Convenient Synthesis of the 1,4-Bishomo-6-secoheptaprismane Ring System[1]

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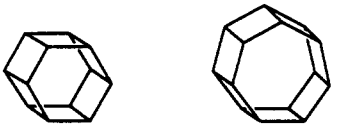
The facile synthesis of **13**, a highly functionalized 1,4-bishomo-6-secoheptaprismane, is reported in 45% overall yield, starting with the Diels-Alder adduct of 5,5-dimethoxy-1,2,3,4-tetrachlorocyclopentadiene and *p*-benzoquinone. Initial attempts to functionalize **13** for subsequent transformation to hexaprismane (**1**) are summarized.

Introduction

The [*n*]prismanes are a novel class of $(CH)_n$ polyhedranes whose architectural structure has attracted the attention of chemists for many years. The synthetic conquest of [3]prismane (triprismane),[2] [4]prismane (cubane),[3] and [5]prismane (pentaprismane)[4] has required diverse synthetic strategies and has shifted the focus to higher order prismanes. While considerable experimental[5] and theoretical[6] effort has been expended on hexaprismane (**1**), only recently has significant progress been reported.[7] The intriguing structural characteristics as well as the expected novel reactivity have prompted our group to undertake the synthesis of this fascinating hydrocarbon. Herein, we describe the synthesis of an advanced intermediate that may serve as the cornerstone in the development of a strategy applicable to the synthesis of hexaprismane (**1**). Moreover, synthetic modifications should also permit the preparation of heptaprismane (**2**).



1 **2**

Any synthesis of hexaprismane (**1**) requires the construction of six four-membered rings, and thus at the outset we recognized the pivotal role that the intramolecular [2 + 2] photocycloaddition would play in our synthetic venture. However, we were familiar with the thermochemical restrictions imposed upon intramolecular photoadditions which have been outlined by Osawa and Mehta,[8] and thus our attention was directed to other transformations.

Ring-contraction protocols, particularly the Favorskii ring contraction,[9] have been a reliable method for the syntheses of strained polycyclic compounds. In fact, the final steps in the preparation of the cubane[3] and pentaprismane[4] skeletons were Favorskii ring contractions. Thus, a prudent synthetic plan for securing hexaprismane (**1**), and higher order prismanes such as heptaprismane (**2**), would rely heavily on the Favorskii ring-contraction while implementing the intramolecular [2 + 2] photocycloaddition judiciously in accordance with the imposed restrictions outlined by Osawa and Mehta.

A retrosynthetic analysis consistent with the previous observations is shown in Scheme I. We planned to prepare hexaprismane (**1**) via 4-fold Favorskii ring-contraction of the substituted 1,4-bishomo-6-secoheptaprismanetetraone bis(dimethyl ketal) **3** which in turn was expected to arise from a 2:1 Diels-Alder reaction of an α-halocyclopentadienone ketal with a *p*-benzoquinone followed by an intramolecular [2 + 2] photocycloaddition. Dione **3** is formally a 1,4-bishomo-6-seco[7]prismane and would serve as an advanced intermediate in our synthesis of heptaprismane (**2**).

Synthesis of Advanced Intermediate 3

With the proposed approach to hexaprismane (**1**) established, the initial synthetic problem was reduced to discovering an appropriate Diels-Alder reaction between an α-halocyclopentadienone ketal with a *p*-benzoquinone derivative which furnishes the endo,syn,endo adduct. Although 2:1 Diels-Alder reactions giving the endo,syn,-endo stereochemistry are very rare, Bratby and Fray reported that heating a mixture of 1,4-cyclohexadiene with 5,5-dimethoxy-1,2,3,4-tetrachlorocyclopentadiene (**4**) gave only in the endo,syn,endo Diels-Alder adduct **5**.[10] Although **5** is not appropriately substituted for transformation to hexaprismane (**1**), we felt that this Diels-Alder reaction, which has often been overlooked in the synthesis

(1) This paper is based on a portion of the Ph.D. Dissertation of M.A.F., University of Pennsylvania, 1991.

(2) Katz, T. J.; Acton, N. *J. Am. Chem. Soc.* **1973**, *95*, 2738-2739.

(3) Eaton, P. E.; Cole, T. W. *J. Am. Chem. Soc.* **1964**, *86*, 3157-3158.

(4) (a) Eaton, P. E.; Or, Y. S.; Branca, S. J.; Shankar, B. K. *Tetrahedron* **1986**, 1621-1631. (b) Eaton, P. E.; Or, Y. S.; Branca, S. J. *J. Am. Chem. Soc.* **1981**, *103*, 2134-2136. (c) Dauben, W. G.; Cunningham, A. F. *J. Org. Chem.* **1983**, *48*, 2842-2847.

(5) (a) Yang, N. C.; Horner, G. *Tetrahedron Lett.* **1986**, *27*, 543-546. (b) Mehta, G.; Srikrishna, M. S.; Nair, T. S.; Cameron, W.; Tacreiter, W. *Indian J. Chem.* **1983**, 621-623. (c) Mehta, G.; Nair, M. S.; Srikrishna, A. *Indian J. Chem.* **1983**, *22B*, 959-963. (d) Eaton, P. E.; Chakraborty, U. R. *J. Am. Chem. Soc.* **1978**, *100*, 3634-3635. (e) Yang, N. C.; Horner, M. G.; Hrnjez, B. J. *J. Am. Chem. Soc.* **1987**, *109*, 3158-3159.

(6) (a) Disch, R. L.; Schulman, J. M. *J. Am. Chem. Soc.* **1988**, *110*, 2102-2105. (b) Dailey, W. P. *Tetrahedron Lett.* **1987**, *28*, 5787-5790. (c) Mehta, G.; Padma, S.; Osawa, E.; Barbiric, D. A.; Mochizuki, Y. *Tetrahedron Lett.* **1987**, *28*, 1295-1298. (d) Osawa, E.; Barbiric, D. A.; Lee, O. S. *J. Chem. Soc., Perkin Trans. 2* **1989**, 1161-1165. (e) Srikrishna, A.; Sunderbabu, G. *J. Org. Chem.* **1987**, *52*, 5037-5039.

(7) (a) Mehta, G.; Padma, S. *J. Am. Chem. Soc.* **1987**, *109*, 2212-2213. (b) Mehta, G.; Padma, S. *J. Am. Chem. Soc.* **1987**, *109*, 7230-7232. (c) Mehta, G. In *Strain and Its Implications in Organic Chemistry*; de Meijere, A., Blechert, S., Eds.; Kluwer Academic Publishers: Boston, 1988; pp 269-281. (d) Mehta, G.; Padma, S. *Tetrahedron* **1991**, *47*, 7783. (e) Mehta, G.; Padma, S. *Tetrahedron* **1991**, *47*, 7807. (f) Mehta, G.; Reddy, S. H. K.; Padma, S. *Tetrahedron* **1991**, *47*, 7821. (g) Mehta, G.; Padma, S.; Venkatesan, K.; Begum, N. S.; Moorthy, J. N. *Indian J. Chem.* **1992**, *31B*, 473.

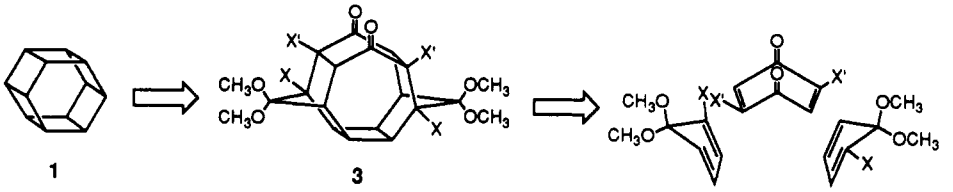
(8) (a) Osawa, E. *J. Org. Chem.* **1977**, *42*, 2621-2626. (b) Reference 5c.

(9) For a review, see: Hunter, D. H.; Stothers, J. B.; Warnoff, E. W. In *Rearrangements in Ground and Excited States*; de Mayo, P., Ed.; Academic Press: New York, 1980; pp 437-461.

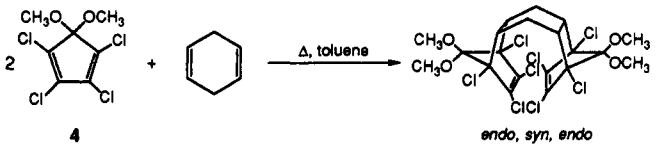
(10) Bratby, D. M.; Fray, G. I. *J. Chem. Soc., Perkin Trans. 1* **1972**, 195-199.

0022-3263/93/1958-1501$04.00/0

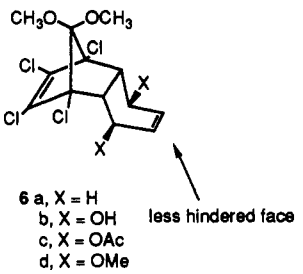
Scheme I



of strained polycycles,[11] would form the basis of our approach to **3** and ultimately to hexaprismane (**1**).



Bratby and Fray rationalized the origin of this rare and remarkable stereoselectivity by assuming that the initially formed 1:1 Diels–Alder adduct **6a** was in a nonplanar boat-type conformation. Molecular models suggested that the exo face of the double bond was more hindered than the endo face so that addition of a second equivalent of 5,5-dimethoxy-1,2,3,4-tetrachlorocyclopentadiene (**4**) would come from the endo face and give the endo,syn,endo adduct. We speculated that the analogous exo,exo dihy-



droxy-substituted cyclohexene **6b** would also possess an endo face which is less sterically hindered and would furnish the desired endo,syn,endo adduct upon reaction with ketal **4**. Therefore, we embarked on a synthesis of the *exo,exo*-cyclohexenediol **6b**.

We started our synthesis (Scheme II) with the known Diels–Alder adduct **7**, readily prepared in 73% from ketal **4** and *p*-benzoquinone.[12] Cerium-mediated borohydride reduction of **7**, as described by Marchand,[13] furnished the endo,endo diol **8a**. Conversion of **8a** to diene **9** followed the literature method[14] with one notable exception. Thus, treatment of the crude diol with methanesulfonyl chloride and triethylamine in CH_2Cl_2 afforded the known dimesylate **8b** in 90% yield for the two steps.[14] When the dimesylate was treated with sodium iodide using refluxing 2-butanone instead of HMPA,[14] diene **9** was obtained in 81% yield. This simple change in solvent now allows hundred-gram lots of **9** to be prepared routinely in 2 days from **7** (Scheme II).

The desired exo,exo stereochemistry of the diol was secured by adding singlet oxygen[15] to the exo face of diene **9**. Reduction of the crude endoperoxide with zinc dust in acetic acid furnished the target exo,exo diol **6b** in 90% yield from diene **9**. As we had hoped, diol **6b** cleanly underwent Diels–Alder reaction with ketal **4** to furnish the highly sought after endo,syn,endo adduct **10** in nearly quantitative yield. NMR analysis of the crude reaction mixture revealed that none of the other three possible isomers were present!

With a convenient preparation of **10** in hand, the synthesis of advanced intermediate **3** still required execution of the intramolecular [2 + 2] photocycloaddition. Sensitized irradiation of **10** under a variety of photochemical conditions yielded only recovered starting material while direct irradiation through quartz produced polymeric material. Initially, we attributed the failure of **10** to undergo cycloaddition to a steric effect caused by having the chlorine atoms present on the reacting double bonds and reasoned that reductive removal of the chlorine atoms would alleviate this problem. Accordingly, addition of a THF solution of diol **10** to a solution of sodium metal in ammonia cooled to −78 °C furnished a 90% yield of the dechlorinated diol **11**. However, irradiation of the dechlorinated diol **11** once again afforded only unreacted starting material.[16]

During our photochemical investigations of the aforementioned dienes, a report by Mehta and Padma offered a possible solution to our impediment. In their synthesis of bishomohexaprismane,[7b,e] Mehta and co-workers successfully carried out the [2 + 2] photocycloaddition of **14** to **15** in 60% yield. The success of this photoaddition suggested to us that we should have ketones, or at least sp^2 centers, located on the cyclohexane ring, for aside from the ketals on the methano bridges, there are no structural differences in the two substrates.

Numerous attempts to oxidize diol **10** were met with failure. This unreactivity is surely due to the extremely hindered nature of the hydroxyl groups of **10**. Molecular mechanics calculations revealed that the hydroxyl oxygen and the bridgehead chlorine atoms of **10** were within van der Waals distance of one another, effectively preventing complex formation and ultimately oxidation. Also consistent with this steric argument was the fact that neither the diacetate (**6c**) nor dimethoxy derivative (**6d**) of diol **6a** would undergo the Diels–Alder reaction with ketal **4**.

Jones oxidation of the dechlorinated diol **11** provided an 85% yield of the diketone **12**, which upon irradiation in 10% acetone/benzene furnished a quantitative yield of the coveted key intermediate **13** (Scheme II). Single-

(11) Srikrishna and Sunderbabu have used this adduct in an attempted secoheptaprismane synthesis. See ref 6e.

(12) Marchand, A. P.; Chou, T.-C. *J. Chem. Soc., Perkin Trans. 1* **1973**, 1948–1949.

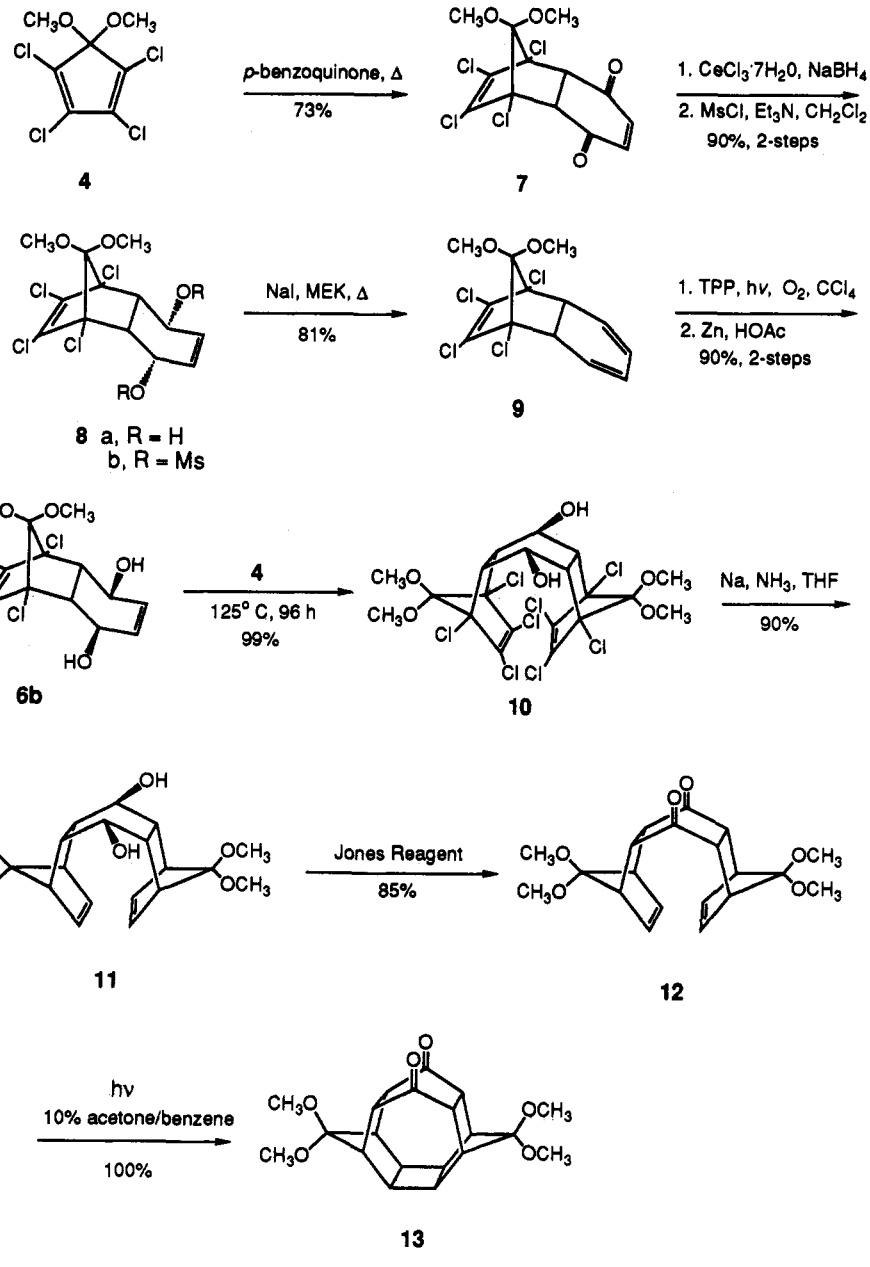
(13) Marchand, A. P.; La Roe, W. D.; Sharma, G. V. M.; Suresh, C. S.; Reddy, D. S. *J. Org. Chem.* **1986**, *51*, 1622–1625.

(14) Chou, T.-C.; Chiou, J. H. *J. Chin. Chem. Soc. (Tapei)* **1986**, *33* (3), 227–234.

(15) *Singlet Oxygen*; Wasserman, H. H., Murray, R. W., Eds.; Academic Press: New York, 1979.

(16) Compound **5** and the corresponding dechlorinated derivative also failed to undergo photochemical [2 + 2] addition.

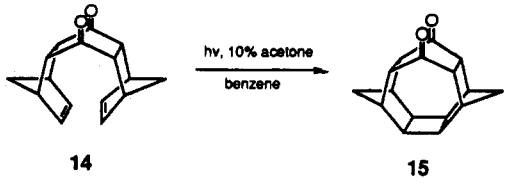
Scheme II



crystal X-ray analysis unambiguously established the structure of **13**.[17]

Attempts To Further Functionalize Intermediate 13

With an efficient synthesis of **13** in hand, there remained the task of bridgehead functionalization in anticipation of ensuing Favorskii ring contractions. To functionalize at the α-carbonyl position, we hoped to rely on the radical bromination methodology developed by Mehta and Padma



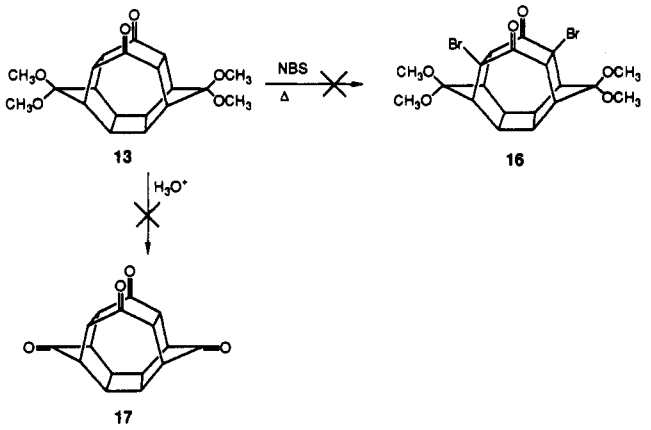
in their synthesis of bishomohexaprismane.[7b,e] They found that the 1,4-bridgehead positions of **15** could be brominated using NBS under radical conditions.

However, when we attempted the analogous radical bromination of **13** for the preparation of **16**, only unreacted starting material was obtained. We attributed this failure to a steric effect caused by the proximity of the methano ketals and reasoned that tetraketone **17**[18] would not suffer this problem. However, hydrolysis of **13** proved to be very troublesome. In fact, only unreacted starting material or total decomposition were observed despite trying a wide range of reaction conditions.

We next attempted to minimize the steric impediment to bromination by converting the dimethyl ketals to ethylene ketals. Refluxing a benzene solution of **12** with ethylene glycol and a catalytic amount of tosic acid afforded the transketalization product **18** in 95% yield (Scheme

(17) The supplementary material contains the X-ray data for this compound.

(18) For recent unsuccessful approaches to the tetraketone **17** or protected derivatives, see ref 7g.



13 16 17

III).[19] Sensitized irradiation of 18 in 10% acetone/benzene furnished the photoadduct 19 in quantitative yield. However, attempted preparation of 20 by radical bromination of 19 with NBS/AIBN in CCl_4 again furnished only unreacted starting material. At this point, it was clear that a modified approach to bridgehead functionalization would be required.

A possible solution to the α-keto bridgehead functionalization problem of 13 lies with functionalization prior to intramolecular [2 + 2] photocycloaddition. Such a strategy would obviate the restrictions imposed by Bredt's rule while not adding additional synthetic steps. The most direct method for installing the α-keto functionality into 12 is via electrophilic capture of the bis-enolate or bis-enol ether form. In the present case, treatment of 12 with 3.5 equiv of LDA followed by addition of trimethylsilyl chloride/triethylamine furnished a good yield of the bis-silyl enol ether derivative 21 (Scheme IV). Addition of NBS or NCS gave the dibromo and dichloro derivatives 22 and 23 in 46% and 35% yields for two steps, respectively. Unfortunately, irradiation of 22 or 23 in 10% acetone/benzene gave complex mixtures of products and in the case of 22 significant decomposition. None of the desired photoadduct was detected in any of the photolysis reactions.

The failure of 22 to undergo the desired photocycloaddition was not unexpected, due to the photolability of α-bromo ketones. However, similar problems with the α-chloro derivative 23 were not anticipated. When the photoaddition of 23 was also found to be unsuccessful, we decided to investigate simple alkylated bridgehead derivatives.

Treatment of 12 with 2.2 equiv of LDA in THF followed by addition of methyl iodide furnished an 85% yield of the dimethyl derivative 25 (Scheme V). Irradiation of 25 in 10% acetone/benzene gave a complex mixture of products, once again, with none of the desired photoadduct present. A single-crystal X-ray structural determination for 25[17] revealed that the two double bonds were parallel to one another and presumably were in an ideal position for intramolecular [2 + 2] photocycloaddition.

Similarly, 25 was treated with 4 equiv of LDA and trapped with excess methyl iodide to furnish tetramethyl derivative 27 in 80% yield (Scheme VI). Irradiation of 27 was also unsuccessful, for a complex mixture of products was obtained. A possible reason for the failure of the substituted derivatives to undergo [2 + 2] photoreaction may be due to an increased tendency for the more highly substituted derivatives to undergo Norish type I photofragmentation reactions. It is known that the C–C bond between the more highly substituted alkyl group and carbonyl carbon of a ketone is preferentially cleaved in a Norish type I reaction.[20] Whatever the reason for the difference in reactivity, the fact remains that only α-unsubstituted ketones such as 12, 14, and 18 will undergo efficient [2 + 2] photochemical ring closure. Substituted derivatives 22, 23, 25, and 27 only yield uncharacterizable material.

(19) We have also prepared the analogous thioethylene ketal adducts.

Conclusions

In summary, we have described a convenient synthesis of 13, a highly functionalized 1,4-bishomo-6-secoheptaprismane, in an overall yield of 45% from cheap and readily available starting materials. Although the synthesis of 13 requires a total of nine steps, these can be carried out in an extremely efficient manner and *without resort to chromatography*. While 13 is structurally very similar to 15,[7b,e] the synthetic route described herein offers several advantages. First, our optimized protocol makes 10-g lots of 13 available in an efficacious manner. The Mehta synthesis, while conceptually novel, is burdened by a bottleneck: a Diels–Alder reaction which furnishes an undesired isomer in large proportion. This step makes acquisition of large amounts of 15 somewhat arduous. Second, our synthesis of 13 provides the 1,4-bishomo-6-secoheptaprismane ring system with ketal groups on the the 1,4-methano bridges whereas 15 is devoid of such functionality. Mehta and Padma have been unable to extend their synthetic plan to 13.[7c,g] Any conversion of this ring system to hexaprismane (1) demands the versatility of oxygen functionality on the 1,4-methylene bridges. Preliminary attempts aimed at transforming 13 to hexaprismane (1) and/or heptaprismane (2) have been unsuccessful despite the fact that we have relied on transformations which have previously been utilized with success in functionalizing polycyclic frameworks. Thus, the functionalization and subsequent transformation of 13 to hexaprismane will likely require the development of new functionalization protocols. Our efforts in this area continue and will be reported in due course.

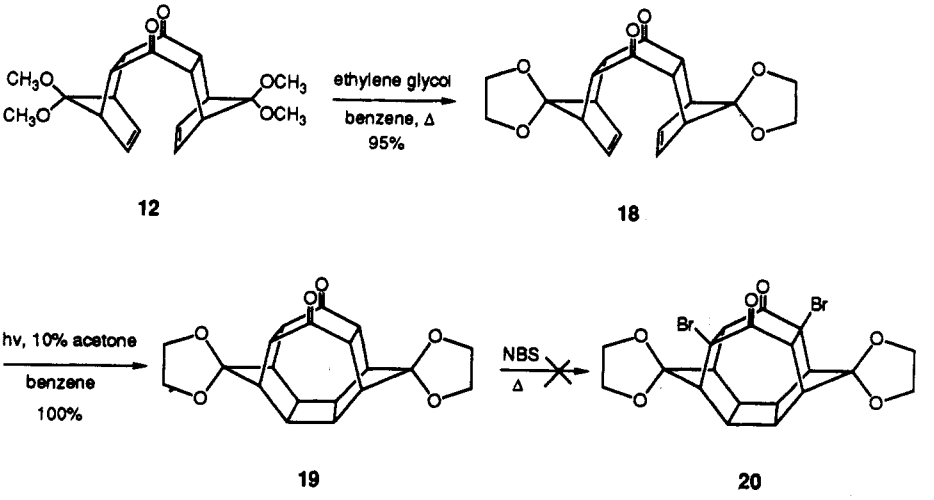
Experimental Section

General Methods. ^1H NMR spectra were obtained in $CDCl_3$ at 250 or 500 MHz with $CHCl_3$ as an internal standard. ^{13}C NMR spectra were obtained at 125 MHz with $CDCl_3$ as an internal standard. Products for which no elemental analyses are reported were judged to be >95% pure by ^1H and ^{13}C NMR. Crude yields are reported for material that was at least 90% pure by ^1H NMR.

(1α,4α,4aβ,8aβ)-1,2,3,4-Tetrachloro-1,4,4a,8a-tetrahydro-9,9-dimethoxy-1,4-methanonaphthalene (9). A mixture of the dimesylate 8b[14] (83.53 g, 0.157 mol), 2-butanone (430 mL), and sodium iodide (81.8 g, 0.546 mol) was heated at reflux. After 30 min, an additional 100 mL of 2-butanone was added to the thick brown mixture, and heating was continued for 30 min. When no starting material remained by TLC, the mixture was cooled and poured onto 2 kg of crushed ice. The mixture was extracted with ether (4 × 225 mL), and the combined organic extracts were washed with water (1 × 1 L), 10% $NaHSO_3$ (2 × 1 L), and brine (1 × 1 L). The colorless solution was dried over $MgSO_4$ and concentrated to yield an off-white crystalline solid (53.4 g, 99%). Recrystallization from 95% ethanol yielded colorless plates of 9 (40.2 g). Concentration of the filtrate and recrystallization yielded

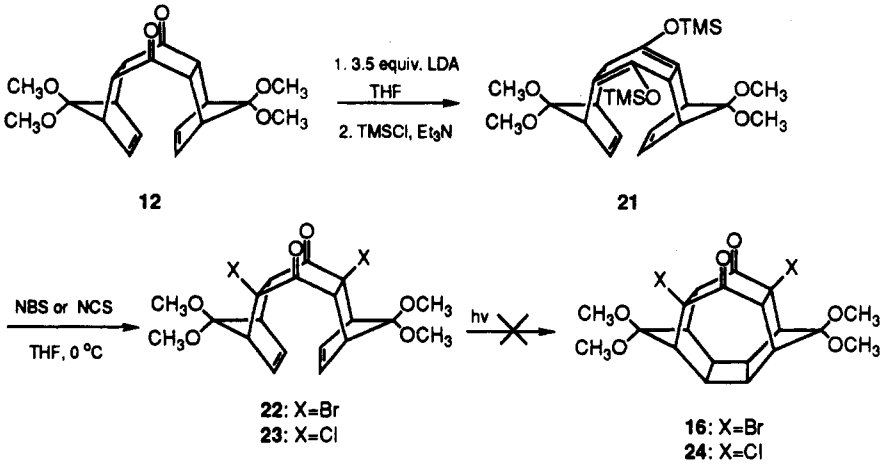
(20) Lowry, T. H.; Richardson, K. S. *Mechanism and Theory in Organic Chemistry*; Harper and Row: New York, 1987; p 1030.

Scheme III



12 18 19 20

Scheme IV

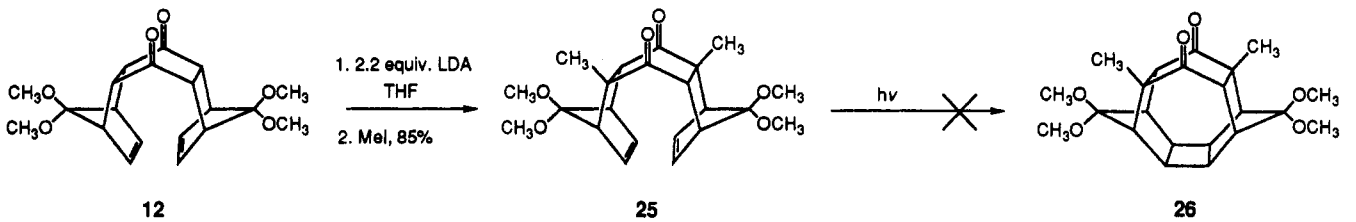


12 21

22: X=Br
23: X=Cl

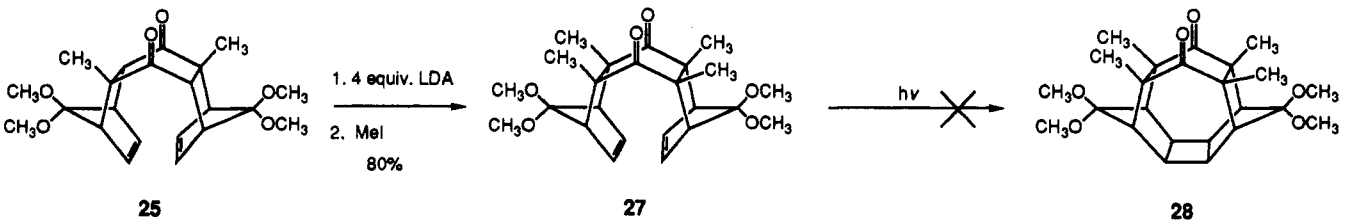
16: X=Br
24: X=Cl

Scheme V



12 25 26

Scheme VI



25 27 28

an additional 3.32 g for a total recrystallized yield of 81%: mp 137–139 °C (lit.[14] mp 141–142 °C); IR ($CDCl_3$) 3015, 2988, 2970, 1601, 1460, 1260, 1195, 1138, 1088, 1020; ^1H NMR δ 5.59–5.78 (m, 4 H), 3.59 (s, 3 H), 3.54 (s, 3 H), 3.49 (m, 2 H); ^{13}C NMR δ 129.46, 124.40, 121.02, 109.16, 79.72, 52.89, 51.83, 47.11; MS 343 (M + 1), 264. Anal. Calcd for $C_{13}H_{12}Cl_4O_4$: C, 45.65; H, 3.54. Found: C, 45.49; H, 3.56.

Endoperoxide Preparation from Diene 9: (1α,4α,4aβ,5β,8β,8aβ)-1,2,3,4-Tetrachloro-1,4,4a,5,8,8a-hexahydro-9,9-dimethoxy-5,8-epidioxy-1,4-methanonaphthalene. To a 3-L, 3-necked flask equipped with a thermocouple, gas dispersion tube, and gas inlet adapter was added a mixture of diene 9 (22.6 g, 66.1 mmol), 5,10,15,20-tetraphenyl-21*H*,23*H*-porphine (TPP) (29 mg), and CCl_4 (1350 mL). The mixture was cooled to 5 °C in an ice bath and was irradiated with a 150-W GE high-pressure sodium street Lucalox lamp while oxygen was bubbled through the dispersion tube. The reaction mixture was periodically raised and lowered out of the ice bath so as to keep the temperature below 15 °C at all times. When TLC (15% ether/hexane) indicated the reaction was finished (usually 1.5–2 h) the solvent was removed under vacuum at 10 °C to give a brown solid (24.7 g, 100%) which was used without further purification: mp 81–91 °C; IR ($CDCl_3$) 2985, 2975, 2940, 1600, 1385, 1370, 1185; ^1H NMR δ 6.47–6.44 (m, 2 H), 4.75–4.70 (m, 2 H), 3.61 (s, 3 H), 3.49 (s, 3

H), 3.32 (m, 2 H); ^{13}C NMR δ 128.17, 127.69, 113.59, 75.82, 69.89, 52.70, 51.67; HRMS (M + 1) calcd for $C_{13}H_{12}Cl_4O_4$ 372.957, obsd 372.963.

(1α,4α,4aβ,5β,8β,8aβ)-1,2,3,4-Tetrachloro-1,4,4a,5,8,8a-hexahydro-9,9-dimethoxy-1,4-methanonaphthalene-5,8-diol (6b). To the crude endoperoxide from diene **9** (36.0 g, 96.8 mmol) was added 200 mL of acetic acid. The green mixture was cooled in ice until the acetic acid just began to crystallize, the ice bath was removed, and zinc dust (30 g) was added all at once with vigorous stirring. After 30 min, the excess zinc was filtered through a bed of Celite and washed with copious amounts of CH_2Cl_2 (250 mL). The filtered solution was washed with water (4 × 250 mL), saturated $NaHCO_3$ (1 × 250 mL), and brine (1 × 250 mL). After drying over $MgSO_4$, the solution was concentrated to give a green solid (34 g, 94% from diene **9**). Recrystallization from cyclohexane yielded soft white needles of diol **6b** (90%): mp 147–147.5 °C; IR ($CDCl_3$) 3600, 2960, 1610, 1205; ^{1}H NMR δ 5.93 (d, J = 1.9, 2 H), 4.16 (br s, 2 H), 3.61 (s, 3 H), 3.53 (s, 3 H), 3.06 (m, 2 H), 2.51 (d, J = 5.1, 2 H); ^{13}C NMR δ 132.0, 129.0, 111.9, 63.6, 53.0, 52.8, 51.8; HRMS (M + NH_4) calcd 391.999, obsd 391.996; (M − OH) calcd 356.962, obsd 356.963. Anal. Calcd for $C_{13}H_{14}O_4Cl_4$: C, 41.52; H, 3.75. Found: C, 41.54; H, 3.73.

(1α,4α,4aβ,5β,8β,8aβ)-1,2,3,4-Tetrachloro-1,4,4a,5,8,8a-hexahydro-9,9-dimethoxy-1,4-methanonaphthalene-5,8-diol Diacetate (6c). To a solution of diol **6b** (0.600 g, 1.60 mmol) in 5 mL of CH_2Cl_2 was added pyridine (774 μL, 9.57 mmol), acetic anhydride (452 μL, 4.79 mmol), and a catalytic amount of (dimethylamino)pyridine (DMAP). The mixture was stirred at rt for 3 h when TLC indicated the reaction had finished (60% ether/petroleum ether). The reaction was then quenched with methanol, diluted with 25 mL of water, and extracted with CH_2Cl_2 (2 × 15 mL). Combined organic extracts were washed with 10% HCl (2 × 30 mL) and brine (1 × 30 mL) and dried over $MgSO_4$. Removal of solvent yielded 0.60 g (82%) of an off-white solid. Recrystallization from 95% ethanol yielded colorless crystals of **6c**: mp 127–128 °C; IR ($CDCl_3$) 2995, 2980, 1740, 1605, 1375, 1240, 1200; ^{1}H NMR δ 5.84 (d, J = 1.8, 2 H), 5.19–5.20 (m, 2 H), 3.60 (s, 3 H), 3.52 (s, 3 H), 3.10 (m, 2 H), 2.03 (s, 6 H); ^{13}C NMR δ 169.7, 130.0, 129.4, 111.5, 76.8, 64.9, 52.9, 51.8, 49.2, 21.1; HRMS (M^+) calcd 457.986, obsd 457.986. Anal. Calcd for $C_{17}H_{18}O_6Cl_4$: C, 44.37; H, 3.94. Found: C, 44.37; H, 3.99.

(1α,4α,4aβ,5β,8β,8aβ)-1,2,3,4-Tetrachloro-1,4,4a,5,8,8a-hexahydro-5,8,9,9-tetramethoxy-1,4-methanonaphthalene (6d). To a suspension of KH (194 mg, 4.84 mmol) in 3 mL of dry THF at 0 °C was added diol **6b** (757 mg, 2.01 mmol) in 5 mL of THF over 2 min. After stirring at 0 °C for 15 min, MeI (300 μL, 4.82 mmol) was added and the mixture was allowed to warm to rt. After 25 min, TLC showed no diol. The mixture was diluted with water and extracted with CH_2Cl_2 (3 × 10 mL), and combined organic extracts were washed with brine (1 × 30 mL), dried over $MgSO_4$, and concentrated to a pale yellow solid (797 mg, 97%). Recrystallization from 95% ethanol yielded white crystals (85%) of **6d**: mp 97.5–98 °C; IR ($CDCl_3$) 2290, 2972, 2963, 1600, 1460, 1378, 1270, 1195, 1098, 900; ^{1}H NMR δ 5.95 (d, J = 2.0, 2 H), 3.64 (m, 2 H), 3.59 (s, 3 H), 3.53 (s, 3 H), 3.35 (s, 6 H), 2.99 (s, 2 H); ^{13}C NMR δ 129.9, 129.1, 111.5, 77.3, 71.2, 56.4, 52.8, 51.7, 49.8; HRMS (M + NH_4) calcd 420.0304, obsd 420.0270. Anal. Calcd for $C_{15}H_{18}O_4Cl_4$: C, 44.58; H, 4.49. Found: C, 44.61; H, 4.49.

(1α,4α,4aβ,5α,8α,8aβ,9b,9aβ,10β,10aβ)-1,2,3,4,5,6,7,8-Octachloro-1,4,4a,5,8,8a,9,9a,10,10a-decahydro-11,11,12,12-tetramethoxy-1,4:5,8-dimethanoanthracene-9,10-diol (10). A neat mixture of diol **6b** (24.57 g), ketal **4** (17.20 g), and $CaCO_3$ (1.75 g) was heated with stirring at 125 °C for 96 h. After cooling, the mixture was dissolved in hot ethanol and treated with decolorizing carbon. The mixture was filtered through Celite, the filter cake washed with copious amounts of ethyl acetate, and the filtrate concentrated to give **10** as an off-white solid (42.0 g, 100%). This crude material was pure enough for the next step. However, slightly better yields were obtained in the dechlorination by recrystallizing **10** from ethyl acetate/hexane: mp 206–207 °C; IR ($CDCl_3$) 3590, 2993, 2977, 1603, 1385, 1283, 1200, 1160, 1112, 1060; ^{1}H NMR δ 3.58 (s, 3 H), 3.53 (s, 3 H), 3.28–3.33 (m, 2 H), 2.78–2.85 (m, 4 H), 2.30 (d, J = 2.8, 2 H); ^{13}C NMR δ 129.4, 110.9, 66.6, 52.8, 52.0, 51.9; MS 636 (M^+), 605. Anal. Calcd for $C_{20}H_{20}O_6Cl_8$: C, 37.53; H, 3.15. Found: C, 37.36; H, 3.07.

(1α,4α,4aβ,5α,8α,8aβ,9b,9aβ,10β,10aβ)-1,4,4a,5,8,8a,9,9a,10,10a-Decahydro-11,11,12,12-tetramethoxy-1,4:5,8-dimethanoanthracene-9,10-diol (11). A solution of 15.0 g (23.4 mmol) of diol **10** in 240 mL of dry THF was added over 60–90 min to a dark blue solution of 20.0 g of sodium in 350 mL of NH_3 cooled to −78 °C in a dry ice/acetone bath. The mixture was stirred at this temperature for 4 h, and granular NH_4Cl was added until the blue color faded. The ammonia was allowed to evaporate overnight, 250 mL of water was added, and the mixture was continuously extracted with ether for 72 h to yield 7.93 g of a tan solid (93%) of **11**. The solid was used without purification for the preparation of **12**. An analytical sample of **11** was obtained by flash chromatography (5% methanol/CH_2Cl_2): mp 199–200 °C; IR ($CDCl_3$) 3602, 3590, 3430 (br), 2990, 2969, 1270, 1120; ^{1}H NMR δ 6.10 (t, J = 1.8, 4 H), 3.20 (s, 6 H), 3.08 (s, 6 H), 2.94 (br s, 4 H), 2.63–2.59 (m, 2 H), 2.25–2.23 (m, 4 H), 1.7–1.9 (br s, 2 H); ^{13}C NMR δ 132.9, 119.3, 69.7, 51.8, 49.8, 46.8, 45.9; HRMS (M^+) calcd for $C_{20}H_{28}O_6$ 364.189, obsd 364.183.

(1α,4α,4aβ,5α,8α,8aβ,9aβ,10aβ)-1,4,4a,5,8,8a,9,9a,10,10a-Decahydro-11,11,12,12-tetramethoxy-1,4:5,8-dimethanoanthracene-9,10-dione (12). A solution of unpurified dechlorinated diol **11** (6.94 g, 19.04 mmol) in 280 mL of acetone was mechanically stirred and cooled to 0 °C. Jones reagent (22.8 mL, 2.6 M)[21] was added dropwise over 20 min with vigorous stirring. The mixture was stirred at 0 °C for 40 min and then for 1.5 h at rt. The excess reagent was quenched with 2-propanol to dissipate all brown color, solid $NaHCO_3$ was added, and the mixture was stirred for several hours. The solids were filtered through a pad of Celite, the filter cake was washed with $CHCl_3$, and the filtrate was concentrated to yield 5.9 g (85%) of a tan solid. Recrystallization from acetone gave white crystals of **12**: mp >260 °C; IR ($CDCl_3$) 3005, 2977, 2957, 1715, 1290, 1117, 1100; ^{1}H NMR δ 5.96 (br s, 4 H), 3.59 (br s, 4 H), 3.21 (br s, 4 H), 3.15 (s, 6 H), 3.08 (s, 6 H); ^{13}C NMR δ 208.4, 134.3, 116.8, 52.3, 52.0, 49.9, 46.4; MS 360 (M^+), 329. Anal. Calcd for $C_{20}H_{24}O_6$: C, 66.65; H, 6.71. Found: C, 66.51; H, 6.75.

2,3,3a,4a,5,6,7,8,8a,9a-Decahydro-2,2,10,10-tetramethoxy-1,7,3,6-ethanediylidene-5,8-methano-1*H*-benz[*f*]indene-4,9-dione (13). A solution of 3.5 g of dione **12** in 450 mL of 10% acetone/benzene was irradiated until NMR indicated complete reaction (ca. 7 h). The mixture was concentrated to yield 3.5 g (100%) of **13** as an off-white solid. Slow evaporation from methanol/ether yielded colorless crystals of **13**: mp 197–199 °C; IR ($CDCl_3$) 2972, 2942, 1695, 1127; ^{1}H NMR δ 3.33 (br s, 4 H), 3.23 (s, 6 H, OCH_3), 3.19 (s, 6 H, OCH_3), 3.13 (br s, 4 H), 2.43 (br s, 4 H); ^{13}C NMR δ 210.0, 115.4, 52.1, 51.0, 50.9, 46.0, 38.5; HRMS (M + H) calcd 361.165, obsd 361.166. Anal. Calcd for $C_{20}H_{24}O_6$: C, 66.65; H, 6.71. Found: C, 66.66; H, 6.57.

(1′α,4′α,4′aβ,5′α,8′α,8′aβ,9′aβ,10′aβ)-1′,4′,4′a,5′,8′,8′a,9′,9′a,10′,10′a-Decahydrodispiro[1,3-dioxolane-2,11′-[1,4:5,8]dimethanoanthracene-12′,2″-[1,3]dioxolane]-9′,10′-dione (18). A mixture of dione **12** (48.0 mg, 0.133 mmol), ethylene glycol (331 mg, 5.3 mmol, 40 equiv), catalytic *p*-TsOH, and 1 mL of benzene was heated at reflux for 17 h. The mixture was cooled, poured onto saturated $NaHCO_3$, and extracted with CH_2Cl_2 (3 × 10 mL). Combined organic extracts were washed with brine (1 × 20 mL), dried over $MgSO_4$, and concentrated to an off-white crystalline solid (45 mg, 95%). Recrystallization from acetone yielded an analytical sample of **18**: mp >275 °C; IR ($CDCl_3$) 2980, 1704, 1300, 1106, 1078, 1012; ^{1}H NMR δ 6.05 (t, J = 2.1, 4 H), 3.79–3.89 (m, 8 H), 3.69 (s, 4 H), 2.96 (d, 4 H); ^{13}C NMR δ 207.6, 134.9, 123.2, 65.0, 64.7, 52.2, 47.8; HRMS (M + H) calcd for $C_{20}H_{20}O_6$ 357.1338, obsd 357.1320.

2′,3′,3′a,4′a,5′,6′,7′,8′,8′a,9′a-Decahydrodispiro[1,3-dioxolane-2,2′-[1,7,3,6]ethanediylidene[5,8]methano[1*H*]benz[*f*]indene-10′,2″-[1,3]dioxolane]-4′,9′-dione (19). A deoxygenated solution (argon) of ethylene ketal **18** (100 mg) in 5 mL of 10% acetone/benzene was irradiated for 15 h with a 450-W medium-pressure Hanovia mercury vapor lamp equipped with a Pyrex filter. The clear solution was concentrated to yield 100 mg of an off-white solid of **19**: mp >260 °C; IR ($CDCl_3$) 2980, 1696, 1298; ^{1}H NMR δ 3.89 (s, 8 H), 3.46 (s, 4 H), 3.25 (s, 4 H), 2.11 (s, 4 H); ^{13}C NMR

(21) Prepared according to Fieser, L. F.; Fieser, M. *Reagents for Organic Synthesis*; Wiley: New York, 1967; Vol. 1, pp 142–144.

δ 209.0, 120.6, 65.3, 64.9, 52.2, 47.0, 38.5; HRMS (M + H) calcd for $C_{20}H_{20}O_6$ 357.1338, obsd 357.1329.

(1α,4α,4aβ,5α,8α,8aβ)-1,4,4a,5,8,8a-Hexahydro-11,11,12,12-tetramethoxy-9,10-bis[(trimethylsilyl)oxy]-1,4:5,8-dimethanoanthracene (21). To a solution of freshly prepared LDA (prepared by adding 185 μL (0.49 mmol) of 2.63 M *n*-butyllithium in hexanes to a 0 °C solution of 78 μL (0.69 mmol) of diisopropylamine in 3 mL of dry distilled THF and stirring for 30 min) cooled to −78 °C was added solid dione **12** (50.0 mg, 0.14 mmol) via spatula. Residual dione was added with the aid of 1–2 mL of dry THF via pasteur pipet. The mixture was allowed to warm to rt during which time a thick slurry formed. The mixture was stirred at rt for 45 min and recooled to −78 °C. To the cold slurry was added a centrifuged mixture of 2.11 mL (1.81 g, 16.6 mmol) of freshly distilled chlorotrimethylsilane and 4.22 mL (3.06 g, 30.3 mmol) of triethylamine. The mixture was allowed to warm to rt for 30 min and then was quenched by addition of saturated $NaHCO_3$ solution. The mixture was then extracted with ethyl acetate (3 × 15 mL), and the combined organic extracts were washed with water (1 × 25 mL) and brine (1 × 25 mL) and dried over $MgSO_4$. Concentration yielded a yellow solid of **21** (70 mg, 100%) which could be used in subsequent steps without purification. However, purification could be accomplished by flash column chromatography in 10% ethyl acetate/petroleum ether to yield colorless crystals of **21**: mp 134–135 °C; IR ($CDCl_3$) 2997, 2960, 1680, 1330, 1255, 1217, 1165, 1140, 1125, 1109, 1067, 1014; ^1H NMR δ 6.02–5.99 (m, 2 H), 5.83–5.81 (m, 2 H), 3.33–3.32 (m, 2 H), 3.26 (t, 2 H), 3.17 (s, 6 H), 3.13 (s, 6 H, OCH_3), 2.98 (s, 2 H), 0.22 (s, 18 H); ^{13}C NMR δ 141.9, 133.0, 130.3, 121.1, 119.2, 51.5, 50.0, 47.4, 47.2, 44.3, 0.43.

(1α,4α,4aβ,5α,8α,8aβ,9aβ,10aβ)-4a,8a-Dibromo-1,4,4a,5,8,8a,9,9a,10,10a-decahydro-11,11,12,12-tetramethoxy-1,4:5,8-dimethanoanthracene-9,10-dione (22). To a mixture of 128.0 mg (0.254 mmol) of bis-TMS derivative **21** in 2.5 mL of dry THF cooled to 0 °C was added 99.3 mg (0.56 mmol) of *N*-bromosuccinimide. The mixture was stirred at 0 °C for 90 min. After it was diluted with water, the mixture was extracted with CH_2Cl_2 (4 × 10 mL). Combined organic extracts were washed with brine, dried over $MgSO_4$, and concentrated to a yellow oil. Flash chromatography (20% ethyl acetate/petroleum ether) yielded 60.0 mg (46%) of a white solid of **22**: mp 160 °C dec; IR ($CDCl_3$) 2945, 1713, 1285, 1210, 1125, 1100, 1060, 1050, 1003; ^1H NMR δ 6.00–5.98 (m, 2 H), 5.93–5.91 (m, 2 H), 4.57 (d, J = 3.9, 2 H), 3.43 (m, 2 H), 3.36–3.31 (m, 2 H), 3.30 (s, 3 H), 3.14 (s, 3 H); ^{13}C NMR δ 197.8, 136.0, 133.6, 116.3, 64.2, 58.0, 54.2, 51.9, 50.6, 47.8; HRMS (M + H) calcd for $C_{20}H_{22}O_6Br_2$ 516.9861, obsd 516.9837.

(1α,4α,4aβ,5α,8α,8aβ,9aβ,10aβ)-4a,8a-Dichloro-1,4,4a,5,8,8a,9,9a,10,10a-decahydro-11,11,12,12-tetramethoxy-1,4:5,8-dimethanoanthracene-9,10-dione (23). To a mixture of 36.5 mg (0.072 mmol) of bis-TMS derivative **21** in 1 mL of dry THF cooled to 0 °C was added 21.2 mg (0.159 mmol) of *N*-chlorosuccinimide. The mixture was allowed to warm to rt and was stirred for 90 min. After it was diluted with water, the mixture was extracted with CH_2Cl_2 (3 × 10 mL). Combined organic extracts were washed with brine, dried over $MgSO_4$, and concentrated to 30 mg of a yellow oil. Flash chromatography (15% ethyl acetate/petroleum ether) yielded 11 mg of a white solid **20** (35% for 2 steps): IR ($CDCl_3$) 2950, 1725, 1285, 1130; ^1H NMR δ 5.97–5.99 (m, 2 H), 5.91–5.93 (m, 2 H), 4.48 (d, J = 3.6, 2 H), 3.32–3.35 (m, 4 H), 3.28 (s, 6 H), 3.14 (s, 6 H); ^{13}C NMR δ 197.8, 135.3, 133.5, 116.6, 72.3, 58.5, 53.8, 51.9, 50.6, 47.5; HRMS (M^+) calcd for $C_{20}H_{22}O_6Cl_2$ 428.0793, obsd 428.0818.

(1α,4α,4aβ,5α,8α,8aβ,9aβ,10aβ)-1,4,4a,5,8,8a,9,9a,10,10a-Decahydro-11,11,12,12-tetramethoxy-4a,8a-dimethyl-1,4:5,8-dimethanoanthracene-9,10-dione (25). To a solution of freshly prepared LDA (prepared by adding 751 μL (1.43 mmol) of 1.91 M *n*-butyllithium in hexanes to a 0 °C solution of 219 μL (1.56 mmol) of diisopropylamine in 4.5 mL of dry distilled THF and stirring for 30 min) cooled to −78 °C was added solid dione **12** (235.0 mg, 0.652 mmol) via spatula. Residual dione was added with the aid of 1–2 mL of dry THF via pasteur pipet. The mixture was allowed to warm to rt during which time a thick slurry formed. The mixture was stirred at room temperature for 30 min and recooled to −78 °C. To the cold slurry was added methyl iodide (97 μL, 1.56 mmol), and the mixture was allowed to warm to rt. As the mixture warmed, the slurry became a homogeneous orange solution. The solution was then quenched with water and extracted with CH_2Cl_2 (4 × 15 mL). The combined organic extracts were washed with brine, dried over $MgSO_4$, and concentrated to yield 258.2 mg of an off-white solid (85%). Recrystallization from 95% ethanol or acetone yielded colorless crystals of **21**: mp 162–163 °C; IR ($CDCl_3$) 2990, 2960, 2935, 2900, 1699, 1283, 1225; ^1H NMR δ 6.04 (m, 2 H), 5.77 (m, 2 H), 3.31 (d, J = 3.6, 2 H), 3.28 (s, 2 H), 3.18 (s, 6 H), 3.08 (s, 3 H), 2.89 (d, J = 2.0, 2 H), 1.68 (s, 6 H); ^{13}C NMR δ 212.2, 138.0, 131.5, 116.4, 58.9, 55.5, 52.3, 51.7, 49.8, 48.3, 25.6; HRMS (M^+) calcd for $C_{22}H_{28}O_6$ 388.189, obsd 388.183.

(1α,4α,4aβ,5α,8α,8aβ,9aβ,10aβ)-1,4,4a,5,8,8a,9,9a,10,10a-Decahydro-11,11,12,12-tetramethoxy-4a,8a,9a,10a-tetramethyl-1,4:5,8-dimethanoanthracene-9,10-dione (27). To a solution of freshly prepared LDA (prepared by adding 251 μL (0.66 mmol) of 2.63 M *n*-butyllithium in hexanes to a 0 °C solution of 115 μL (0.824 mmol) of diisopropylamine in 4.0 mL of dry distilled THF and stirring for 30 min) cooled to −78 °C was added solid dimethyl dione **25** (64.0 mg, 0.165 mmol) via spatula. Residual dione was added with the aid of 1–2 mL of dry THF via pasteur pipet. The mixture was allowed to warm to rt during which time a thick slurry formed. The mixture was stirred at rt for 3 h and recooled to −78 °C. To the cold slurry was added methyl iodide (410 μL, 6.6 mmol), and the mixture was allowed to warm to rt and stir for 45 min. As the mixture warmed, the slurry became a homogeneous orange solution. The solution was then quenched with water and extracted with ethyl acetate (2 × 10 mL). The combined organic extracts were washed with brine, dried over $MgSO_4$, and concentrated to yield an off-white solid (68 mg, 80%). Recrystallization from methanol yielded colorless cubes of **27**: mp 234–235.5 °C; IR ($CDCl_3$) 2998, 2955, 1690, 1283, 1200, 1135, 1105, 1090, 1073, 1010; ^1H NMR δ 5.82 (t, 4 H, J = 2.1), 3.14 (s, 3 H), 3.02 (s, 3 H), 2.96 (t, J = 2.2), 1.56 (s, 6 H); ^{13}C NMR δ 217.7, 136.0, 115.9, 59.2, 54.7, 51.3, 50.3, 23.8; HRMS (M + H) calcd for $C_{24}H_{32}O_6$ 516.9861, obsd 516.9837.

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Supplementary Material Available: ^{13}C NMR spectra for the endoperoxide from **9** and compounds **11**, **18**, **19**, **21**, **22**, **23**, **25**, and **27** as well as X-ray data for **13** and **25** (20 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.