyme under nitrogen at 0 °C. After a 3-h stirring period at 0 °C, a solution of **9a** (8.97 g, 0.0329 mol) in 50 mL of diglyme was added dropwise to the heterogeneous mixture at 0 °C. After being stirred for an additional 0.5 hr at 0 °C, the reaction mixture was permitted to warm to room temperature where it was stirred for 20.5 h under nitrogen before being cooled to 0 °C and treated cautiously with 33 mL of water (gas evolution) followed by 330 mL of a 10% aqueous sodium hydroxide solution and 330 mL of a 30% aqueous hdyrogen peroxide solution. After being stirred for 3 h at room temperature, the aqueous reaction mixture was extracted with dichloromethane (6 × 200 mL). The combined organic layers were washed with saturated sodium bicarbonate solution (3 × 250 mL) and dried. Concentration under reduced pressure (35 mm) afforded a diglyme solution of diol diesters which was further concentrated at 45 °C and 0.3 mm to yield 7.56 g of a white solid. Continuous extraction of the aqueous layer with dichloromethane for 3 days afforded an additional 1.26 g (87% total) of diol mixture: ^{1}H NMR ($CDCl_3$) δ 4.21 (br d, J = 6 Hz, 2 H), 3.60 (very dominant), 3.56 (2 s, 6 H), 2.98 (br s, 2 H, OH), 2.74–2.08 (br m, 10 H).

To an ice-cooled, heterogeneous mixture of diol diester (5.32 g, 0.0172 mol) in 110 mL of acetone, 49.5 mL of a stock solution of chromic acid (prepared from 10 g of sodium dichromate dihydrate, 13.6 g of concentrated sulfuric acid, and 50 mL of water) was added dropwise with stirring. The brownish solution was stirred at room temperature for 10 min prior to decanting the acetone from the chromium salt residue. The residue was rinsed with acetone (3 × 40 mL) and decanted each time. The combined acetone extracts were concentrated under reduced pressure and then treated with an excess of saturated aqueous sodium bicarbonate solution. The resulting aqueous mixture was extracted with dichloromethane (6 × 100 mL). The combined extracts were washed with water and brine before drying. Removal of the solvent afforded 4.78 g (91%) of a mixture of diketo diesters. ^{1}H NMR analysis established the composition of the mixture as 38% of **13** and 62% of **12**.

The isomerically pure diketo diesters were obtained by high-pressure liquid chromatography on silica gel (80:20 ethyl acetate–ether elution). For **13**: R_f 0.59; recrystallization from acetone afforded white, cubic crystals, mp 221.5–222 °C; ν_{max} (KBr) 1755, 1733, 1320 cm^{-1}; ^{1}H NMR ($CDCl_3$, 100 MHz) δ 3.66 (s, 6 H), 3.11–2.93 (m, 6 H), 2.80 ($^1/_2$ ABq (endo), J_{AB} = 19 Hz, $\Delta\nu_{AB}$ = 51.6 Hz, 2 H), 2.28 ($^1/_2$ ABq (exo), J_{AB} = 19 Hz, $\Delta\nu_{AB}$ = 51.6 Hz, J_{AX} = 5 Hz, 2 H); ^{13}C NMR ($CDCl_3$) 211.32 (s), 169.29 (s), 68.64 (d), 61.09 (s), 53.17 (d), 52.28 (d), 48.02 (d), and 36.93 (t) ppm; m/e calcd 304.0947, obsd 304.0952.

Anal. Calcd for $C_{16}H_{16}O_6$: C, 63.15; H, 5.30. Found: C, 63.16; H, 5.33.

For **12**: R_f 0.48; recrystallization from benzene yielded white, cubic crystals, mp 203–204 °C; ν_{max} (KBr) 1753, 1735, 1723, 1192 cm^{-1}; ^{1}H NMR ($CDCl_3$, 100 MHz) δ 3.70 (s, 3 H), 3.63 (s, 3 H), 3.25–2.84 (m, 6 H), 2.67 ($^1/_2$ ABq (endo), J_{AB} = 19 Hz, $\Delta\nu_{AB}$ = 24.5 Hz, 2 H), 2.27 ($^1/_2$ ABq (exo), J_{AB} = 19 Hz, $\Delta\nu_{AB}$ = 24.5 Hz, J_{AX} = 4 Hz, 2 H); ^{13}C NMR ($CDCl_3$) 210.13, 169.98, 168.81, 67.76, 61.62, 60.50, 54.15, 52.43, 52.23, 48.33, 37.85 ppm; m/e calcd 304.0947, obsd 304.0952.

Anal. Calcd for $C_{16}H_{16}O_6$: C, 63.15; H, 5.30. Found: C, 63.16; H, 5.38.

Dimethyl Octahydro-2,2″-*endo*,*endo*-dioxodispiro[cyclobutane-1,1′-[3,4,7]-metheno[1*H*]cyclopenta[*a*]pentalene-5′(7′*H*),1″-cyclobutane]-7′,8′-dicarboxylate (16). To a nitrogen-blanketed solution of **13** (6.7 g, 0.022 mol) and cyclopropyldiphenylsulfonium tetrafluoroborate (67.96 g, 0.216 mol) in 200 mL of anhydrous dimethyl sulfoxide was added 4.83 g of

powdered potassium hydroxide (85%, 0.0734 mol; prepared under an argon atmosphere in a glovebag), and the resulting yellow solution was stirred for 30 h at room temperature. The reaction mixture was slowly poured into 100 mL of an aqueous 1 M fluoroboric acid solution. After dilution with 280 mL of water, the acidic mixture was extracted with dichloromethane (6 × 120 mL). The combined organic layers were washed with water (2 × 150 mL) and brine (1 × 250 mL) before drying.

Removal of the solvent produced a slightly yellow solid. This crude product was triturated with pentane (5 × 100 mL) and the residual solid collected on a sintered-glass funnel. The collected solid was then leached with dichloromethane (1 × 75 mL, 2 × 25 mL, 1 × 10 mL) until the filtrate was colorless. The remaining solid (26.7 g) was pure cyclopropyldiphenylsulfonium tetrafluoroborate.

The concentrated pentane extracts were chromatographed on a silica gel column. Elution with 10% ether in petroleum ether yielded 11.79 g of a mixture of diphenyl sulfide and cyclopropyl phenyl sulfide. The dichloromethane extracts were concentrated and placed on the same silica gel column by using the adsorbent coating technique. Continued elution with 10% ether in petroleum ether afforded an additional 0.5 g of sulfides (total yield >90%). The mixture of cyclobutanones (6.51 g, 77%) was recovered from the column with 70% ethyl acetate in chloroform. Recrystallization from benzene yielded colorless cubic crystals highly enriched in **16**: mp 220–224 °C; ν_{max} (KBr) 1779, 1759, 1742, 1718 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.74, 3.63 (very dominant, 2 s, 6 H), 1.24–3.54 (br m, 18 H); *m/e* calcd 384.1573, obsd 384.1572.

Anal. Calcd for $C_{22}H_{24}O_6$: C, 68.73; H, 6.29. Found: C, 68.35; H, 6.22.

Methanolic elution of the column yielded an additional 20.63 g of sulfonium salt (recovered yield 88%).

Decahydro-3,6-bis[3-(trimethylsilyl)allyl]-1*H*-6,4,5,7b-(epoxyethanylylidyne)cyclopenta[2,3]pentaleno[6,1-*bc*]-furan-1,9-dione (19). A solution of allyltrimethylsilyl anion was prepared by adding *sec*-butyllithium in cyclohexane (6.38 mmol) to dry tetrahydrofuran (30 mL) with stirring under nitrogen at −78 °C. Tetramethylethylenediamine (740 mg, 6.38 mmol) and allyltrimethylsilane (730 mg, 6.38 mmol) were introduced, and the solution was kept at −20 °C for 30 min. After cooling to −40 °C, 500 mg (1.645 mmol) of **13** was added. Stirring was maintained for 1 h, and the reaction mixture was kept at −20 °C for 1 h. Following the addition of solid ammonium chloride, the solution was allowed to warm to 0 °C, poured onto water (30 mL), and extracted with ether (3 × 30 mL). The combined organic extracts were washed with water (2×) and brine prior to drying. Evaporation of the solvent left 880 mg of a yellow oil which was subjected to preparative layer chromatography on silica gel (elution with 20% ether in hexane). There was isolated 200 mL (23%) of **20** and 80 mg (10%) of **19**. Recrystallization of the dilactone from benzene–hexane afforded white needles: mp 176–177 °C; ν_{max} (KBr) 2955, 1750, 1615, 1332, 840 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.95 (d of t, J = 19 and 6 Hz, 2 H), 5.71 (d, J = 19 Hz, 2 H), 3.1–2.2 (m, 10 H), 2.25 (d, J = 19 Hz, 2 H), 1.7 (d of d, J = 19 and 3.4 Hz, 2 H), 0.15 (s, 18 H); ^{13}C NMR ($CDCl_3$) 171.03, 139.17, 137.70, 89.67, 65.02, 59.77, 54.90, 49.28, 45.11, 33.79, −1.23 ppm; *m/e* calcd 468.2150, obsd 468.2164.

Anal. Calcd for $C_{26}H_{36}O_4Si$: C, 66.62; H, 7.74. Found: C, 66.60; H, 7.84.

Dimethyl Octahydro-1,5-dihydroxy-2,5-bis[3-(trimethylsilyl)allyl]-3,4,7-metheno-1*H*-cyclopenta[*a*]pentalene-7,8(7a*H*)-dicarboxylate (20). Method A. A solution of *sec*-butyllithium in tetrahydrofuran was prepared from 2.64 mol of *sec*-butyllithium dissolved in cyclohexane, 5 mL of tetrahydrofuran, and 310 mg (2.64 mmol) of tetramethylethylenediamine at −78 °C under nitrogen. To this mixture was added allyltrimethylsilane (301 mg, 2.64 mmol), and the solution was warmed to −20 °C with stirring for 30 min. After cooling to −45 °C, 200 mg (0.66 mmol) of **13** was introduced, stirring was maintained for 1 h, solid ammonium chloride (1 g) was added, and the solution was allowed to warm to 0 °C. The solution was poured onto water (10 mL) and extracted with ether (3 × 10 mL). The combined organic extracts were washed with water (2×) and brine before drying. Solvent removal under reduced pressure gave 360 mg of yellow oil which was subjected to preparative layer chromatography on silica gel (elution with 50% ether–hexane). There was obtained 130 mg (25%) of **20**: mp 108–109 °C; ν_{max} (KBr) 3507, 2955, 1730, 1615, 855, 830 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.10 (d of t, J = 19 and 6 Hz, 2 H), 5.70 (d, J = 19 Hz, 2 H), 3.73 (s, 6 H), 2.8–1.5 (series of m, 16 H), 0.1 (s, 18 H); ^{13}C NMR ($CDCl_3$) 173.85, 142.00, 134.53, 77.34, 66.85, 59.18, 58.85, 52.04, 49.91, 48.26, 37.43, −1.16 ppm.

Anal. Calcd for $C_{28}H_{44}O_6Si_2$: C, 63.12; H, 8.31. Found: C, 62.73; H, 8.45.

Method B. A solution of **19** (100 mg, 0.21 mmol) in dry methanol (4 mL) under nitrogen was treated dropwise with a solution of sodium methoxide in methanol until the pH was approximately 10. After being stirred for 4 h at 25 °C, the reaction mixture was poured into water (10 mL) and extracted with ether (3 × 10 mL). The combined organic layers were washed with water (2×) and brine, dried, and evaporated to give 105 mg (94%) of pure **20**.

Dimethyl Dodecahydro-5,5″-*endo*,*endo*-dioxodispiro-[furan-2(3*H*),1′-[3,4,7]-metheno[1*H*]cyclopenta[*a*]pentalene-5′(7′*H*),2″(3″*H*)-furan]-7′,8′-dicarboxylate (17). A. Baeyer–Villiger Ring Expansion of 16. To a solution of unpurified **16** (6.51 g, 0.0169 mol) in 200 mL of methanol was added aqueous 30% hydrogen peroxide solution (9.06 g, 0.08 mol). Following the addition of 3.38 mL (0.0338 mol) of a 10 N sodium hydroxide solution, the reaction mixture was stirred for 2.25 h at room temperature. After the addition of 250 mL of a 10% aqueous hydrochloric acid solution, the reaction mixture was repeatedly extracted with dichloromethane (8 × 100 mL). The combined extracts were washed with water (2 × 100 mL) and dried. Concentration yielded 7.1 g (100%) of a mixture of dilactones; ^{1}H NMR ($CDCl_3$) δ 3.82, 3.74, 3.66 (very dominant, s, 6 H), 3.10–1.50 (br m, 18 H). Recrystallization from acetone–dichloromethane afforded 295 g of isomerically pure dilactone **17**: mp 296.5–298.5 °C dec; ν_{max} (KBr) 1775, 1740, 1735 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.69 (s, 6 H), 2.81 (br s, 2 H), 2.68–2.34 (br m, 8 H), 2.19 (d, J = 3.5 Hz, 4 H), 2.08–1.50 (m, 4 H); ^{13}C NMR ($CDCl_3$) 175.84, 169.44, 89.08, 64.42, 59.11, 57.33, 51.74, 47.53, 36.69, 35.69, 29.38 ppm; *m/e* calcd 416.1471, obsd 416.1480.

Anal. Calcd for $C_{22}H_{24}O_8$: C, 63.45; H, 5.89. Found: C, 63.19; H, 5.87.

B. Oxidative Cyclization of 20. To a solution of **20** (100 mg, 0.188 mmol) in acetic acid (3 mL) under nitrogen were added 286 mg (1.50 mmol) of peracetic acid and 6 drops of sulfuric acid. After being stirred for 4 h at room temperature, the acidic solution was neutralized with saturated sodium bicarbonate solution, extracted with dichloromethane (3 × 10 mL), washed with sodium thiosulfate solution, water, and brine, and then dried. Removal of solvent under reduced pressure left 50 mg of a clear residue. Trituration with ether afforded 19 mg (24%) of **17**.

Dimethyl 1,2,3,3b,4a,5,6,7,8,8a,8b,9-Dodecahydro-1,5-dioxo-4,8,9-metheno-4*H*-cyclopenta[1,2-*a*:4,3-*a*′]dipentalene-4,10-dicarboxylate (18). Recrystallized dilactone **17** (>95% isomeric purity, 2.0 g, 4.80 mmol) was added in small portions at room temperature to 240 g of an 8% solution of phosphorus pentoxide in methanesulfonic acid under nitrogen. The colorless reaction mixture was stirred at 50 °C for 36.5 h. After being cooled, the reddish reaction mixture was added dropwise from a separatory funnel into 1 L of water with occasional stirring. The aqueous mixture was then extracted with dichloromethane (5 × 100 mL). The combined extracts were washed with water (3 × 300 mL) and brine (1 × 100 mL) before drying. Removal of the solvent afforded 2.05 g of crude **18** which was chromatographed on silica gel. Elution with 50% ethyl acetate in chloroform furnished 1.51 g (83%) of pure **18**: mp 234–235 °C (from benzene); ν_{max} (KBr) 1730, 1690, 1627, 1297 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.64 (m, 4 H), 3.50 (s, 6 H), 3.17 (br s, 2 H), 2.93–2.50 (m, 8 H); ^{13}C NMR ($CDCl_3$) 201.98, 185.25, 170.44, 147.19, 70.84, 63.58, 63.15, 59.48, 52.04, 39.84, 25.98 ppm; *m/e* calcd 380.1260, obsd 380.1264.

Anal. Calcd for $C_{22}H_{20}O_6$: C, 69.46; H, 5.30. Found: C, 69.66; H, 5.41.

Hydrogenation of 18. Dimethyl Hexadecahydro-1,5-dioxo-4,8,9-methenocyclopenta[1,2-*a*:4,3-*a*′]dipentalene-4,10-dicarboxylate (22). Bis(cyclopentenone) **18** (1.58 g, 4.15 mmol) was dissolved in 100 mL of ethyl acetate with gentle heating on a steam bath. Acidic 10% palladium-on-carbon catalyst was prepared by adding glacial acetic acid to a stirred mixture of the commercial catalyst in distilled water until a pH of 5–6 was

reached. After collection by filtration and thorough washing with distilled water, the catalyst was dried in vacuo for 7 h. The acidic catalyst (150 mg) was added to the solution of **18** in a standard Paar hydrogenation bottle, and shaking was initiated at an initial pressure of 47 psi of hydrogen. After 16 h, the catalyst was removed by filtration through Celite, and the filtrate was concentrated to yield 1.60 g (100%) of **22**. Depending upon the acidity and age of the catalyst, 1–2% transesterification can be observed. Recrystallization of the product from ethyl acetate afforded white crystals, dec pt 213 °C; ν_{max} (KBr) 1730, 1287 cm^{-1}; ^{1}H NMR ($CDCl_3$, 100 MHz) δ 3.55 (s, 6 H), 2.96 (br, s), 2.80 (br s), 2.69 (m), 2.43–2.29 (m), 2.24 (br s), 2.15–1.70 (m) (total 18 H); ^{13}C NMR ($CDCl_3$) 217.25 (s), 171.90 (s), 62.32 (d), 61.48 (d), 57.01 (s), 53.08, 51.86, 51.32, 43.22, 38.88, 24.40 (t) ppm; *m/e* calcd 384.1573, obsd 384.1577.

Anal. Calcd for $C_{22}H_{24}O_6$: C, 68.73; H, 6.29. Found: C, 68.56; H, 6.38.

Dimethyl Octahydro-1,5-dioxo-5*H*,8*H*-3a,9a:4b,7a-diepoxy-4,8,9-metheno-1*H*-cyclopenta[1,2-*a*:4,3-*a'*]dipentalene-4,11(4a*H*)-dicarboxylate (21). A solution of **18** (100 mg, 0.263 mmol) in 95% ethanol (5 mL) was treated with a solution of sodium carbonate (32 mg, 0.302 mmol) and hydrogen peroxide (0.13 mL, 1.5 mmol) in water (1 mL). The reaction mixture was stirred at 50 °C for 10 min prior to dilution with water (10 mL). The precipitated solid was separated by filtration and recrystallized from ethyl acetate–dichloromethane. There was obtained 82 mg (76%) of **21**: mp 304–305 °C; ν_{max} (KBr) 1750, 1320 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.60 (s, 6 H), 3.25–3.0 (m, 4 H), 2.7–2.3 (m, 10 H); ^{13}C NMR ($CDCl_3$) 203.48, 170.04, 67.50, 62.51, 62.48, 56.82, 56.31, 51.76, 43.92, 38.46, 21.61 ppm.

Anal. Calcd for $C_{20}H_{20}O_8$: C, 64.08; H, 5.84. Found: C, 63.94; H, 4.94.

Methyl Tetradecahydro-8β-hydroxy-5-oxo-5*H*-1,10,5a,9-ethanediylidene-1*H*-cyclopenta[*b*]cyclopenta[5,6]pentalene[2,1-*d*]pyran-12-carboxylate (23). To a cold (0 °C) solution of **22** (272 mg, 0.708 mmol) in 17 mL of dry methanol was added sodium borohydride (37 mg, 0.97 mmol) under nitrogen, and the resulting solution was stirred for 8 h at 0 °C. The reaction mixture was neutralized with aqueous 2 N acetic acid solution (2 mL) at 0 °C, diluted with 100 mL of water, and extracted with dichloromethane (4 × 25 mL). The combined extracts were washed with water (1 × 35 mL) and brine (1 × 35 mL) before drying. Removal of the solvent afforded 282 mg of **23** which was recrystallized from ethyl acetate to yield 204 mg (81%) of white needles: mp 182–183 °C; ν_{max} (KBr) 3470, 1741, 1295 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.92 (br, s, 1 H), 4.13 (br s, 1 H), 3.68 (s, 3 H), 2.94–2.45 (m, 11 H), 2.35–1.97 (m, 3 H), 1.93–1.34 (m, 5 H); ^{13}C NMR ($CDCl_3$) 172.00, 84.98, 74.99, 63.50, 62.96, 61.67, 59.03, 52.77, 51.31, 50.99, 50.18, 46.78, 45.81, 42.41, 41.38, 37.55, 33.77, 24.33, 22.93 ppm; *m/e* calcd 356.1624, obsd 356.1629.

Anal. Calcd for $C_{21}H_{24}O_5$: C, 70.76; H, 6.79. Found: C, 70.76; H, 6.71.

Tetradecahydro-5*H*,6*H*-1,5b,12:5a,10,11-dimethenodicyclopenta[*e*,*e'*]benzo[2,1-*c*:3,4-*c'*]dipyran-5,6-dione (7). A. Reduction of 22 with Sodium Borohydride. To a cold (0 °C) solution of **22** (639 mg, 1.66 mmol) in 35 mL of dry methanol was added sodium borohydride (95 mg, 2.49 mmol), and the resulting solution was stirred at 0 °C under nitrogen for 8.5 h. After the reaction mixture was slowly acidified at 0 °C with aqueous 2 N hydrochloric acid solution, the solution was concentrated under reduced pressure until a precipitate had formed. This residue was diluted with 80 mL of water and extracted with dichloromethane (3 × 40 mL). The combined organic extracts were washed with water (1 × 25 mL), dried, and concentrated to afford a mixture of dilactone **7**, hydroxy ester **23**, and a small amount of overreduced material (^{1}H NMR analysis). The crude product was dissolved in 250 mL of benzene along with 20 mg of *p*-toluenesulfonic acid. The resulting solution was heated at the reflux temperature for 8 h under nitrogen with periodic removal of benzene (100 mL in 5-mL aliquots) via a Dean–Stark trap. After dilution with 125 mL of water and separation of the layers, the aqueous phase was extracted with dichloromethane (3 × 30 mL). The combined organic layers were dried and concentrated to give a solid mixture (534 mg) which consisted (^{1}H NMR analysis) of **7** (93%) and the overreduction product (7%). Recrystallization from ethyl acetate afforded 460 mg (86%) of pure dilactone **7**: mp 225–226.5 °C dec; ν_{max} (KBr) 1732, 1111, 1090 cm^{-1}; ^{1}H NMR ($CDCl_3$, 100 MHz) δ 4.91 (m, 2 H), 3.13–2.47 (m, 12 H), 2.36–2.03 (m, 4 H), 1.78–1.46 (m, 2 H); ^{13}C NMR ($CDCl_3$) 172.13 (s), 86.52 (d), 59.61 (d), 59.09 (d), 54.80 (s), 52.78 (d), 45.83, 41.54, 37.44 (t), 23.86 (t) ppm; *m/e* calcd 324.1361, obsd 324.1365.

Anal. Calcd for $C_{20}H_{20}O_4$: C, 74.05; H, 6.22. Found: C, 73.98; H, 6.27.

B. Reduction of 22 with Sodium Cyanoborohydride. To a solution of **22** (4.23 g, 0.011 mol) in 180 mL of absolute methanol was added the indicator bromocresol green followed by sodium cyanoborohydride (2.76 g, 0.044 mol). To this blue solution was added methanolic 2 N hydrochloric acid solution dropwise with stirring under nitrogen as needed to maintain the yellow endpoint. After 8.5 h, the yellow color had become persistent. An additional 2 mL of acid was added, and the solution was concentrated under reduced pressure. The residue was treated with 225 mL of water and extracted with dichloromethane (4 × 100 mL). The combined organic layers were washed with water (1 × 100 mL) and brine (1 × 100 mL) before drying and concentration. A white solid (4.05 g) resulted. At times, cyclization to the dilactone was not complete. When this occurred, the crude product was dissolved in 500 mL of benzene containing a catalytic amount of *p*-toluenesulfonic acid (7 mg) and heated at the reflux temperature for 8.5 h under nitrogen with periodic removal of benzene (volume reduced by 50%) via a Dean–Stark trap. After removal of the benzene under reduced pressure, the residue was dissolved in 400 mL of dichloromethane and extracted with water (2 × 100 mL) and brine (1 × 100 mL) before drying. Concentration afforded 3.77 g of slightly yellow **7**, which was contaminated by overreduction products to the extent of 2% (^{1}H NMR analysis). Recrystallization from ethyl acetate yielded pure dilactone **7** (3.04 g, 85%).

C. Acid-Catalyzed Cyclization of 23. A solution of **23** (120 mg, 0.337 mmol) and *p*-toluenesulfonic acid (7 mg) in 50 mL of benzene was heated at the reflux temperature under nitrogen for 8.5 h with periodic removal of benzene (25 mL in 5-mL aliquots) via a Dean–Stark trap. Following the addition of 50 mL of water to the reaction mixture, the layers were separated and the aqueous portion was extracted with dichloromethane (3 × 20 mL). The combined organic phases were washed with brine (1 × 50 mL), dried, and concentrated to yield white needles (109 mg, 100%) of pure **7**.

Octadecahydro-3,7-dioxadicyclopenta[*cd*,*c'd'*]pentaleno[2,1,6-*hia*:5,4,3-*h'i'a'*]diindene-4,8-dione (8). In a dry 250-mL three-necked reaction flask which was equipped with a condenser, a Herschberg stirrer, and a nitrogen inlet, freshly cut sodium (1.7 g, 0.074 g-atom) in 80 mL of dry toluene was heated with rapid stirring under nitrogen until a fine dispersion had formed. In order to minimize contamination from mineral oil, the Herschberg stirrer was replaced by a magnetic stirring bar at this point. Trimethylchlorosilane (10 mL, 0.079 mol) was added followed by 500 mg (1.54 mmol) of **7**. The resulting solution was refluxed for 7 h. After the condenser was replaced with a distillation setup, the reaction solution was distilled until pure toluene (bp 110 °C) was collected. The residual solution was filtered through a Celite pad directly into methanol (50 mL). The filtrate was concentrated under reduced pressure to yield a yellow solid, which was dissolved in 100 mL of dichloromethane and extracted with water and brine prior to drying. Removal of the solvent afforded crude **8**, recrystallization of which from ethyl acetate yielded 410 mg (82%) of pure dilactone: mp 255–259.5 °C dec; ν_{max} (KBr) 1715, 1227 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.85 (br s, 2 H), 4.03–2.68 (br m, 12 H), 2.45–1.52 (br m, 8 H); ^{13}C NMR ($CDCl_3$) 173.03 (s), 84.06 (d), 65.12, 51.47, 50.45, 46.94, 45.48, 41.27, 39.44, 27.25 ppm; *m/e* 326.1518, obsd 326.1513.

Anal. Calcd for $C_{20}H_{22}O_4$: C, 73.60; H, 6.79. Found: C, 73.42; H, 6.80.

Reduction of 18 with Sodium in Toluene Containing Chlorotrimethylsilane. Dimethyl 1,2,3,3''β,4α,5α,5'β,6,7,8,-9,9'β,9''α,10-Tetradecahydro-3,6-dioxodicyclopent[*b*,*h*]-*as*-indacene-4β,5β-dicarboxylate (27). A sodium dispersion (300 mg, 130.0 mg-atom) was prepared in dry toluene (10 mL) contained in a 50-mL, three-necked flask fitted with a condenser, nitrogen-inlet tube, and Herschberg stirrer. After the mixture was cooled to room temperature without stirring, chlorotrimethylsilane (3.5 mL, 26.9 mmol) was added through the condenser follwed by dropwise addition of a solution of **18** (100 mg,

0.36 mmol) in 1 mL of dry toluene. The resulting yellow mixture was heated at reflux with stirring for 4 h, cooled to room temperature, and filtered through Celite into 15 mL of anhydrous methanol. After concentration of the filtrate under reduced pressure, the residue was dissolved in dichloromethane (50 mL), washed with aqueous sodium bicarbonate solution, and dried. Solvent evaporation left 70 mg (50.6%) of **27**: mp 215 °C dec (from ethyl acetate); ν_{max} (KBr) 1740, 1695, 1645 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.74 (s, 3 H), 3.53 (s, 3 H), 3.64–2.91 (br m, 5 H), 2.82–2.09 (br m, 13 H); ^{13}C NMR ($CDCl_3$) 203.27, 202.68, 184.12, 183.67, 173.04, 172.33, 149.02, 148.08, 52.23, 51.65, 45.73, 44.33 (2 C), 41.73, 40.98, 40.82, 40.04, 37.77, 37.60, 37.05, 25.90, 25.74 ppm; *m/e* calcd 384.1573, obsd 384.1577.

Anal. Calcd for $C_{22}H_{24}O_6$: C, 68.73; H, 6.29. Found: C, 68.54; H, 6.24.

Reduction of 18 with Sodium in Liquid Ammonia. Dimethyl 1,2,3,3′′β,4α,5β,5′α,6,7,8′′,9,9′α,9′′β,10-Tetradecahydro-3,6-dioxodicyclopent[*b,h*]-*as*-indacene-4β,5α-dicarboxylate (28). Freshly cut sodium metal (1.86 g, 0.0809 g-atom) was dissolved in 450 mL of ammonia (dried over and distilled from sodium) under nitrogen. A solution of **18** (0.93 g, 2.45 mmol) in 60 mL of dry tetrahydrofuran was added dropwise during 1.5 h at −78 °C. The reaction mixture was stirred for an additional hour and then allowed to come to room temperature with evaporation of the ammonia during 2.5 h. Saturated aqueous ammonium chloride solution (179 mL) was added dropwise to the residue, the resulting yellow solution was extracted with dichloromethane (5 × 100 mL), and the combined organic layers were washed with brine (1 × 100 mL) prior to drying. Concentration gave 1.34 g of a white foam, recrystallization of which from ethyl acetate delivered 619 mg (66%) of **28** as a colorless solid, mp 248 °C dec; ν_{max} (KBr) 1740, 1690, 1640 cm^{-1}; ^{1}H NMR ($CDCl_3$, 100 MHz) δ 3.67 (s, 6 H), 3.33–2.97 (m, 2 H), 2.93–2.28 (m, 16 H); ^{13}C NMR ($CDCl_3$) 202.23, 184.35, 173.82, 149.84, 52.26, 45.57 (2 C), 40.43, 39.52, 36.92, 25.94 ppm; *m/e* calcd 384.1573, obsd 384.1577.

Anal. Calcd for $C_{22}H_{24}O_6$: C, 68.73; H, 6.29. Found: C, 68.51; H, 6.34.

Base-Promoted Epimerization of 27. To a solution of **27** (39 mg, 0.102 mmol) in dry methanol (15 mL) was added 1 mL of a dilute sodium methoxide solution in methanol, and stirring was maintained for 6 days at room temperature under nitrogen. The solvent was removed under reduced pressure, and the residue was dissolved in dichloromethane (5 mL). After washing with water (4 mL) and brine (4 mL), the organic phase was dried and concentrated to give 30 mg (78%) of **28**.

Hydrogenation of 28. A solution of **28** (500 mg, 1.30 mmol) in 200 mL of ethyl acetate (distilled from potassium carbonate) was deoxygenated by bubbling nitrogen through it. A 166.5-mg sample of 10% palladium on carbon (previously treated with glacial acetic acid in water to pH 5, washed thoroughly with water, and dried overnight at 0.1 mm) was then added. After this magnetically stirred mixture contained in a hydrogenation bottle was cooled to −23 °C in a dry ice–carbon tetrachloride slush bath, connection was made to a Paar apparatus, and the hydrogenation was begun at 50 psig. After 10 h, the reaction mixture was disconnected from the hydrogenator and allowed to come to room temperature while bubbling nitrogen through it. The catalyst was separated by filtration through Celite and washed with a small amount of ethyl acetate, methanol (50 mL), and dichloromethane (200 mL). Evaporation of the ethyl acetate wash followed by recrystallization, in combination with the solid obtained by concentration of the latter two fractions, gave 422 mg (83.6%) of **29**: mp 246 °C dec; ν_{max} (KBr) 1740, 1730 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.66 (s, 6 H), 3.25 (m, 2 H), 3.01–1.61 (br m, 18 H), 1.35–0.91 (br m, 2 H); ^{13}C NMR ($CDCl_3$) 220.82, 174.60, 54.41, 51.81, 44.46, 43.75, 42.90, 41.08, 37.44, 36.99, 25.29 ppm; *m/e* calcd 388.1886, obsd 388.1891.

Anal. Calcd for $C_{22}H_{28}O_6$: C, 68.02; H, 7.26. Found: C, 67.70; H, 7.26.

Borohydride Reduction of 29. A suspension of **29** (200 mg, 0.515 mmol) in absolute ethanol (138 mL) was gently heated under nitrogen until complete disolution was achieved and allowed to return to room temperature. Sodium borohydride (80.5 mg, 2.13 mmol) was introduced in one portion, the mixture was stirred for 16 h, and 25 mL of 10% hydrochloric acid was then slowly added. The ethanol was removed in vacuo, and the residue was diluted with water (75 mL) and extracted with dichloromethane (4 × 75 mL). The combined organic layers were washed with brine (75 mL), dried, and evaporated to furnish 214 mg of white solid, recrystallization of which from ethyl acetate gave 64.7 mg (38.3%) of **30**: mp 283 °C dec; ν_{max} (KBr) 1755, 1735 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.90 (q, J = 8.5 Hz, 2 H), 3.90–1.38 (br m, 22 H); ^{13}C NMR ($CDCl_3$) 172.23, 82.77, 44.73, 42.20, 42.07, 41.94, 37.64, 37.26, 32.57, 27.44 ppm; *m/e* calcd 328.1674, obsd 328.1679.

Anal. Calcd for $C_{20}H_{24}O_4$: C, 73.14; H, 7.37. Found: C, 73.37; H, 7.19.

Acid-Catalyzed Isomerization of 8. A solution of **8** (50 mg) in 4 mL of concentrated sulfuric acid was heated at 90 °C with stirring under nitrogen for 4.25 h. After being cooled, the mixture was poured into ice–water (30 mL) and extracted with dichloromethane (3 × 30 mL). The combined organic layers were washed with water (50 mL), dried, and evaporated. There remained 34 mg of a pale yellow solid, recrystallization of which from ethyl acetate afforded dilactone **34a** as colorless crystals: mp 248.5–250 °C; ν_{max} (KBr) 1760 cm^{-1}; ^{1}H NMR ($CDCl_3$, 100 MHz) δ 3.8–3.08 (m, 6 H), 3.0–2.6 (m, 4 H), 2.4–1.25 (m, 12 H); *m/e* calcd 326.1518, obsd 326.1521.

Anal. Calcd for $C_{20}H_{22}O_4$: C, 73.60; H, 6.79. Found: C, 73.33; H, 6.78.

5,9-Dimethyloctadehydro-3,7-dioxadicyclopenta[*cd,c′d′*]pentaleno[2,1,6-*hia*:5,4,3-*h′i′a′*]diindene-4,8-dione (32). Into a flame-dried three-necked 500-mL flask was condensed 150 mL of anhydrous liquid ammonia. Tetrahydrofuran (50 mL) was introduced, followed by 356 mg (15.5 mg-atom) of sodium metal. To the blue solution was added dropwise 500 mg (1.54 mmol) of **7** dissolved in tetrahydrofuran (30 mL). After an additional 20 min at −35 °C, excess methyl iodide (4 mL) was added. The alkylation was allowed to proceed for 30 min prior to addition of saturated ammonium chloride solution. The product was extracted into dichloromethane (3 × 100 mL), and the combined organic layers were washed with water (75 mL) and brine (100 mL) prior to drying and solvent removal. The resultant yellowish solid was recrystallized from ethyl acetate to give 419 mg (76.6%) of **32** as colorless crystals: mp 303–306 °C dec; ν_{max} (KBr) 1715, 1173 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.80 (m, 2 H), 4.21–3.60 (m, 2 H), 3.41–2.49 (m, 8 H), 2.45–1.60 (m, 8 H), 1.45 (s, 6 H); ^{13}C NMR ($CDCl_3$) 176.59, 83.25, 64.31, 63.23, 54.39, 50.39, 47.75, 46.89, 39.39, 37.33, 26.76 ppm; *m/e* 354.1831, obsd 354.1836.

Anal. Calcd for $C_{22}H_{26}O_4$: C, 74.56; H, 7.3. Found: C, 74.43; H, 7.49.

Acid-Catalyzed Isomerization of 32. A solution of **32** (80 mg) in concentrated sulfuric acid (3 mL) was heated at 78–80 °C for 20 h. The reaction mixture was poured into water (20 mL) and extracted with chloroform (3 × 25 mL). The combined organic layers were washed with water (2 × 20 mL), dried, and evaporated. The residual solid (58 mg) was recrystallized from ethyl acetate to give **34b** as colorless needles: mp 207–209 °C; ν_{max} (KBr) 1760 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.90–3.26 (m, 2 H), 3.08–2.36 (br m, 4 H), 2.4–1.55 (br m, 14 H), 1.36 (s, 6 H); ^{13}C NMR ($CDCl_3$) 179.40, 104.99, 65.34, 65.18, 61.29, 61.13, 54.66, 40.47, 34.91, 26.06, 25.90 ppm; *m/e* calcd 354.1831, obsd 354.1836.

Anal. Calcd for $C_{22}H_{26}O_4$: C, 74.56; H, 7.39. Found: C, 74.42; H, 7.45.

Bromination of 22 with *N*-Bromosuccinimide. Dimethyl 4b,8a-Dibromohexadecahydro-1,5-dioxo-4,8,9-metheno-4*H*-cyclopenta[1,2-*a*:4,3-*a′*]dipentalene-4,10-dicarboxylate (41). A refluxing solution of **22** (100 mg, 0.26 mmol) and *N*-bromosuccinimide (93 mg, 0.522 mmol) in 5 mL of carbon tetrachloride was irradiated with a UV-rich tungsten lamp. After 15 min, the reaction mixture was cooled to room temperature, and the precipitated succinimide was separated by filtration. Removal of the solvent in vacuo yielded a solid which when recrystallized from ethanol afforded 70 mg (50%) of **41** as long white needles: mp 114–140 °C dec; ν_{max} (KBr) 1745, 1730 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.60 (s, 6 H), 3.50–3.00 (br m, 8 H), 3.54–3.10 (m, 4 H), 2.30–1.70 (m, 4 H); mass spectrum, *m/e* 544, 542, 540 (1:2:1).

Anal. Calcd for $C_{22}H_{22}Br_2O_6$: C, 48.73; H, 4.09; Br, 29.47. Found: C, 48.23; H, 4.15; Br, 29.49.

Bromination of 22 with 2,4,4,6-Tetrabromocyclohexa-2,5-dienone. Dimethyl 2α,4b,6α-Tribromohexadecahydro-

1,5-dioxo-4,8,9-metheno-4*H*-cyclopenta[1,2-*a*:4,3-*a*']dipentalene-4,10-dicarboxylate (42a). A solution of **22** (100 mg, 0.26 mmol) and 2,4,4,6-tetrabromocyclohexa-2,5-dienone (203 mg, 0.496 mmol) in 10 mL of dichloromethane cooled to −20 °C was treated dropwise with a saturated solution of hydrogen bromide in dichloromethane (2–3 mL). Upon being warmed to room temperature, the homogeneous solution was extracted with 5% aqueous sodium carbonate solution (4 × 10 mL) and brine (1 × 10 mL) before drying. Removal of the solvent afforded an oil which when permitted to stand overnight in ethanol yielded 50 mg of tribromide **42a**: mp 135–150 °C dec; ν_{max} (KBr) 1750, 1744, 1724 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.34 (m, 2 H), 3.60 (d, separation 0.4 Hz, 6 H), 3.50–1.90 (br m, 13 H).

Anal. Calcd for $C_{22}H_{21}Br_3O_6$: C, 42.54; H, 3.41. Found: C, 42.84; H, 3.58.

The ethanolic filtrate was concentrated, and the resulting oil was dissolved in ether. When the mixture was allowed to stand, small needles of dibromide **40** (50 mg) were formed: mp 144–154 °C dec; ^{1}H NMR ($CDCl_3$) δ 4.35 (m, 1 H), 3.60 (s, 6 H), 3.50–1.84 (br m, 15 H); mass spectrum, *m/e* 544, 542, 540 (1:2:1).

Bromination of 22 with Pyridinium Hydrobromide Perbromide. Dimethyl 2α,4b,6α,9α-Tetrabromohexadecahydro-1,5-dioxo-4,8,9-metheno-4*H*-cyclopenta[1,2-*a*:4,3-*a*']dipentalene-4,10-dicarboxylate (42b). To a solution of **22** (100 mg, 0.26 mmol) in 50 mL of dichloromethane was added 350 mg (1.09 mmol) of pyridinium hydrobromide perbromide at 0 °C. After 1 h, the yellowish solution was washed with an aqueous sodium bicarbonate–sodium thiosulfate solution. The aqueous layer was further extracted with dichloromethane (3 × 2 mL). The combined organic layers were dried and concentrated to yield, after drying at 0.1 mm, 180 mg (98.5%) of tetrabromide **42b**. Recrystallization from acetonitrile afforded white crystals: dec pt 150 °C; ν_{max} (KBr) 1758, 1730, 1294 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.41 (d, J = 6 Hz, 2 H), 3.59 (s, 6 H), 3.57–3.02 (br m, 8 H), 2.72–2.02 (m, 4 H); ^{13}C NMR ($CDCl_3$) 204.22 (s), 170.68 (s), 67.84 (d), 63.23 (s), 61.99 (d), 57.96 (s), 53.54 (d), 52.50 (t), 48.86 (d), 46.52 (d), 34.62 (t) ppm; mass spectrum, *m/e* 696, 698, 700, 702, 704 (1:4:6:4:1).

Anal. Calcd for $C_{22}H_{20}Br_4O_6$: C, 37.75; H, 2.88. Found: C, 37.92; H, 3.05.

Hexadecahydro-7β-hydroxy-4*H*-4a,8-methano-1*H*-3-oxacyclopenta[*cd*]pentaleno[1',2',3':3,4]pentaleno[2,1,6-*hia*]indene-4,9-dione (43). A heterogeneous mixture of 50% sodium hydride dispersion (52 mg, 1.08 mmol) and dilactone **8** (226 mg, 0.693 mmol) in 18 mL of dry toluene was heated at reflux for 12 h under nitrogen. The resulting yellow solution was quenched at 0 °C with a 10% aqueous ammonium chloride solution (10 mL). Upon further dilution with 50 mL of water, the reaction mixture was extracted with dichloromethane (4 × 20 mL). The combined extracts were washed with brine and dried. Removal of the solvent yielded a white solid which upon recrystallization from ethyl acetate–hexane afforded pure **43** (180 mg, 80%), mp 193–194 °C; ν_{max} (KBr) 3530, 1755, 1700 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.40–4.97 (m, 1 H), 4.20 (m, 1 H), 3.57–2.66 (m, 11 H), 2.54 (br s, 1 H, OH), 2.41–1.98, (m, 2 H), 1.98–1.50 (m, 6 H); ^{13}C NMR ($CDCl_3$) 211.88 (s), 170.12 (s), 87.24 (d), 73.59 (d), 66.20 (s), 58.43, 58.14, 57.54, 56.49, 55.38 (2 C), 53.14, 50.31, 49.23, 47.80, 45.89, 41.03, 39.09, 25.30, 23.52 ppm; *m/e* calcd 326.1518, obsd 326.1524.

Anal. Calcd for $C_{20}H_{22}O_4$: C, 73.60; H, 6.79. Found: C, 73.90; H, 6.79.

Methyl Hexadecahydro-1,4,8,5-(epoxymethynooxy)dipentaleno[1,2,3-*cd*:1',2',3'-*gh*]pentalene-4(1*H*)-carboxylate (44). A. Treatment of Dilactone 8 with Saturated Methanolic Hydrogen Chloride. To a saturated methanolic hydrogen chloride solution (24 mL) cooled to 0 °C was added dilactone **8** (400 mg, 1.22 mmol) under nitrogen. After stirring for 29 h at room temperature, the acidic reaction mixture was slowly added to 200 mL of water and then extracted with dichloromethane (5 × 40 mL). The combined extracts were washed with water (2 × 100 mL) and brine (1 × 100 mL) before drying. Removal of the solvent in vacuo afforded a mixture (450 mg) of **44** and a minor product. Recrystallization of this crude product from ether yielded 356 mg (86%) of pure **44**: mp 168.5–169.5 °C; ν_{max} (KBr) 1739, 1710, 1082 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.38–4.09 (br s, 2 H), 3.71 (s, 3 H), 3.18–1.17 (br m, 19 H); ^{13}C NMR ($CDCl_3$) 174.62 (s), 100.21 (s), 74.58 (d), 74.24 (d), 58.90 (d), 55.70 (s), 54.74 (d), 54.46 (d), 54.12, 52.38, 51.71, 48.28, 47.94, 46.31 (2 C), 45.75, 44.79, 38.05 (2 C), 24.05, 22.82 ppm; *m/e* calcd 340.1674, obsd 340.1680.

Anal. Calcd for $C_{21}H_{24}O_4$: C, 74.09; H, 7.11. Found: C, 74.18; H, 7.25.

B. Treatment of 43 with Saturated Methanolic Hydrogen Chloride. A solution of **43** (78 mg, 0.239 mmol) in 10 mL of dry methanol was saturated with anhydrous hydrogen chloride gas at 0 °C. The resultant solution was permitted to stir at room temperature for 20 h at which point it was diluted with 100 mL of water and extracted with dichloromethane (4 × 20 mL). The combined extracts were washed with water (2 × 40 mL) and brine (1×) prior to drying. After removal of the solvent, the crude product was purified by preparative TLC on silica gel (ether elution). Extraction of the band at R_f 0.5 with ether–methanol afforded 31 mg (38%) of **44**. The minor product (R_f 0.13, 8 mg) was recovered from the plate with dichloromethane–methanol and not further characterized.

C. Reaction of Dilactone 8 with Trimethyloxonium Tetrafluoroborate. A heterogeneous mixture of trimethyloxonium tetrafluoroborate (150 mg, 1.015 mmol) and **8** (100 mg, 0.306 mmol) in 5 mL of dry dichloromethane was stirred at room temperature for 20 h.

To a cold (0 °C) sodium methoxide solution (prepared by dissolving 34 mg of sodium (1.52 mmol) in 2 mL of dry methanol) was added the oxonium slurry in one portion. After 45 min, 10 mL of a 10% aqueous sodium carbonate solution was added. The reaction mixture was extracted with dichloromethane. After the extract was dried, removal of the solvent afforded 77 mg (74%) of slightly impure **44**. Purification was accomplished by recrystallization from ether. The minor component has not been identified: *m/e* calcd 354.1831, obsd 354.1836 ($C_{22}H_{26}O_4$).

Methyl 1α,5α-Dibromohexadecahydro-9-oxo-4,8-methanodipentaleno[1,2,3-*cd*:1',2',3'-*gh*]pentaleno-4(1*H*)-carboxylate (45). A. Treatment of Dilactone 8 with Triphenylphosphine Dibromide. To a solution of triphenylphosphine (1.13 g, 4.302 mmol) in 24 mL of dry, degassed acetonitrile was added dropwise 220 μL of bromine (4.3 mmol) at room temperature under nitrogen. To this bright yellow solution was added **8** (650 mg, 1.99 mmol) in one portion prior to heating at the reflux temperature for 24 h. The reddish, homogeneous solution was treated with 520 μL of pyridine (6.45 mmol) and 25 mL of dry methanol. After the resulting solution had been refluxed for 3.5 h, the solvent was removed under reduced pressure to yield a slightly brownish solid (3.12 g).

The crude product was chromatographed on silica gel (140 g). Upon elution with 30% ether–hexane, 0.62 g (64.4%) of **45** was isolated. Recrystallization from ethyl acetate–hexane afforded a highly crystalline, white solid: mp 152.5–153.5 °C; ν_{max} (KBr) 1751, 1738, 1724, 1704 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.74–3.83 (br m, 2 H), 3.77 (s, 3 H), 3.54–1.22 (br m, 19 H); ^{13}C NMR ($CDCl_3$) 208.34 (s), 170.24 (s), 66.66 (s), 59.80 (d), 58.28, 58.11, 57.89, 57.44, 56.03, 55.70, 54.91, 53.45, 52.44, 48.22 (d), 48.11 (d), 46.37 (2 C, d), 43.39 (2 C, t), 26.36 (t), 25.85 (t) ppm; *m/e* calcd 482.0093, obsd 482.0099.

Anal. Calcd for $C_{21}H_{24}Br_2O_3$: C, 52.08, H, 5.00; Br, 33.01. Found: C, 52.32; H, 5.06; Br, 32.62.

B. Treatment of 43 with Triphenylphosphine Dibromide. To a solution of triphenylphosphine (139 mg, 0.529 mmol) in 3 mL of dry, degassed acetonitrile was added bromine (27 μL, 0.529 mmol) dropwise at room temperature under nitrogen. To this orange solution was added **43** (75 mg, 0.23 mmol) in one portion. The resulting solution was heated at the reflux temperature for 21 h. After the addition of 3 mL of dry methanol to the brownish reaction mixture, heating was continued for an additional 3 h. The contents were diluted with 35 mL of water and extracted with dichloromethane (4 × 20 mL). The combined extracts were washed with dilute aqueous sodium bicarbonate solution (1×), water (1×), and brine (1×) prior to drying and solvent evaporation. The resultant brownish solid was purified by preparative TLC on silica gel (40% ether–hexane elution) and 70 mg (63%) of dibromo keto ester **45** (R_f 0.40) was obtained.

Eicosahydro-3,7-dioxadicyclopenta[*cd*,*c'd'*]pentaleno-[2,1,6-*hia*:5,4,3-*h'i'a'*]diindene-4α,8α-diol (46). To a solution of **8** (100 mg, 0.306 mmol) in 20 mL of dry tetrahydrofuran was added lithium aluminum hydride (33 mg, 0.870 mmol) at 0 °C under nitrogen. After 30 min at 0 °C, the reaction mixture was stirred for 2 h at room temperature. Excess hydride was destroyed

by adding slowly 20 mL of a 10% aqueous ammonium chloride solution. Following filtration through Celite, the resulting layers were separated, and the aqueous layer was extracted with dichloromethane (2 × 20 mL). The combined extracts were washed with water (1 × 20 mL), dried and evaporated. A solid was obtained which when recrystallized from acetone afforded 48 mg (47.5%) of **46**: mp 188–189.5 °C; ν_{max} (KBr) 3370, 1060, 997, 951 cm^{-1}; ^{1}H NMR ($CDCl_3$, 90 MHz) δ 6.05 (br s, 2 H), 4.30–4.12 (m, 2 H), 3.23–2.90 (m, 4 H), 2.82–2.15 (br m, 6 H), 2.04–1.12 (br m, 12 H); mass spectrum, m/e 312 (P − H_2O).

Anal. Calcd for $C_{20}H_{28}O_4$: C, 72.73; H, 7.88. Found: C, 72.43; H, 7.89.

Reaction of Dilactone 7 with Trimethyloxonium Tetrafluoroborate. Formation of 47. A heterogeneous mixture of dilactone **7** (110 mg, 0.34 mmol) and trimethyloxonium tetrafluoroborate (104 mg, 0.70 mmol) in 10 mL of dry dichloromethane was stirred under nitrogen for 17 h. The reaction mixture was treated with aqueous sodium bicarbonate solution and extracted with dichloromethane. The combined extracts were washed with water and dried. Removal of the solvent provided a clear oil which was chromatographed on silica gel (40% ether–hexane elution). Crystalline **47** (97 mg, 83.5%) was obtained which was recrystallized from ether–hexane: mp 159–160 °C; ν_{max} (KBr) 3061, 1746, 1113, 1074 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.66 (m, 1 H), 5.39 (m, 1 H), 4.90 (m, 1 H), 3.96 (m, 0.5 H), 3.60 (br s, 3.5 H), 3.28–2.42 (br m, 10 H), 2.35–1.19 (br m, 5 H); m/e calcd 338.1518, obsd 338.1522.

Catalytic Hydrogenation of the 47/48 Mixture. A 90-mg sample of unpurified **47/48** mixture in 10 mL of ethyl acetate containing 50 mg of 10% palladium on carbon was hydrogenated at atmospheric pressure, filtered through Celite, and freed of solvent. There was isolated 85 mg of **50**: mp 172–174 °C (from ethyl acetate); ν_{max} (KBr) 1742 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.8 (m, 1 H), 3.6 (s, 3 H), 2.8–1.0 (br m, 20 H); ^{13}C NMR ($CDCl_3$) 174.32, 172.44, 84.98, 64.96, 62.64, 60.97, 58.97, 53.58, 52.70, 52.34, 51.42, 50.55, 45.48, 43.54, 43.16, 42.68, 37.66, 29.03, 28.92, 26.22, 23.36 ppm; m/e calcd 340.1674, obsd 340.1680.

Anal. Calcd for $C_{21}H_{24}O_4$: C, 74.09; H, 7.11. Found: C, 73.73; H, 7.06.

Methyl 8α-Bromotetradecahydro-5-oxo-5*H*-1,10,5α,9-ethanediylidene-1*H*-cyclopenta[*b*]cyclopenta[5,6]pentaleno[2,1-*d*]pyran-12-carboxylate (51). A. Treatment of Dilactone 7 with Methanolic Hydrogen Bromide. To 80 mL of saturated methanolic hydrogen bromide solution cooled to 0 °C was added **7** (400 mg, 1.23 mmol) under nitrogen. After being stirred at 0 °C for 1.5 h, the solution was slowly poured into 100 mL of water and extracted with dichloromethane (3 × 100 mL). The organic extracts were washed with water (1 × 100 mL) and brine (1 × 100 mL) and dried, and the solvent was removed. There remained 470 mg of a white foam, which on recrystallization from ether–hexane provided 230 mg of pure **51**: mp 135–136 °C; ν_{max} (KBr) 1735, 1285, 1110, 1070 cm^{-1}; ^{1}H NMR ($CDCl_3$, 100 MHz) δ 4.95 (m, 1 H), 4.12 (m, 1 H), 3.74 (s, 3 H), 3.2–1.3 (m, 18 H); ^{13}C NMR ($CDCl_3$) 174.16, 171.81, 85.09, 62.51, 62.15, 60.48, 58.70, 58.59, 54.84, 53.17, 52.04, 51.85, 51.04, 50.28, 45.32, 42.57, 42.49, 40.95, 37.71, 26.63, 23.31 ppm; m/e calcd 418.0781, obsd 418.0788.

Anal. Calcd for $C_{21}H_{23}BrO_4$: C, 60.15; H, 5.53; Br, 19.06. Found: C, 60.28; H, 5.58; Br, 18.88.

The mother liquor from the recrystallization was chromatographed on silica gel (50% ether–hexane elution). Initially, 50 mg of a clear oil, which appeared to be a mixture of bromo and olefinic products, was obtained. Subsequently, an additional 156 mg of **51** (total yield 75%) was recovered from the column.

B. Esterification of Anhydride 53. A suspension of anhydride **53** (50 mg, 0.107 mmol) in 5 mL of dry methanol containing a catalytic amount of *p*-toluenesulfonic acid was heated at the reflux temperature for 96 h. The homogeneous solution was treated with an ethereal solution of excess diazomethane. After removal of the solvent, the reaction mixture was dissolved in 50 mL of dichloromethane and washed with water (1×) and brine (1×) prior to drying

The crude product was purified by preparative TLC on silica gel (ether elution). An unidentified mixture (35 mg) was obtained at an R_f value of 0.8–1.0. The bromo ester **51** (29 mg, 65%) was isolated at an R_f value of 0.5.

Dimethyl 1α,5α-Dichlorohexadecahydro-4,8,9-metheno-4*H*-cyclopenta[1,2-*a*:4,3-*a*']dipentalene-4,10-dicarboxylate (52). To a saturated methanolic hydrogen chloride solution (24 mL) cooled to 0 °C was added **7** (400 mg, 1.23 mmol) under nitrogen. After being stirred for 10–26 h at room temperature, the acidic methanol solution was added to 200 mL of water and extracted with dichloromethane (5 × 40 mL). The combined extracts were washed with water (2 × 100 mL) and brine (1 × 100 mL) prior to drying. Concentration of the solution produced 550 mg of a yellow oil which was chromatographed on silica gel (100 g). Dichloro diester **52** (325 mg, 62%) was collected with 10% ether–hexane. Recrystallization from hexane afforded high-density, white crystals: mp 151.5–153 °C; ν_{max} (KBr) 1755, 1732, 1254, 1104 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.50–4.08 (br m, 2 H), 3.73 (s, 6 H), 3.10–1.36 (br m, 18 H); ^{13}C NMR ($CDCl_3$) 172.60 (s), 63.61 (d), 61.67 (d), 59.97 (d), 56.14 (s), 53.74, 52.07, 51.53, 43.00, 40.57, 23.39 (t) ppm; m/e calcd 424.1208, obsd 424.1216.

Anal. Calcd for $C_{22}H_{26}Cl_2O_4$: C, 62.12; H, 6.16; Cl, 16.67. Found: C, 62.22; H, 6.19; Cl, 16.74.

With 70% ether–hexane, 122 mg of a complex mixture of olefinic products was obtained.

1α,5α-Dibromohexadecahydro-4,8,9-metheno-4*H*-cyclopenta[1,2-*a*:4,3-*a*']dipentalene-4,10-dicarboxylic Anhydride (53). A. Treatment of Dilactone 7 with Triphenylphosphine Dibromide. To a solution of triphenylphosphine (850 mg, 3.2 mmol) in 10 mL of dry, degassed acetonitrile was added 520 mg (3.2 mmol) of bromine at room temperature. The mixture was cooled to 0 °C where a solution of **7** (942 mg, 2.92 mmol) in 10 mL of dry acetonitrile was added slowly. This homogeneous solution was heated at the reflux temperature for 72 h under nitrogen. Upon being cooled, the solvent was evaporated and replaced by dry methanol. The heterogeneous solution was cooled to −20 °C where the precipitated **53** (200 mg) was isolated by filtration. This impure anhydride was recrystallized from acetonitrile (or ethyl acetate) to yield pure product: dec pt 230 °C; ν_{max} (KBr) 1850, 1840, 1770, 1262, 899, 878, 762, 749 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.40–3.84 (br m, 2 H), 2.89 (br m, 10 H), 2.69–1.17 (br m, 8 H); ^{13}C NMR ($CDCl_3$) 172.62, 61.86, 59.54, 58.13, 57.81, 54.79, 46.91, 42.76, 42.16, 25.71 ppm; m/e calcd 465.9780, obsd 465.9787.

Anal. Calcd for $C_{20}H_{20}Br_2O_3$: C, 51.31; H, 4.31; Br, 34.14. Found: C, 51.50; H, 4.50; Br, 33.94.

The filtrate afforded a very complex mixture of products which could not be identified even after column chromatography on silica gel.

B. Conversion of 51 into 53 with Triphenylphosphine Dibromide. To a solution of triphenylphosphine (66 mg, 0.252 mmol) in 3 mL of dry, degassed acetonitrile was added 14 μL (0.274 mmol) of bromine at 0 °C. To this yellow solution was added 50 mg (0.12 mmol) of **51**, and the resulting solution was heated at the reflux temperature for 18 h under nitrogen. Dry methanol (0.5 mL) was added, and the solution was heated again for 0.5 h. The reaction mixture was diluted with 50 mL of water and extracted with dichloromethane (3 × 50 mL). The combined extracts were washed with water (50 mL) and brine (50 mL) before drying and solvent evaporation. There resulted a brown solid which was recrystallized from dichloromethane–hexane to give 23 mg (41%) of anhydride **53**.

Dimethyl Hexadecahydro-4,8,9-metheno-4*H*-cyclopenta[1,2-*a*:4,3-*a*']dipentalene-4,10-dicarboxylate (57). A. Reduction of 52 with Tri-*n*-butyltin Hydride. To a heated solution of **52** (111 mg, 0.261 mmol) in 1 mL of dry benzene was added a solution of tri-*n*-butyltin hydride (174 mg, 0.60 mmol) and azobis(isobutyronitrile) (3 mg) in 1 mL of dry benzene very slowly over a 9-h period under nitrogen. After being heated for an additional 15.5 h, the reaction mixture was concentrated to yield a clear oil which was repeatedly subjected to preparative TLC on silica gel (20% ether–hexane elution). This afforded 40 mg (43%) of pure diester **57** (R_f 0.43), which was recrystallized from hexane: mp 122–122.5 °C; ν_{max} (KBr) 1757, 1738 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.66 (s, 6 H), 2.80–2.23 (br m, 9 H), 2.17–1.78 (br m, 2 H), 1.75–1.26 (br m, 11 H); m/e 356.1987, obsd 356.1991.

Anal. Calcd for $C_{22}H_{28}O_4$: C, 74.13; H, 7.92. Found: C, 74.03; H, 7.96.

B. Attempted Cyclization of 52 with Activated Magnesium. Reductive Formation of 57. Dry tetrahydrofuran (5 mL) was distilled from lithium aluminum hydride directly into a 25-mL three-necked flask (previously flame dried) which contained 51.4 mg (2.116 mg-atom) of sublimed magnesium under nitrogen.

Ethylene bromide (182 μL, 2.116 mmol) was added, and the mixture was heated to reflux for 1.5 h. To the resulting solution was added 156 mg (3.99 mmol) of potassium metal, and the mixture was heated at the reflux temperature for 4 h. To the resulting grayish black precipitate was added dichloro diester **52** (75 mg, 0.176 mmol) in one portion. The mixture was then heated at reflux for 15.5 h. The reaction mixture was slowly poured into a cold (0 °C) saturated aqueous ammonium chloride solution. Following the addition of 50 mL of water, the aqueous mixture was extracted with dichloromethane (4 × 30 mL). The combined extracts were washed with water (1 × 30 mL) and brine (1 × 30 mL) before drying. Removal of solvent afforded 86 mg of a yellow solid which was subjected to preparative TLC on silica gel (40% ether–hexane elution). The only identifiable material isolated (R_f 0.4) was **57** (22 mg, 35%), slightly contaminated with the monochloride reduction product.

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Registry No. 7, 61223-90-3; **8**, 61223-91-4; **9a**, 53282-97-6; **9b**, 61206-25-5; **10b**, 61231-15-0; **12**, 61206-31-3; **13**, 61206-28-8; **14**, 61206-26-6; **15**, 61206-27-7; **16**, 61231-13-8; **17**, 61231-14-9; **18**, 71341-97-4; **19**, 71341-98-5; **20**, 71341-99-6; **21**, 71425-92-8; **22**, 61206-30-2; **23**, 71393-20-9; **27**, 71342-00-2; **28**, 71392-35-3; **29**, 71342-01-3; **30**, 71369-94-3; **32**, 71425-98-4; **34a**, 71342-02-4; **34b**, 71369-92-1; **40**, 71342-03-5; **41**, 71342-04-6; **42a**, 71342-53-5; **42b**, 71342-54-6; **43**, 71342-55-7; **44**, 71342-56-8; **45**, 71342-57-9; **46**, 71342-58-0; **47**, 71393-21-0; **48**, 71393-22-1; **50**, 71342-48-8; **51**, 71342-49-9; **52**, 71342-50-2; **53**, 71342-51-3; **57**, 71342-52-4; chromic acid, 13530-68-2; dimethyl decahydro-1,5-dihydroxy-3,4,7-metheno-7*H*-cyclopenta[*a*]pentalene-7,8-dicarboxylate, 71342-59-1; dimethyl decahydro-1,6-dihydroxy-3,4,7-metheno-7*H*-cyclopenta[*a*]pentalene-7,8-dicarboxylate, 71342-60-4; cyclopropyldiphenylsulfonium tetrafluoroborate, 33462-81-6; allyltrimethylsilane, 762-72-1; methyl iodide, 74-88-4.

Topologically Spherical Molecules. Rearrangement Reactions of Functionalized C_2-Symmetric Hexaquinane Systems and Synthesis of (C_2)-Dioxa-C_{20}-octaquinane, a Heterocyclic Trisecododecahedrane

Leo A. Paquette,* William J. Begley,[1a] Douglas Balogh, Matthew J. Wyvratt,[1b] and David Bremner

Evans Chemical Laboratories, The Ohio State University, Columbus, Ohio 43210

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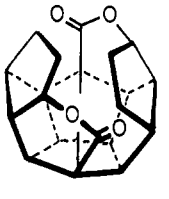
A scheme is described which culminates in an efficient synthesis of (C_2)-dioxa-C_{20}-octaquinane (**3**). Because all of the intermediates employed show a marked tendency to undergo symmetry-destroying transannular reactions, the strategy involved uncovering those transformations which would not trigger these unwanted processes. Lithium aluminum hydride reduction of dilactone **1** or diketo diester **6** gave dilactol **5a**, dissolution of which in thionyl chloride provided the highly reactive α-chloro ether **9**. This substance is particularly prone to 1,2 Wagner–Meerwein shift of its internal σ bond since considerable nonbonded steric strain is thereby relieved. Nevertheless, **9** did undergo successful 1,4-reduction in liquid ammonia with generation of bis(dihydropyran) **15**. Both **15** and its doubly cyclopropanated congener **35** are shown to be particularly prone to transannular bonding. In contrast, the derived diepoxide **39** experienced ring contraction under comparable electrophilic conditions and provided dialdehyde **41**. Decarbonylation of the latter intermediate under rather specific conditions afforded **3**.

Molecules whose carbon skeletons take on a high degree of convex polyhedral topology are of considerable interest, though they remain little-studied at the present time. The preceding paper described a ready solution to the problem of incorporating 20 carbon atoms into six fused five-membered rings with strict control of all-cis stereochemistry at the ten ring junctions and maintenance of a C_2 axis of symmetry.[2] Certain features of the chemical reactivity of dilactones **1** and **2** were disclosed, the weight of evidence being sufficient to justify the deployment of new conceptual schemes to arrive ultimately at our target molecule, the pentagonal dodecahedrane.[3] The purpose of the present study was elucidation of synthetic pathways which would ultimately permit efficient transformation of



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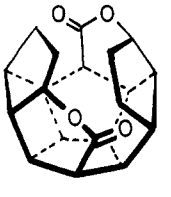

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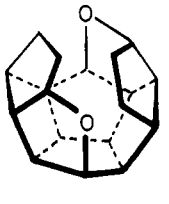

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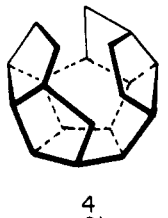

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existing hexaquinanes such as **1** and **2** into higher order polyquinanes.[4] Such new studies are detailed, and the

(1) (a) Postdoctoral Fellow of the Science Research Council, 1975–1977. (b) National Science Foundation Graduate Fellow, 1972–1975.

(2) Paquette, L. A.; Wyvratt, M. J.; Schallner, O.; Muthard, J. L.; Begley, W. J.; Blankenship, R. M.; Balogh, D., previous paper in this issue.

(3) For an earlier synopsis of a portion of this study, see: Paquette, L. A. *Pure Appl. Chem.* **1978**, *50*, 1291.

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