Aureolic Acid Antibiotics: Synthesis of Naphthocyclobutene Precursors

Subhash C. Datta,† Richard W. Franck,* and Paul D. Noire‡

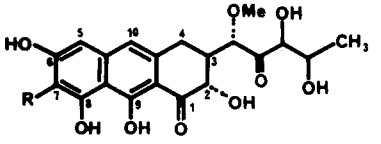
Department of Chemistry, Fordham University, Bronx, New York 10458

Received January 3, 1984

The use of the dianion of 1,2-dicarbomethoxycyclobutane, a method introduced by Garratt, has been exploited to produce naphthocyclobutenes with methoxy groups in the naphtho moiety. A highly regioselective functionalization of the cyclobutene ring has been demonstrated by using NBS followed by solvolysis of the reactive cyclobutyl bromide. The site of substitution of the cyclobutyl ring was proven by a NOEDs experiment. The substituted naphthocyclobutenes were subjected to conditions for ring opening and cycloaddition. Only one derivative, the 2-(trimethylsilyl)ethyl ether **31**, was successfully opened and captured.

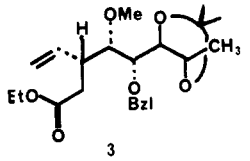
Introduction

The aureolic acid class of antibiotics is comprised of three subgroups. One group, the olivomycins, is isolated from *Streptomyces olivoreticuli* and contains the anthracenoid aglycone olivin (**1**) linked to a trisaccharide at C-2 and a disaccharide at C-6. A second group, the

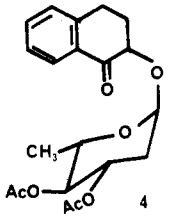


1 R = H
2 R = CH_3

chromomycins, comes from *Streptomyces* and has 7-methylolivin or chromomycinone (**2**) as the aglycone with di- and trisaccharides corresponding in glycoside composition and stereochemistry to those of the olivomycins. The third group, aureolic acid itself, or mithramycin, also *Streptomyces* derived has chromomycinone as its aglycone but has some sugars and glycosidic stereochemistries different from other family members.[1] Since the appearance of our recent paper on a model aglycone synthesis in which there is a reasonably complete review of the synthetic literature in the area,[2] there have appeared some noteworthy contributions to the field. The Weinreb group has completed a synthesis of 6,8,9-trimethylolivin.[3] The preparation of potential side-chain precursors such as **3**



3

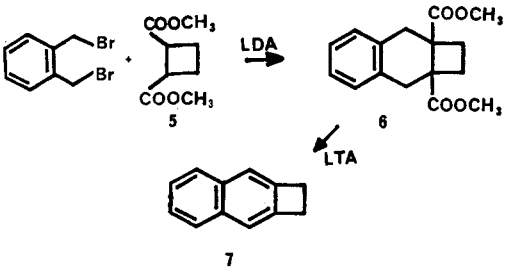


4

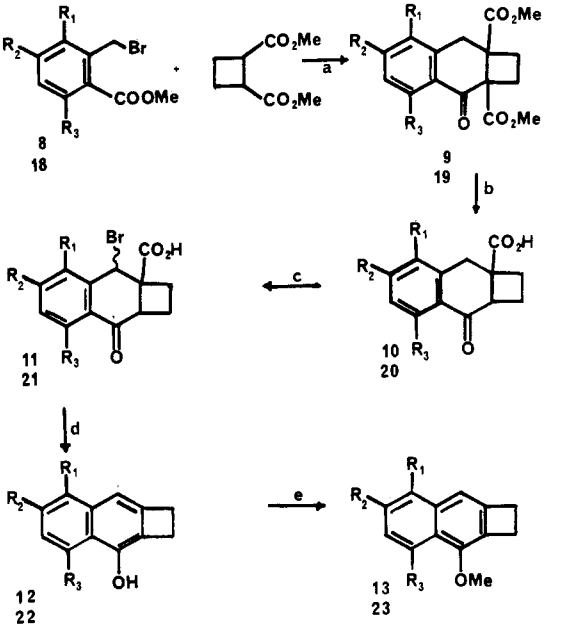
has been reported by Roush.[4] Finally, the first success at forging a glycosidic link between a sugar and a model aglycone to produce **4** has been described by Thiem.[5]

Our strategy for the synthesis of an aglycone, inspired by Cava's anthracycline work,[6] required the merging of a sugar-derived dienophile **A** with an *o*-quinone methide **B**. Our model studies had demonstrated the practicality of our scheme using benzoquinone methides. Also Cava had shown the parent naphthoquinone methide could add to *N*-phenylmaleimide.[6] Therefore, it remained for us to develop a preparation of the properly substituted naphthoquinone methide precursor and to demonstrate its utility in our proposed scheme. It is our synthesis of highly

Scheme I



Scheme II[a]



8–**13** $R_1 = R_2 = R_3 = H$
18–**23** $R_1 = Br$ $R_2 = R_3 = OMe$

[a] a, LDA, THF; b, HOAc, H_2SO_4, H_2O; c, NBS; d, Et_3N, SiO_2; e, KO-*t*-Bu, CH_3SO_3F or K_2CO_3, $(CH_3)_2SO_4$.

* Address correspondence to R. W. Franck, Hunter College, 695 Park Avenue, New York, NY 10021.

† Subhash C. Datta on sabbatical leave from Hans Raj College, Delhi University, Delhi, India.

‡ Current address, Givaudan Corp., Research Department, Clifton, NJ 07014.

(1) (a) Remers, W. "The Chemistry of Antitumor Antibiotics"; Wiley: New York, 1979; Vol. 1. (b) Thiem, J.; Meyer, B. *J. Chem. Soc., Perkin Trans. 2* **1979**, 1331–1336. (c) Thiem, J.; Meyer, B. *Tetrahedron* **1981**, *37*, 551–558. (d) Riccio, R.; Nakanishi, K. *J. Org. Chem.* **1982**, *47* 4589–4592.

(2) Franck, R. W.; John, T. V. *J. Org. Chem.* **1983**, *48*, 3269–3276.

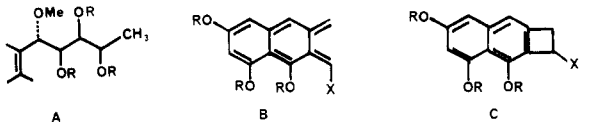
(3) Dodd, J. H.; Starrett, J. E., Jr.; Weinreb, S. M. *J. Am. Chem. Soc.* **1984**, *106*, 1811–1812.

(4) (a) Roush, W. R.; Harris, D. J.; Lesur, B. M. *Tetrahedron Lett.* **1983**, 24, 2227–2230. (b) Roush, W. R.; Lesur, B. M. *Ibid.* **1983**, *24*, 2231–2234.

(5) Thiem, J.; Gerken, M.; Snatzke, G. *Liebigs Ann. Chem.* **1983**, 448–461.

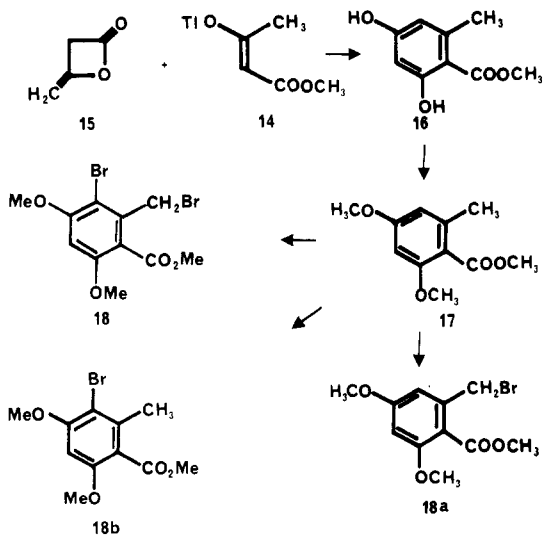
0022-3263/84/1949-2785$01.50/0

substituted naphtho[b]cyclobutenes of type C that is the subject of this article.[7]



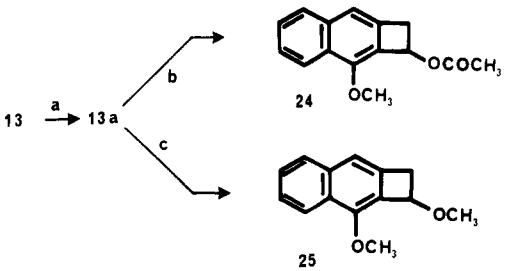
Results and Discussion

The parent naphtho[b]cyclobutene has been prepared in four independent ways;[6,8] we chose the Garratt route, outlined in Scheme I as most convergent and thus suitable for our work.[8b] Since Garratt had shown that the dianion of 1,2-dicarbomethoxycyclobutane (**5**) condensed with both diesters and dihalides to form symmetrical naphtho-fused cyclobutanes, we reasoned that the dianion should condense with a halo ester to form a product that would afford an unsymmetrical napthocyclobutane of the type needed for aureolic acids. As shown in Scheme II, methyl *o*-bromotoluate (**8**) condenses smoothly with dianion **5** to produce the naphthcyclobutane framework **9** in 65% yield. Aqueous acid hydrolysis of diester **9** afforded the keto acid **10** in good yield. Acid **10** was then subjected to bromination with NBS to afford a mixture of stereoisomers **11**, which without further purification was subjected to a Grob fragmentation to yield the air-sensitive 3-hydroxynaphtho[b]cyclobutane (**12**). Naphthol **12** was easily methylated with methyl fluorosulfonate and potassium *tert*-butoxide to form the methyl ether **13**. The cyclobutenes in this series were all characterized by their AA'BB' NMR patterns, and the remainder of their NMR spectra as well as their mass spectra. With a viable route for preparing 8-alkoxy-substituted naphthocyclobutenes in hand, we turned to its application to a system whose functionality corresponded to that of the aromatic segment of the aureolic acid antibiotics. The required toluic acid derivative was easily obtained by using a procedure of Hase.[9] Thus, condensation of the thallium salt of methyl



acetoacetate (**14**) with diketene **15** produced methyl dihydroxytoluate **16** which on methylation and careful column chromatography yielded methoxytoluate **17** in 38% yield. Then one ring carbon and the benzylic methyl were brominated with NBS to afford **18** in 97% yield. We found it expedient to perform the bromination in two steps in one flask. With the first equivalent of NBS, with no light or peroxides, there took place the electrophile bromination; with the second equivalent under free-radical initiating conditions, the benzylic position was substituted. Although, under carefully controlled conditions, it was possible to obtain about a 75% yield of benzylic bromination product **18a** without ring substitution, there was always some contamination with the product of electrophilic bromination of the ring **18b**. Since we were to be using NBS in subsequent steps, we reasoned that intentional ring bromination at the outset would avoid problems of inadvertent aromatic substitution later in the synthesis. Repetition of the Garratt condensation of dianion **5** with bromo ester **18** produced the substituted naphthocyclobutene framework in 82% yield. To obtain these good yields, it was necessary to use less than 2 full equiv of LDA. Typical reactant ratios for 18:5:LDA were 1:1.4:2.6. Using our methods developed for the model series, we proceeded via acid **20**, bromo acid **21**, and naphthol **22** which was methylated to afford the required naphthocyclobutene starting material **23** in 44% yield from **19** (Scheme II).

We next proceeded to functionalize the cyclobutene carbons of **13** and **23**. Cava had shown that the parent naphtho[b]cyclobutene could be functionalized via NBS.[10] Solvolysis of the simple bromonaphthocyclobutene required silver trifluoroacetate in aqueous acetonitrile to form the 1-hydroxy compound. Also, potassium *tert*-butoxide in *tert*-butyl alcohol at reflux formed a 1-*tert*-butyl ether. However, Cava showed that the ether formation mechanism was not a simple displacement, but proceeded via naphthocyclobutadiene and an elimination–addition pathway. In our unsymmetrical system, the latter mechanistic possibility with its loss of differentiation between C-1 and C-2 could give us product mixture, or at worst, the wrong regioisomeric substitution on the cyclobutane ring. Although, there was no precedent for substituent effects on the regioselectivity of functionalization of the cyclobutanes of unsymmetrical benzo- or naphthocyclobutenes, we had no reason to doubt that the *o*-methoxyl in **13** would stabilize the transition state for hydrogen



a, NBS; b, KOAc, HOAc; c, MeOH

abstraction at C-1. In any event, NBS treatment of **13** afforded a bromide which was solvolyzed with potassium acetate and acetic acid at reflux temperature. A single product, tentatively assigned structure **24**, was obtained. The intermediate bromide from **13** was also solvolyzed with methanol to afford a single methyl ether **25**. When the NBS, KOAc–HOAc sequence was applied to **23**, and the product was subjected to chromatography, two acetates were obtained. The NMR spectra of the products differed

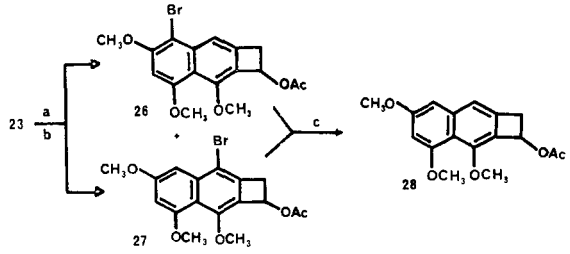
(6) (a) Kerdesky, F. A. J.; Ardecky, R. J., Lakshmikantham, M. V.; Cava, M. P. *J. Am. Chem. Soc.* **1981**, *103*, 1992. (b) Cava, M. P.; Shirley, R. L. *J. Am. Chem. Soc.* **1960**, *82*, 654–656.

(7) The model experiments for this work have been described in a communication: Noire, P. D.; Franck, R. W. *Tetrahedron Lett.* **1982**, *23*, 1031–1034.

(8) (a) Ewing, G. D.; Boekelheide, V. *Synthesis* **1979**, 427–428. (b) Bilyard, K. G.; Garratt, P. J.; Underwood, A. J.; Zahler, R. *Tetrahedron Lett.* **1979**, 1815–1818. (c) Thummel, R. P.; Cravey, W. E.; Nutakel, W. *J. Org. Chem.* **1978**, *43*, 2473–2477.

(9) Hase, T. A.; Suokas, E.; McCoy, K. *Acta Chem. Scand. Ser. B* 1978, *32*, 701-702.

(10) Cava, M. P.; Hsu, A-F. C. *J. Am. Chem. Soc.* **1972**, *94*, 6441–6444.

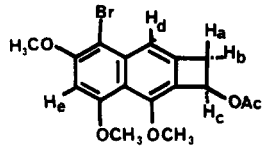


a, NBS; b, KOAc, HOAc; c, Bu_3SnH

in the aromatic region. One isomer exhibited two singlets, essentially identical with those of **23**. The other isomer revealed a pair of meta-coupled doublets. Hence, we assumed that our two products were identically functionalized on the cyclobutane carbon, but differed in naphthalene substitution caused by a bromine migration.

Considering the precedent for rearrangements of bromonaphthols,[11] we hypothesized a ring bromination followed by a HBr-catalyzed debromination to relieve buttressing which converts **23** to **23a** (Scheme III). The rate of this electrophilic process must be competitive with the free-radical substitution on the side chain. Evidence for this hypothesis came with the isolation from a bromination reaction mixture of a very small quantity of naphthocyclobutene **23a**, isomeric with **23**, which exhibited the meta-coupled aromatic protons identical to one of the acetates. Both **23** and **23a** were debrominated with Bu_3SnH to yield **23b**. Similarly, acetates **26** and **27** were both converted to acetate **28** by treatment with Bu_3SnH (94% yield).

In order to demonstrate that the regiochemistry of the acetates was as we have indicated, we undertook a differential NOE experiment with acetate **26**.[12] The en-

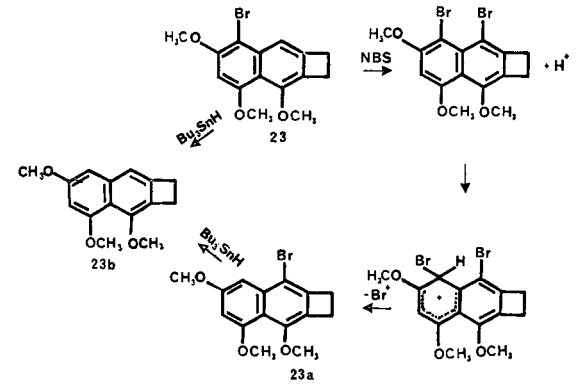


26

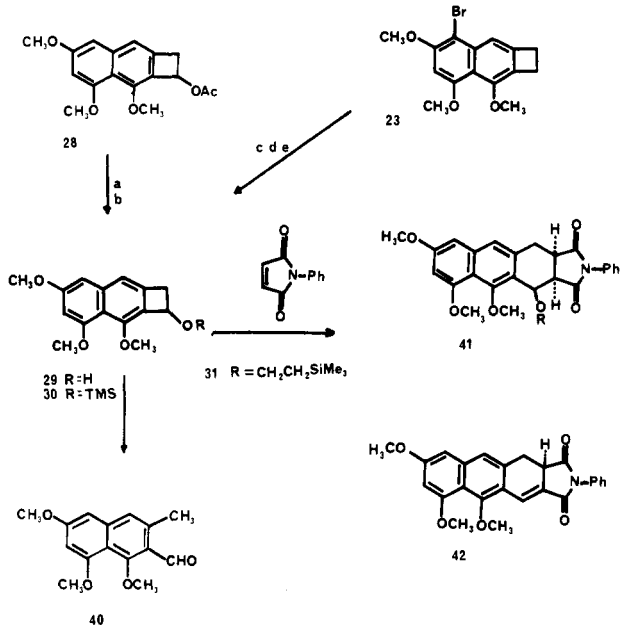
hancement shown in Table I confirmed our structure assignment. Note in particular the effect of irradiating the aromatic methoxyl (δ 4.09) which is not adjacent to an aromatic hydrogen. This methoxyl at C-8 causes the 30% enhancement of the signal of the unique cyclobutane proton (δ 6.30) which carries the acetate substituent.

The acetate **28** (Scheme IV) was converted to alcohol **29** via $LiAlH_4$ reduction at −30 °C. The alcohol could be isolated and trimethylsilated with standard conditions to produce **30**. With a view to making an alkyl naphthocyclobutenyl ether, the bromide obtained by NBS treatment of **23** was solvolyzed with 2-(trimethylsilyl)ethanol and then debrominated with Bu_3SnH to yield **31**. Thinking that a bridged reagent such as **32** would be more suitable, we modified our scheme towards attaining diol **33** (Scheme V). Naphthol **22** was acetylated to form **34**. Then execution of the previously described NBS, KOAc–HOAc sequence afforded naphthocyclobutene diacetate **35**. In this case, there was no bromine migration because the 3-position is not activated by acetate toward electrophilic bromination which initiates the rearrangement. However, a small amount of the regioisomeric bromination product **36** was detected. Apparently, the effect of the *o*-naphthyl acetate function is less stabilizing for the

Scheme III



Scheme IV[a]



[a] a, $LiAlH_4$, −20 °C; b, Me_3SiCl; c, NBS; d, $Me_3SiCH_2CH_2OH$; e, Bu_3SnH.

free-radical bromination step than the *o*-methoxyl in our earlier examples. Also, the solvolysis of bromide **36** is no longer assisted, thus it is stable to our conditions for acetolysis and can be isolated. Tri-*n*-butyltin hydride debromination of **35** produced **37** which was subjected to mild acid-catalyzed ester exchange with MeOH to form **38**. Unfortunately, the conditions required to deacylate the phenolic ester were sufficiently electrophilic so that ring opening via successive ipso protonation and dealkylation produced the dimethyl acetal **39**.

All three derivatives **28**, **29**, and **30**, upon heating at 175–190 °C in sealed tubes with or without dienophiles present, were converted mainly to the brilliantly fluorescent aldehyde **40**. The minor products isolated did not exhibit characteristics expected of diene–dienophile adducts. It is known that the ring opening of benzocyclobutenols to carbonyls is highly exothermic (−20 kcal/mol in one determination).[13a] It has also been observed that blocked benzocyclobutenols usually afford better cycloaddition yields than their parent alcohols.[13b] Hence, we conclude that some deblocking of **28** and **30** takes place in the presence of adventitious nucleophiles, despite our

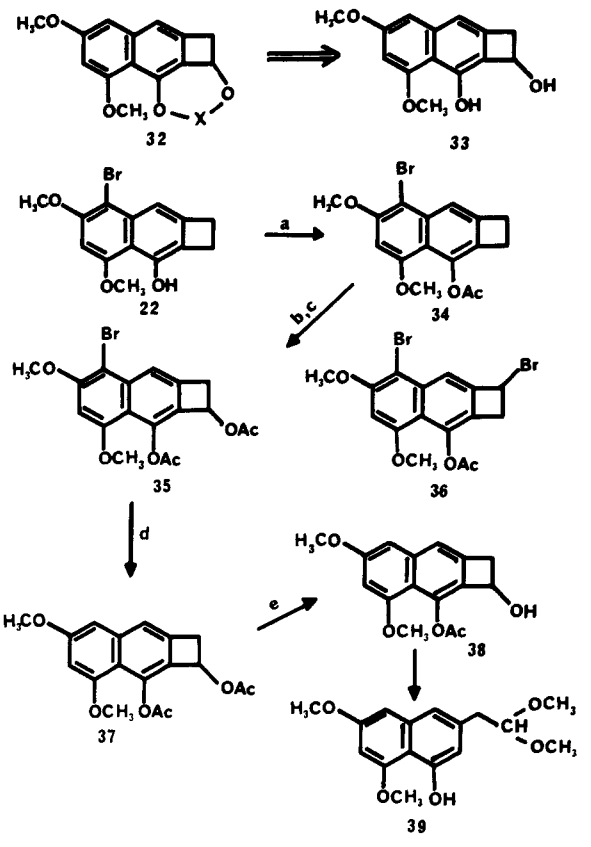
(11) Cooke, R. G.; Jihnsin, B. L.; Owen, W. R. *Chem. Ind. (Berlin)* **1957**, 1623–1624.
(12) Kotovych, G.; Harts, G. H. M. *Can. J. Chem.* **1980**, *58*, 2649–2659.
(13) (a) Ito, Y.; Umehara, Y.; Hijiya, T.; Yamada, Y.; Matsuura, T. *J. Am. Chem. Soc.* **1980**, *102*, 5917. (b) Amaro, A.; Carreno, M. C.; Farina, F. *Tetrahedron Lett.* **1979**, 3983. (c) We thank a referee for suggesting ref 13a.

Table I. Proton Nuclear Overhauser Effects Difference Data of the Acetate 26

		protons undergoing NOE enhancement[a]							
^{1}H irratd	δ	OCH_3 (4.09)	OCH_3 (4.02)	OCH_3 (3.97)	H_{AB} (3.8)	H_{AB} (3.2)	H_C (6.3)	H_D (7.4)	H_E (6.6)
H_D	7.84		no effect						
H_E	6.62		8.9	7.3					
H_C	6.30	trace			6.8				
OCH_3	4.09						30.6		
OCH_3	4.02								40.0
OCH_3	3.97								44.6
H	3.8					19.0		2.6	
H	3.2				11.3				
$OCOCH_3$	2.15						3.0		

[a] obsd values recorded as percent of N_{max}.

Scheme V[a]



[a] a, Ac_2O; b, NBS; c, KOAc, HOAc; d, Bu_3SnH; e, MeOH, H^+.

scrupulous pretreatment of the Pyrex reaction tubes. Hence, the liberated naphthocyclobutenol simply rearranged to aldehyde **40**. Alkyl ether **31** was thermally more stable than the other derivatives in the series. When heated to 220 °C in the presence of *N*-phenylmaleimide, **31** underwent cycloaddition to form adduct **41**, in low yield. The adduct was characterized by its NMR which included the expected shift of the benzylic methine from a cyclobutyl value to a cyclohexyl (5.28 to 5.63) and its high-resolution mass spectrum which included a significant M^+ of 533.2235. A minor product from this reaction, which became the principal isolated product when the reaction time was extended from 4 to 24 h, was the result of the elimination of 2-(trimethylsilyl)ethanol, the alkene **42**. It was characterized by its NMR which had a characterisitic vinyl singlet δ 8.04 and its high-resolution mass spectrum with an M^+ of 415.144 3 (calcd 415.1420). The success of this step suggests that a complete synthesis of the aureolic acid aglycone might be developed via the naphthocyclobutene approach. At this time, however, the temperature conditions for ring opening of **31** are too high for the survival of our sugar-derived dienophiles. Hence, an alternate construction of the aromatic portion of the aglycone is underway in our laboratory.

Experimental Section

Melting points are uncorrected and were determined on Fisher-Johns melting point apparatus. NMR spectra were taken on a Varian XL-100 instrument at Fordham University, a Bruker WM 360 at Penn State for NOEDs, and a Bruker WM 500 at Yale. H NMR spectra were recorded in $CDCl_3$ with Me_4Si as internal standard; IR spectra were recorded in $CHCl_3$ on a Perkin Elmer 710B spectrometer. Elemental analyses were done by Spang Microanalytical Lab., Eagle Harbor, MI. High-resolution mass spectra were determined by the Mass Spectrometry Center of the University of Pennsylvania. Silica Gel 60 (70–230 mesh) (E Merck) and Florisil (60–100 mesh, Sigma) were used for column chromatography. For analytical and preparative TLC, Silica Gel 60 PF_{254} (E Merck) was used. Chromatotron plates were prepared by using Kieselgel 60 PF_{254} gipshalting (E Merck).

CCl_4 was freshly distilled from P_2O_5. THF was first distilled from $LiAlH_4$ followed by distillation from potassium benzophenone ketyl. Benzene was dried over sodium metal, whereas ether was distilled from $LiAlH_4$ (after preliminary drying over $MgSO_4$ followed by CaH_2). Photobrominations used GE EBV no. 2 photoflood lamps.

In some experiments when 1 or 1.2 equiv of NBS was used, a small quantity of the starting material remained unchanged.

Dimethyl 8-Oxo-1,2,2a,3,8,8a-hexahydrocyclobuta[*b*]naphthalene-2a,8a-dicarboxylate (9). Dry diisopropylamine (13.2 mL, 0.094 mol) was added to a 1-L 3-necked flask under N_2 and equipped with septum inlets. The flask was cooled to 0–5 °C and BuLi in hexane (90 mL, 1.1 M) was added dropwise over 15 min. The resulting LDA solution was stirred for an additional 30 min and was brought to −78 °C, and dry THF (250 mL) was slowly added. Dimethyl *trans*-1-2-cyclobutanedicarboxylate (**5**, 7.7 g, 0.045 mol) in 20 mL of dry THF was added dropwise over 15 min. The orange dianion solution was stirred at −78 °C for 30 min. The bromo ester **8** (10.63 g, 0.046 mol) in 10 mL of THF was added dropwise. The mixture was stirred at −78 °C for 6 h and quenched by addition of 25 mL of 1:1 HOAc:H_2O. The mixture was extracted with ether, and the extract was washed with brine and dried. The residue left after evaporation of the solvent was chromatographed on Florisil eluting with 5% EtOAc:petroleum ether to give 8.8 g (69%) of of the compound **9**: mp 83–85 °C; IR 3040, 2970, 1740, 1685, 1610, 1290, 1260, 1230, 1130 cm^{-1}; NMR δ 7.98 (d, J = 7 Hz, 1 H), 7.40 (m, 3 H), 3.76 (s, 3 H), 3.70 (s, 3 H), 3.46 (half of AB quartet, J = 16 Hz, 1 H), 3.33 (m, 1 H), 3.00 (half of AB quartet, J = 16 Hz, 1 H), 2916 (m, 3 H); mass spectrum, m/z 288 (M^+), 229, 170.

8-Oxo-1,2,2a,3,8,8a-hexahydrocyclobuta[*b*]naphthalene-2a-carboxylic Acid (10). A 100-mL round-bottomed flask under an N_2 atmosphere containing diester **9** (300 mg, 1.0 mmol) and a mixture of HOAc:H_2O:H_2SO_4 in the ratio 7:5:1 (39 mL) was heated at 100 °C for 16 h. The solution was cooled and poured into ice and water. Ethyl acetate (100 mL) was added and most of the acid was carefully neutralized with solid $NaHCO_3$ (pH 5.0). The mixture was extracted with ethyl acetate and the extract was washed with brine and water and dried (Na_2SO_4). After removal of solvent under vacuum, the residue was purified by PLC, eluting with 20% EtOAc/$CHCl_3$, to afford 0.204 g (91%) of acid **10**: IR

broad bands at 2950, 1700, 1675, 1275 cm^{-1}; NMR δ 11.50 (s, br, 1 H), 7.86 (d, J = 8 Hz, 1 H), 7.40 (m, 3 H), 3.60 (m, 1 H), 3.28 (half of AB quartet, J = 16 Hz, 1 H), 2.98 (half of ABq, J = 16 Hz, 1 H), 2.54 (m, 2 H), 2.10 (m, 2 H); mass spectrum, m/z 216 (M^+), 188.

3-Bromo-8-oxo-1,2,2a,3,8,8a-hexahydrocyclobuta[*b*]-naphthalene-2a-carboxylic Acid (11). To the solution of the keto acid **10** (0.62 g, 2.8 mmol) in 40 mL of dry CCl_4 in a dry 50-mL round-bottomed flask under N_2 was added NBS (0.525 g, 2.9 mmol) and 10 mg of $(PhCOO)_2$. The contents was refluxed and also irradiated for 1.5 h. The reaction was followed by TLC ($CHCl_3$:MeOH/98:2). The reaction mixture was cooled and the precipitated succinimide was collected and washed with CCl_4. The filtrate was washed with cold water and dried over Na_2SO_4. Removal of the solvent gave 0.694 g (82%) of **11** which was labile and was used in the next step without further purification: NMR δ 9.0 (s, br, 1 H), 7.96 (m, 1 H), 7.45 (m, 3 H), 5.94 (s, 0.17 H), 5.58 (s, 0.83 H), 4.64 (m, 1 H), 2.7 (m, 2 H), 2.3 (m, 3 H).

8-Hydroxy-1,2-dihydrocyclobuta[*b*]naphthalene (12). A solution of bromo carboxylic acid **11** (0.234 g, 0.8 mmol) in distilled acetonitrile (35 mL) under N_2 was treated with 2 g of silica gel and then with Et_3N (0.5 mL). The mixture was stirred at room temperature for 1 h and was refluxed for 3 h. The mixture was filtered and the silica gel was washed with CH_3CN. The combined filtrate was evaporated in vacuo and the residue was taken up in ether. The ether solution was washed with cold 5% HCl, cold water, cold $NaHCO_3$, and brine and dried. Removal of the solvent under vacuum gave 0.113 g (83%) of the naphthol **12**: IR 3550, 3300 (br), 2920, 1600, 1410, 1280, 1260, 1090 cm^{-1}; NMR δ 8.08 (m, 1 H), 7.7 (m, 1 H), 7.34 (m, 2 H) 7.08 (s, 1 H), 5.22 (b, 1 H), 3.24 (s, 4 H).

8-Methoxy-1,2-dihydrocyclobuta[*b*]naphthalene (13). To a solution of the naphthol **12** (170 mg, 1 mmol) at 0 °C in 2 mL of dry DME in a 25-mL two-necked flask under nitrogen was added K-O-*t*-Bu (124 mg, 1.1 equiv). The solution at 0 °C was treated with 90 mL of FSO_3CH_3 followed by 80 mL after 20 min. The reaction mixture was poured onto ice and 10% NaOH solution (20 mL), and the mixture was extracted with CH_2Cl_2. The extract was washed with brine, dried over sodium sulfate, and concentrated under reduced pressure to yield 99 mg (54%) of **13**: IR 2910, 1585, 1320, 1270, 1100 cm^{-1}; NMR δ 8.14 (m, 1 H), 7.68 (m, 1 H), 7.35 (m, 2 H), 7.04 (s, 1 H, 3-CH), 4.04 (s, 3 H), 3.50 (m, 2 H), 3.28 (m, 2 H).

1-Acetoxy-8-methoxy-1,2-dihydrocyclobuta[*b*]naphthalene (24). To a solution of methyl ether **13** (92 mg, 0.5 mmol) in 10 mL of dry CCl_4 in a 25-mL two-necked dry flask, was added NBS (98 mg 1.1 equiv, 6 mmol). The mixture was refluxed gently and simultaneously irradiated for about 45 min. When no more starting material was left, the contents were cooled and KOAc (0.5 g) and glacial acetic acid (5 mL) were added. The mixture was refluxed for 1.5 h and was poured onto ice water. The mixture was extracted with ether. The ether solution was thoroughly washed with $NaHCO_3$ and brine and dried. The solvent was distilled and the residue was column chromatographed over Florisil eluting with ethyl acetate/petroleum ether (2:8) to give 74 mg (63%) of **24**: NMR δ 8.14 (m, 1 H), 7.66 (m, 1 H), 7.35 (m, 2 H), 7.06 (s, 1 H), 6.22 (m, X of ABX, 1 H, H of C-1), 4.04 (s, 3 H), 3.8, 3.2 (m, A and B of ABX, 2 H, H's of C-2), 2.08 (s, 3 H).

1,8-Dimethoxy-1,2-dihydrocyclobuta[*b*]naphthalene (25). To a solution of the methyl ether **13** (50 mg, 0.27 mmol) in 10 mL of dry CCl_4 was added NBS (54 mg, 1.1 equiv) and the mixture was gently refluxed and simultaneously irradiated as above. After the evaporation of CCl_4 under N_2, methanol (5 mL) was added and the mixture was gently refluxed for 3 h. Methanol was distilled in vacuo and the residue was purified on a silica gel PLC plate to yield 26 mg (45%) of **25**: NMR δ 8.16 (m, 1 H), 7.68 (m, 1 H), 7.36 (m, 2 H), 7.06 (s, 1 H), 5.24 (mX of ABX, 1 H, H of C-1), 4.14 (s, 3 H), 3.40 (s superimposed on m, 5 H, OCH_3 and A and B protons of ABX).

Methyl 4,6-Dimethoxy-3-bromo-2-(bromomethyl)benzoate (18). To a solution of methyl 2,4-dimethylorsellinate (4.2 g, 0.02 mol) in 100 mL of dry CCl_4, maintained in a nitrogen atmosphere, was added *N*-bromosuccinimide (2.6 g, 1.1 equiv). The mixture was refluxed without any peroxide or proton source for about 45 min, until there was no more starting material detectable by TLC. The flask was cooled and additional NBS (3.6 g, 1.1 equiv) was added. The mixture was subjected to photolysis and simultaneously refluxed for 45 min. The flask was cooled and succinimide which separated was filtered and washed with a small quantity of CCl_4. The filtrate was evaporated and the residue was crystallized from methanol to give colorless shining crystals: mp 117 °C (7.1 g 97%) (lit.[14] mp 118.5–119 °C); NMR δ 6.44 (s, 1 H), 4.66 (s, 2 H, CH_2), 3.96, 3.94 (each s, 9 H 3 OCH_3).

In some experiments, prior to the photolysis step, the intermediate nuclear brominated compound **18b** was isolated: NMR δ 6.34 (s, 1 H), 3.88, 3.82 (each s, 6 H, 2 OCH_3), 2.36 (s, 3 H, CH_3).

Dimethyl 4-Bromo-5,7-dimethoxy-8-oxo-1,2,2a,3,8,8a-hexahydrocyclobuta[*b*]naphthalene-2a,8a-dicarboxylate (19). Diisopropylamine (3.9 mL, 0.028 mol) was placed in a cooled (−20 °C) flame dried 250-mL two-necked round-bottomed flask. BuLi in hexane (21.5 mL, 0.026 mol) was added to the stirred solution dropwise over a period of 20 min. After the addition, stirring was continued for a further 0.5 h. The contents was cooled to −78 °C and the LDA solution was diluted with 75 mL of absolute THF by slow addition, taking care that the temperature did not rise above −20 °C. Dimethyl *trans*-cyclobutane-1,2-dicarboxylate (2.41 g, 0.014 mol) in 15 mL of absolute THF was added dropwise with stirring and efficient cooling over a 0.5-h period. The contents were stirred for 0.75 h and a solution of methyl 4,6-dimethyl-3-bromo-2-(bromomethyl)benzoate (3.68 g, 0.01 mmol) in 25 mL of absolute THF was added dropwise over a 0.5-h period. The mixture was stirred at −78 °C for 24 h, was slowly brought to 0 °C, and was quenched with acetic acid:H_2O (1:2, 20 mL). The mixture was thoroughly extracted with ethyl acetate and the combined extracts were washed with sodium carbonate and brine and dried ($MgSO_4$). Upon concentration and cooling a pale yellow solid separated (2.29 g, 82%), which was recrystallized from EtOAc:petroleum ether: mp 208–10 °C; IR 1740, 1665 cm^{-1}; NMR δ 6.46 (s, 1 H), 3.98, 3.90, 3.72, 3.68 (each s, 12 H, 4 OCH_3), 3.34 (m, 6 H, 3 CH_2); mass spectrum, exact mass calcd for $C_{18}H_{19}O_7Br$ m/z 426.0313, 428.0293, found m/z 426.0323, 428.0303.

4-Bromo-5,7-dimethoxy-8-oxo-1,2,2a,3,8,8a-hexahydrocyclobuta[*b*]naphthalene-2a-carboxylic Acid (20). A solution of dimethyl ester **19** (3.0 g) in 130 mL of a mixture of HOAc:H_2O:concentrated H_2OSO_4 (7:5:1) under N_2 was refluxed at 110–115 °C for 36 h. The mixture was cooled and poured slowly with stirring onto ice in a 1-L beaker. Much of the acid was neutralized with solid $NaHCO_3$ after covering the solution with a layer of EtOAc to avoid frothing, but still keeping the pH at 5.0. The aqueous phase was repeatedly extracted with EtoAc. The combined extract was washed with brine, dried, and concentrated under reduced pressure. The residues was absorbed on silica gel and chromatographed by first eluting with chloroform and then with 5% MeOH–$CHCl_3$, affording the acid **20** (1.99 g, 80%): mp 193–194 °C; IR 3535, 1720, 1680, 1580 cm^{-1}; NMR δ 10.06 (br s, 1 H, COOH), 6.40 (s, 1 H, aromatic), 3.968 3.85 (6 H, 2 OCH_3), 3.7, 3.06 (m, 3 H), 2.5 (m, 2 H), 2.08 (s, 2 H); mass spectrum, exact mass calcd for $C_{15}H_{15}O_5Br$ m/z 354.0102, 365.0082, found m/z 354.0095, 356.0040.

It was found that if this hydrolytic decarboxylation was carried out for a lesser time, the work up of an aliquot showed two spots of polar compounds, presumably two acids, one monocarboxylic and the other dicarboxylic acid.

4-Bromo-5,7-dimethoxy-8-hydroxy-1,2-dihydrocyclobuta-[*b*]naphthalene (22). To a solution of naphthocyclobutene-carboxylic acid **20** (1.0 g, 2.8 mmol) in 250 mL of dry CCl_4 under N_2 was added NBS (0.56 g, 1.1 equiv) and the mixture was simultaneously irradiated and refluxed for 1 h. The mixture was cooled and succinimide which separated was filtered and washed with CCl_4. The filtrate was evaporated in vacuo and the residue was dissolved in 100 mL of CH_3CN. To this solution was added silica gel (3 g) and the mixture was refluxed under N_2 for 3 h. The mixture was cooled and silica gel was collected and washed with CH_3CN. The filtrate was evaporated, and the residue was taken up in EtOAc. The organic phase was washed with $NaHCO_3$ and brine, dried, and chromatographed on silica gel, eluting with ethyl acetate:petroleum ether (3:7) to give naphthol **22** (0.65 g, 74%): mp 176–177 °C; IR 3395, 2930, 1610, 1360, 1100 cm^{-1}; NMR δ 9.2

(14) Rana, N. M.; Sargent, M. V.; Elix, J. A. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1992–1995.

(s, 1 H, OH, D_2O exchangable), 7.42 (s, 1 H), 6.54 (s, 1 H) 4.06, 3.96 (6 H, 2 OCH_3), 3.26 (s, 4 H, CH_2CH_2); mass spectrum, exact mass calcd for $C_{14}H_{13}O_3Br$ m/z 308.0048, 310.0028, found m/z 308.0035, 310.0023.

4-Bromo-5,7,8-trimethoxy-1,2-dihydrocyclobuta[*b*]naphthalene (23). To a solution of the naphthol **22** (1.0 g) in 150 mL of dry acetone and anhydrous potassium carbonate (2 g) was added dimethyl sulfate (0.5 mL). The mixture was refluxed under N_2 for 24 h until no starting material was detected by TLC. Potassium carbonate was filtered and washed with acetone. Acetone was evaporated under vacuum and water and 10 mg of K_2CO_3 was added to the residue. The contents were stirred at room temperature for 2 h and extracted with CH_2CL_2. The extract after concentration was passed over a small bed of silica gel and the product was crystallized from ethyl acetate:petrol to give pale yellow crystals (0.94 g, 90%): mp shrinking at 162–165 °C, melting at 197–198 °C; IR 2950, 1585, 1345, 1335, 1120, 1080 cm^{-1}; NMR δ 7.58 (s, 1 H), 6.60 (s, 1 H), 4.08, 3.98, 3.94 (each s, 9 H, 3 OCH_3), 3.6, 3.3 (m, 4 H, CH_2CH_2); mass spectrum, exact mass calcd for $C_{15}H_{15}O_3Br$ m/z 322.0204, 324.0184, found m/z 322.0200, 324.0173.

1-Acetoxy-4-bromo-5,7,8-trimethoxy-1,2-dihydrocyclobuta[*b*]naphthalene (26) and 1-Acetoxy-3-bromo-5,7,8-trimethoxy-1,2-dihydrocyclobuta[*b*]naphthalene (27). In a flame-dried two-necked 50-mL round-bottomed flask flushed with N_2 was placed the trimethoxynaphtho[*b*]cyclobutane **23** (100 mg, 0.0308 mmol) and dry CCl_4 (10 mL) was injected. It was warmed to completely dissolve the compound and cooled and NBS (78 mg, 1.4 equiv) was added. The mixture was gently refluxed and simultaneously irradiated for 45 min. The reaction mixture was cooled, CCl_4 was removed under reduced pressure, and the flask was kept under N_2 atmosphere after the vacuum was broken. To the residue under N_2 were added KOAc (1 g) and acetic acid (5 mL) and the mixture was gently refluxed for 2 h. Acetic acid was removed under vacuum and water was added to the residue. The mixture was extracted with EtOAc. The extract was washed with $NaHCO_3$ and brine and dried over Na_2SO_4. TLC showed two major and one minor product. These were separated by preparative TLC to yield in order of decreasing R_f (EtOAc:petroleum ether 4.5:5.5): **23a** (0.9), **27** (0.8), **26** (0.7).

23a: 15 mg; 13%; mp 172–173 °C; IR 2945, 1615, 1585, 1325, 1110 cm^{-1}; NMR δ 7.04 (d, J = 3 Hz, 1 H), 6.44 (s, J = 3 Hz, 1 H), 4.02, 3.90, 3.88 (each s, 9 H, 3 CH_3), 3.50, 3.20 (m, 4 H, CH_2CH_2); mass spectrum, exact mass calcd for $C_{15}H_{15}O_3Br$ m/z 322.0204, 324.0184, found m/z 322.0185, 324.0057.

27: 35 mg; 30%; mp 166–167 °C; IR 2975, 1740, 1610, 1585, 1310, 1020 cm^{-1}; NMR δ 7.06 (d, J = 3 Hz, 1 H), 6.48 (d, J = 3 Hz, 1 H), 6.22 (m, X of ABX, 1 H, H of C-1), 3.80 (m, A of ABX, 1 H at C-2), 3.20 (m, B of ABX, 1 H, H of C-2), 2.12 (s, 3 H, $OCOCH_3$); mass spectrum, exact mass calcd for $C_{17}H_{17}O_5Br$ m/z 380.0259, 382.0239, found m/z 380.0275, 382.0281.

26: 55 mg; 57%; mp 162–164 °C; IR 3010, 1738, 1585, 1340 cm^{-1} NMR δ 7.64 (s, 1 H), 6.60 (s, 1 H), 6.28 (m, X of ABX, 1 H, H of C-1), 3.80 (m, A of ABX, 1 H at C-2), 3.20 (m, B of ABX, 1 H, H of C-2), 2.14 (s, 3 H, $OCOCH_3$); mass spectrum, exact mass calcd for $C_{17}H_{17}O_5Br$ m/z 380.0259, 382.0239, found m/z 380.0286, 382.0199.

Preparation of 1-Acetoxy-5,7,8-trimethoxy-1,2-dihydrocyclobuta[*b*]naphthalene (28) from 26. To a solution of the acetate **26** (50 mg, 0.13 mmol) in absolute benzene (5 mL) in a dry flask under N_2 was added AIBN (3 mg). Tributyltin hydride (70 μL, 2 equiv) was added into the mixture. The mixture was refluxed in an oil bath under N_2 (100 °C) for 3 h. Benzene was evaporated under vacuum, and the residue was purified by preparative TLC (silica gel) with ethyl acetate:petroleum ether (3:7) to give 37 mg (92%) of **26**: IR 2935, 1735, 1582, 1335, 1320, 1110, 1080 cm^{-1}; NMR δ 6.98 (s, 1 H), 6.64 (d, J = 3 Hz, 1 H), 6.44 (d, J = 3 Hz, 1 H), 6.28 (m, X of ABX, 1 H, H of C-1), 4.08 (s, 3 H, OCH_3), 3.94 (s, 6 H, 2 OCH_3), 3.8 (m, B of ABX, 1 H, H of C-2), 3.20 (m, A of ABX, 1 H, H of C-2), 2.16 (s, 3 H, $OCOCH_3$); mass spectrum, exact mass calcd for $C_{1718}O_5$ m/z 302.1154, found m/z 302.1149.

Preparation of 1-Acetoxy-5,7,8-trimethoxy-1,2-dihydrocyclobuta[*b*]naphthalene (28) from 27. To a solution of the acetate **27** (40 mg, 0.105 mmol) in absolute benzene (5 mL) in a dry flask under N_2 was added AIBN (3 mg). Tributyltin hydride (56 μL, 2 equiv) was added and the mixture was refluxed in an oil bath for 3 h. Workup followed by preparative TLC on silica gel gave 30 mg of **28** (94%) whose NMR was identical to a sample prepared from **26**.

Preparation of 5,7,8-Trimethoxy-1,2-dihydrocyclobuta-[*b*]naphthalene (23b) from 23a (Prepared Above). To a solution of the bromonaphtho[*b*]cyclobutene **23a** (30 mg, 0.092 mmol) in absolute benzene (3 mL) was added tributyltin hydride (50 μL) and the mixture was refluxed for 3 h and worked up as above to give 22 mg (93%) of **23b**: mp 132–134 °C; IR 2940, 1618, 1585, 1325, 1140, 1100 cm^{-1}; NMR δ 6.94 (s, 1 H), 6.64 (d, J = 3 Hz, 1 H), 6.40 (d, J = 3 Hz, 1 H), 4.06, 3.90, 3.86 (each s, 9 H, 3 OCH_3), 3.58 (m, 2 H), 3.24 (m, 2 H); mass spectrum, exact mass calcd for $C_{15}H_{16}O_3$ m/z 244.1099, found m/z 244.1112.

Preparation of 5,7,8-Trimethoxy-1,2-dihydrocyclobuta-[*b*]naphthalene 23b from 23. To a solution of methyl ether **23** (50 mg) in benzene (5 mL) in a dry flask under N_2 was added AIBN (3 mg). To this solution was added tri-*n*-butyltin hydride (85 μL, 2 equiv) and the mixture was refluxed for 3 h. Workup as above gave 34 mg of **23b** (90%), mp 132–133 °C, identical with the sample prepared from **23a**.

1-Acetoxy-5,7,8-trimethoxy-1,2-dihydrocyclobuta[*b*]naphthalene (28) by NBS Acetoxylation and Debromination of the Crude Mixture. To a solution of methyl ether **23** (97 mg, 0.30 mmol) in a dry flask under N_2 in 10 mL of dry CCl_4 was added NBS (75 mg, 1.4 equiv) and the mixture was gently refluxed with simultaneous irradiation for 45 min. After solvent removal KOAc (1 g) and glacial acetic acid (5 mL) were added under N_2 and the mixture was refluxed for 2 h. After the workup as described above the crude product was azeotroped three times with 10 mL of benzene. Then under N_2 was added 10 mL of absolute benzene, followed by AIBN (94 mg). To this mixture was added tri-*n*-butyltin hydride (162 L, 2 equiv) and the solution was refluxed for 3 h. Benzene was removed under vacuum and the residue on TLC showed two spots, one major and one minor. These two compounds were separated on a silica gel preparative TLC plate to afford 12 mg (14%) of **23b**, mp 131–133 °C, and 69 mg (76%) of **28**, identical with samples described above.

1-Hydroxy-5,7,8-trimethoxy-1,2-dihydrocyclobuta[*b*]naphthalene (29). The acetate **28** (133 mg, 0.44 mmol) in absolute THF (20 mL) was cooled to −25 to −23 °C and $LiAlH_4$ (100 mg, 3 mmol) was added carefully. The mixture was stirred at −25 to −23 °C (CCl_4, dry ice) for 4 h. A small scale workup of a test portion showed no acetate. The bulk of the solution at −25 °C was diluted with ether (50 mL) and carefully and slowly quenched with a minimum quantity of saturated solution of sodium sulfate, keeping the temperature of the solution below −20 °C, until the grey color disappeared to give a white bulky precipitate. The ethereal solution was decanted and the residue thoroughly and repeatedly washed with ether. The combined ether extracts were dried over sodium sulfate, which after concentration gave a white solid: 112 mg; 98%; mp 168–169 °C; IR 3630, 2950, 1620, 1585, 1330 cm^{-1}; NMR δ 6.92 (s, 1 H), 6.60 (d, J = 2.5 Hz, 1 H), 6.40 (d, J = 2.5 Hz, 1 H), 5.44 (m, 1 H), 4.20 (s, 3 H, OCH_3), 3.92, 3.90 (6 H, 2 OCH_3), 3.7, 3.1 (m, 2 H); mass spectrum, exact mass calcd for $C_{15}H_{16}O_4$ m/z 260.1048, found m/z 260.1041.

1-(Trimethylsiloxy)-5,7,8-trimethoxy-1,2-dihydrocyclobuta[*b*]napthalene (30). To the hydroxy compound **29** (104 mg, 0.4 mmol) in absolute THF (15 mL) was added dry triethylamine (115 μL, 1.2 equiv of Me_4Si) followed by chlorotrimethylsilane (66 μL, 1.3 equiv). The mixture was stirred at room temperature for 30 h. THF was evaporated and water was added to the residue. The product was extracted with ether and the extract washed with brine and dried over Na_2SO_4. The crude product was purified by rapid preparative TLC on a Chromatotron. The fastest moving fraction was the silyl ether which was eluted with ethyl acetate:petroleum ether (9:1):130 mg; 98%; NMR δ 6.94 (s, 1 H), 6.60 (d, J = 2.5 Hz, 1 H), 6.40 (d, J = 2.5 Hz, 1 H), 5.52 (m, X of ABX, 1 H, H of C-1), 4.12, 3.88, 3.84 (each s, 9 H, 3 OCH_3), 3.8 (m, A of ABX, 1 H, H of C-2), 3.2 (m, B of ABX, 1 H, H of C-2), 0.8 (s, 9 H, $(CH_3)_3Si$); mass spectrum, exact mass calcd for $C_{18}H_{24}O_4Si$ m/z 332.1444, found m/z 332.1419.

4-Bromo-5,7-dimethoxy-8-acetoxy-1,2-dihydrocyclobuta-[*b*]naphthalene (34). To the solution of the phenol **22** (11 mg) in acetic anhydride (freshly distilled over fused sodium acetate, 4 mL) was added 2 drops of pyridine and the mixture was stirred

for about $^1/_2$ h. The solidified product was extracted with EtOAc and the extract washed with $NaHCO_3$ and brine and the solvent evaporated. The residue was crystallized from EtOAc:petroleum ether to afford colorless needles (90 mg, 80%): mp 193–194 °C. Anal. Calcd for $C_{16}H_{15}O_4Br$: C, 54.72; H, 4.30; Br, 22.75. Found: C, 54.84; H, 4.24; Br, 22.72. IR 2915, 2840, 1745, 1610, 1355, 1320, 1100 cm^{-1}; NMR 7.84 (s, 1 H), 6.40 (s, 1 H), 3.98, 3.92 (each s, 6 H, 2 OCH_3), 3.28 (m, 4 H, CH_2CH_2), 2.34 (s, 3 H, $OCOCH_3$).

4-Bromo-1,8-diacetoxy-5,7-dimethoxy-1,2-dihydrocyclobuta[*b*]naphthalene (35). To a solution of the acetate **34** (70 mg, 0.198 mmol) in 20 mL of dry CCl_4 in a 50-mL two-neck flask was added NBS (50 mg, 1.4 equiv). The mixture was gently refluxed and simultaneously irradiated for 1.5 h. Solvent was removed under vacuum and the residue was subsequently kept under N_2. The residue was treated with KOAc (1 g, excess) and glacial acetic acid (5 mL) and gently refluxed for 3 h. The acetic acid was removed under reduced pressure and water was added to the residue. The product was extracted with ethyl acetate which on TLC showed two brown fluorescent spots. These were separated by preparative TLC (silica gel) eluted with ethyl acetate:petroleum ether (4.6) to afford **36**: 15 mg; 18%; NMR δ 8.0 (s, 1 H), 6.62 (s, 1 H), 5.5 (m, X of ABX, 1 H, H on C-2), 4.00, 3.94 (each s, 6 H, 2 OCH_3), 3.6 (m, AB of ABX, 2 H of C-1), 2.36 (s, 3 H, $OCOCH_3$).

35: 36 mg; 44%; IR 2915, 1738, 1600, 1325, 1100 cm^{-1}; NMR δ 7.84 (s, 1 H), 6.56 (s, 1 H), 5.02 (m, X of ABX, 1 H, H of C-2), 3.96, 3.92 (each s, 6 H, 2 OCH_3), 2.75, 2.38 (m, AB of ABX, 2 H on C-2), 2.32, 2.08 (each s, 6 H, 2 $OCOCH_3$); mass spectrum, exact mass calcd for $C_{18}H_{17}O_6Br$ m/z 408.0208, 410.0188, found m/z 408.0244, 410.0189.

1,8-Diacetoxy-5,7-dimethoxy-1,2-dihydrocyclobuta[*b*]naphthalene (37). To a mixture of diacetate **35** (82 mg, 0.20 mmol) and AIBN (3 mg) was added absolute benzene (20 mL), followed by tri-*n*-butyl in hydride (108 μL, 2 equiv). The mixture was refluxed for 48 h. Benzene was removed under vacuum and the residue prep-plated on silica gel (ethyl acetate:petroleum ether, 4:6, 45 mg, to afford **37** and 16 mg of recovered **35**: 85%; mp 144–145 °C; IR 2930, 1740, 1605, 1315, 1100 cm^{-1}; NMR δ 7.24 (s, 1 H), 6.68 (d, J = 3 Hz, 1 H), 6.42 (d, J = 3 Hz, 1 H), 6.04 (m, X of ABX, 1 H, H of C-1), 3.87 (s with m at base, 5 H, OCH_3 and CH_2), 2.34, 2.10 (6 H, 2 $OCOCH_3$); mass spectrum, exact mass calcd for $C_{18}H_{18}O_6$ m/z 330.1103, found m/z 330.1098.

Attempted Synthesis of 1,8-Dihydroxy-5,7-dimethoxy-1,2-dihydrocyclobuta[*b*]naphthalene (33) (Resulting in Formation of 38 and 39). The diacetate **37** prepared above (66 mg. 0.1 mmol) in 10 mL of methanol was treated with *p*-TsOH (1 mg) and the mixture stirred at room temperature for 5 days. The reaction was followed by TLC (EtOAc:petroleum ether, 3:7); first a slower moving spot appeared, then at the end of the third day, a faster moving spot appeared, and starting material still remained. These two products were separated by preparative TLC (silica gel) and characterized as **38** and **39**.

38: 16.5 mg; 48.8%; mp 176–177 °C; IR 3530, 2930, 1745, 1610, 1600, 1325, 1125 cm^{-1}; NMR δ 7.26 (s, 1 H), 6.68 (d, J = 3 Hz, 1 H), 6.44 (d, J = 3 Hz, 1 H), 5.35 (m, X of ABX, 1 H, H on C-1), 3.38 (s, 3 H, OCH_3), 3.7, 3.19 (m, 3 H), 2.38 (3 H, $OCOCH_3$ phenolic); mass spectrum, exact mass calcd for $C_{16}H_{16}O_5$ m/z 288.0998, found m/z 288.1004.

39: semisolid; 17.5 mg; 51.2% (Yields are based on starting material used up in the reaction.); IR 3440, 2930, 2890, 1610, 1300 cm^{-1}; NMR δ 9.98 (s, 1 H, phenolic OH, exchangeable with D_2O), 7.0 (bs, 1 H) 6.62 (d, J = 3 Hz, 1 H), 6.37 (d, J = 3 Hz, 1 H), 4.6 (t, J = 6 Hz, 1 H), 4.00, 3.88 (each s, 6 H, 2 OCH_3), 3.65 (each s, 6 H, OCH_3 of acetal), 2.94 (d, J = 6 Hz); mass spectrum, exact mass calcd for $C_{16}H_{20}O_5$ m/z 292.1311, found m/z 292.1302.

1-(2-(Trimethylsilyl)ethoxy)-5,7,8-trimethoxy-1,2-dihydrocyclobuta[*b*]naphthalene (31). To the solution of the methyl ether **23** (100 mg, 0.309 mmol) in a dry flask 10 mL of CCl_4 and NBS (77 mg, 1.4 equiv) were added and the mixture was subjected to photolysis with simultaneous mild heating for 45 min. To the same solution, after complete bromination, was added trimethylsilylethanol (112 μL, 5 equiv) and the mixture heated gently for 24 h and then left stirring overnight at room temperature. The solvent was removed under vacuum and the residue was taken up in methylene chloride and passed through a small bed of silica gel. The total crude compound on the TLC (ethyl acetate:petroleum ether, 2:8) showed three spots. It was dried in a vacuum desicator and used for debromination.

The crude bromo((trimethylsilyl)ethoxy)naphthocyclobutene (100 mg) was dissolved in 10 mL of absolute benzene and AIBN (5 mg) was added. Tributyltin hydride (84 μL, 2 equiv) was syringed in and the mixture refluxed for 3 h. Benzene was removed under vacuum and the residue was purified on a chromatotron (5% EtOAc:petroleum ether). The second band was isolated to yield 12 mg, 15%, of **31**: NMR δ 6.94 (s, 1 H, 3-H), 6.62 (d, J = 3 Hz, 1 H, 6-H), 5.28 (m, 1 H, 1-H), 4.06 (s, 3 H, OCH_3), 3.84 (s, 3 H, OCH_3), 3.6 (broad m, 2 H, OCH), 0.9 (broad m, 2 H, CH_2Si), 0.4 (s, 9 H, $(CH_3)Si$); mass spectrum, exact mass calcd for $C_{20}H_{28}O_4Si$ m/z 360.1954, found m/z 360.1783.

***cis*-*N*-Phenyl-4-(2-(trimethylsilyl)ethoxy)-5,8-trimethoxy-1,2,3,4-tetrahydro-2,3-anthracenedicarboximide (41) and *cis*-*N*-Phenyl-5,6,8-trimethoxy-1,2-dihydro-2,3-anthracenedicarboximide (42).** In a dry flask were placed a mixture of ((trimethylsilyl)ethoxy)naphthocyclobutene **31** (5 mg) and *N*-phenylmalemide (30 mg, excess) which was heated to 220 °C for 1 h. TLC showed disappearance of the (trimethylsilyl)ethoxy compound and two new spots appeared. The mixture of the products was purified by chromatography with a chromatotron and when the gradient elution reached EtOAc:petroleum ether, 1:9, were isolated 2 mg and 1 mg of **41** and **42**, respectively.

41: δ NMR 7.31–7.54 (m, 5 H, Ph, 1 H, naphth.), 6.73, 6.56 (dd, J = 2.51 Hz, 2 naphth), 5.63 (d, J = 4 Hz, 1 H, OCH), 4.23 (m, 1 H, OCH, A of AA′XX′), 4.01 (s, 3 H, OCH_3), 3.93 (s, 3 H, OCH_3), 3.86 (s, 3 H, OCH_3), 3.53 (m, 1 H, A′ of AA′XX′), 3.33 (m, 3 H, 3C–H?), 3.14 (m, 1 H, C h?), 0.82 (m, 1 H, X of AA′XX′), 0.74 (m, 1 H, X′ of AA′XX′), 0.12 (s, 9 H, Me_3Si); mass spectrum, calcd for $C_{30}H_{55}O_6Si$ 533.2334, found 533.2197.

42: NMR δ 8.04 (d, J = 2 Hz, 1 H, X of ABMX), 7.54–7.32 (M, 6 H, Ph + 1 naphth), 6.71 (d, J = Hz, 1 H naphth), 6.54 (d, J = 2 Hz, 1 H, naphth), 4.01 (s, 3 H, OCH_3), 3.93 (s, 3 H, OCH_3), 3.90 (s, 3 H, OCH_3), 3.74 (M of ABMX, 1 H, CHC=O), 3.49 (A of ABMX, 1 H, CHAr), 3.06 (B of ABMX, 1 H, CHAr); mass spectrum calcd for $C_{25}H_{21}NO_5$ 415.1420, found 415.1443. ***Note***: This ion was also observed with **41**.

Acknowledgment. The research was supported by Grant CA 27116 awarded by the National Cancer Institute, DHHS. The 500-MHz NMR spectra were provided by the Northeast Regional NMR facility at Yale University, supported by NSF Grant CHE 7916210. The NOEDs data was obtained at Penn State by Professor S. M. Weinreb. Useful discussions about experimental conditions were offered by Dr. P. Garratt of University College, London. To all those listed above, we express our appreciation.

Registry No. *trans*-**5**, 7371-67-7; **8**, 2417-73-4; **9**, 90606-47-6; **10**, 90606-48-7; **11**, 90606-49-8; **12**, 82586-21-8; **13**, 82586-22-9; **18**, 58137-74-9; **18b**, 56526-84-2; **19**, 90606-50-1; **20**, 90606-51-2; **22**, 90606-52-3; **23**, 90606-53-4; **23a**, 90606-54-5; **23b**, 90606-55-6; **24**, 90606-56-7; **25**, 90606-57-8; **26**, 90606-58-9; **27**, 90606-59-0; **28**, 90606-60-3; **29**, 90606-61-4; **30**, 90606-62-5; **31**, 90606-63-6; **34**, 90606-64-7; **35**, 90606-65-8; **37**, 90606-66-9; **38**, 90606-67-0; **39**, 90606-68-1; **41**, 90606-69-2; **42**, 90606-70-5; methyl 2,4-dimethylorsellinate, 6110-37-8; *N*-phenylmalemide, 941-69-5.