76-05-1; hexafluoroisopropyl alcohol, 920-66-1; acetone, 67-64-1; α-(trimethylsiloxy)isobutyrophenone, 55418-35-4; α-hydroxyisobutyrophenone, 7473-98-5; benzyl *tert*-butyl ketone, 6721-67-1; mandelic acid acetonide, 6337-34-4; norborneneone ethylene glycol ketal, 31444-18-5; 1-benzoyl-*exo*-2-(trifluoroacetoxy)norbornane, 82027-54-1; *exo*-2-benzoyl-*exo*-6-(trifluoroacetoxy)norbornane, 82027-55-2; 2-phenyl-2-chloropropane, 934-53-2; $PhCH(OCH_2CF_3)COSEt$, 82027-56-3; $PhCH(OCH_2CF_3)CO_2CH_2CF_3$, 82044-33-5; $PhCH(OCH_2CF_3)CO_2H$, 82027-57-4.

Supplementary Material Available: Experimental details for the preparation of mesylates **3** and **5–10** and various solvolyses procedures (6 pages). Ordering information is given on any current masthead page.

Photooxidation of Vitamin K Chromenol Derivatives[1]

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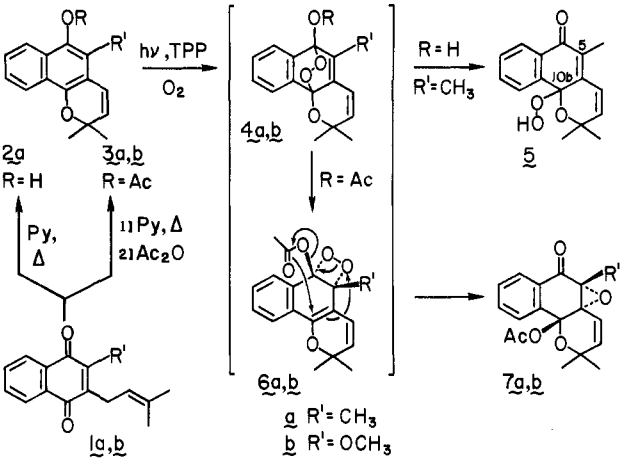
Abstract: The TPP-sensitized photooxidation of the chromenol of menaquinone 1 affords the stable peroxy-*p*-quinol. This oxidation route is blocked in the corresponding chromenol acetates of menaquinone 1 chromenol and *O*-methyllapachol. Photooxidation of these acetates leads to a unique stereoselective 1,4-acetoxy migration and the formation of novel epoxy quinone ketal derivatives. These unstable substances undergo facile hydrolysis reactions to form stable hemiketals in which the chromenol skeleton remains intact. The menaquinone 1 chromanol acetate undergoes the same type of 1,4-acetoxy migration. However, hydrolysis of this epoxy quinone ketal leads to an unstable hemiketal which undergoes pyran ring opening to form the epoxy quinone.

Vitamin K is involved in a wide variety of important biological processes such as oxidative phosphorylation,[2] blood clotting,[3] active transport of amino acids[4] and antibiotics, heme and uracil biosynthesis, and perhaps even bacterial genetic regulation.[5] Several of these processes either require molecular oxygen[2,3] or are disrupted by molecular oxygen upon exposure to ultraviolet light.[2] Consequently, it is surprising that so little information is available bearing on the reactions of vitamin K and its derivatives with oxygen. Recently, we[6] have extended the observations of Snyder and Rapoport[7] dealing with the photooxidative cleavage of vitamin K side chains. In this report, the chemistry associated with the photooxidation of vitamin K chromenol and its derivatives is described.

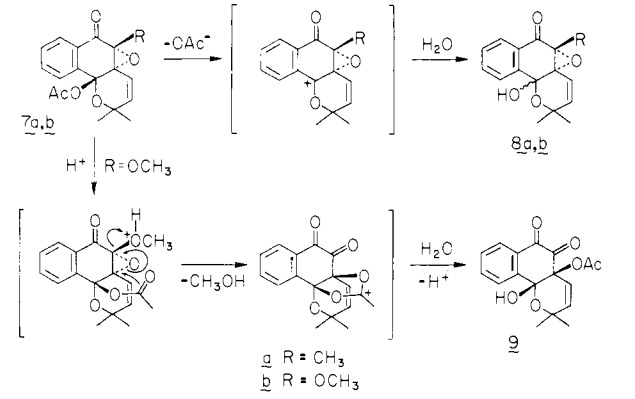
Results

Both menaquinone 1 (MK-1, **1a**) and *O*-methyllapachol (**1b**) undergo a facile base-catalyzed cyclization to chromenols **2a** and **2b**, respectively (Scheme I). These chromenol derivatives with gem-dimethyl groups at the 2-position have been selected for this study, since they do not give rise to the trivial product isomers associated with the long-chain analogues in which an asymmetric carbon atom exists at this position. Tetraphenylporphine- (TPP-) sensitized photooxidation of **2a** in acetone affords a single crystalline hydroperoxide, mp 140–141 °C, in 85% yield. That this substance is the 10b-hydroperoxide **5** rather than the isomeric 5-hydroperoxide (Scheme I) was confirmed by spectroscopic data: IR ($CHCl_3$) 1650 cm^{-1}; ^1H NMR ($CDCl_3$–Me_2SO-d_6) $>C(CH_3)_2$ δ 1.42 and 1.70, $=CCH_3$ 2.10; $\lambda_{max}^{CH_3CN}$ 318 nm (ϵ 10 000).[8]

Scheme I



Scheme II



Under the same conditions, the acetates of these chromenols, **3a** and **b**, give rise to the epoxy ketones **7a** and **b**, respectively, in nearly quantitative yield (Scheme I). Both of these epoxy ketones are quite labile. Fortunately **7b** can be obtained in pure

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(4) Madden, J. J.; Boatwright, D. T.; Jagger, J. *Photochem. Photobiol.* **1981**, *33*, 305.

(5) Haddock, B. A.; Jones, C. W. *Bacteriol. Rev.* **1977**, *41*, 47. Taber, H. "Vitamin K Metabolism and Vitamin-K-dependent Proteins"; Suttie, J. W., Ed.; University Park Press, Baltimore, 1979; p 177.

(6) Wilson, R. M.; Walsh, T. F.; Gee, S. K. *Tetrahedron Lett.* **1980**, 3459.

(7) Snyder, C. D.; Rapoport, H. *J. Am. Chem. Soc.* **1969**, *91*, 731.

(8) The phenyl dienone, 1-phenyl-5-methyl-2,4-hexadien-1-one, exhibits λ_{max}^{EtOH} 315 nm (ϵ 25 000). Montillier, J.-P.; Dreux, J. *Bull. Soc. Chim. Fr.* **1969**, 3638.

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Table I. Comparison of the ^{1}H NMR Properties of Epoxy Ketones **7a** and **7b**

	assignments, δ					
						
7a	1.45 (s) 1.60 (s)	1.74 (s)		1.80 (s)	5.80 (d, J = 10 Hz) 6.45 (d, J = 10 Hz)	7.35–8.00 (m)
7b	1.50 (s) 1.60 (s)	1.80 (s)	3.85 (s)		5.95 (d, J = 10 Hz) 6.45 (d, J = 10 Hz)	7.35–8.15 (m)

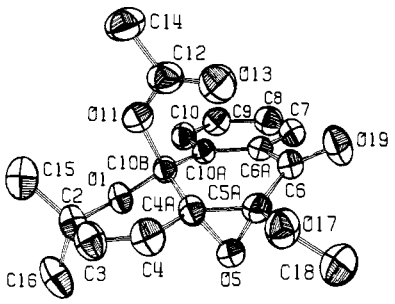

Figure 1. ORTEP drawing of **7b**.

form by direct crystallization from concentrates of the crude reaction mixture (mp 108–108.5 °C) and has spectroscopic properties consistent with the proposed structure: IR ($CHCl_3$) 1730, 1710 cm^{-1}; ^{1}H NMR as outlined in Table I; m/e M^+ = 330. That **7a** is closely related to **7b** is indicated by the similarity of their spectroscopic parameters obtained from freshly prepared samples: **7a**, IR ($CHCl_3$) 1740, 1710 cm^{-1}; ^{1}H NMR as outlined in Table I; m/e M^+ = 314. Unfortunately, these data do not define unequivocally the relative positions and sterochemistry of the acetoxy and epoxy functional groups. Therefore, an X-ray crystallographic structure determination was conducted with **7b**. The structure of **7b** was obtained without difficulty when direct methods were used and is illustrated in Figure 1. The atomic positions from the final refinement are available in Table A,[9] the bond lengths and angles calculated from these appear in Tables B and C, the root-mean-square displacements in Table D, the anisotropic thermal parameters in Table E, the hydrogen fractional atomic positional parameters in Table F, the least-squares planes in Table G, and the observed and calculated structure factors in Table H. These data permit the unequivocal assignment of the epoxide to ring positions **4a** and **5a** and the acetoxy group to position **10b**, as well as the assignment of a trans stereochemistry between the acetoxy and epoxy functional groups in **7b**. The structure of **7a** follows by analogy to that of **7b**. The absence of any detectable cis isomer of **7a** or **b** indicates that these substances arise in a highly stereoselective process.

The instability of the epoxy ketones **7a,b** is due primarily to the solvolytic lability of the acetoxy groups. Exposure of the acetates to water or alcohols leads to epimeric mixtures of alcohols **8a,b** or the corresponding ethers (Scheme II). The stereochemistry of these alcohols has been assigned by comparison of the chemical shifts of their gem-dimethyl groups with those in the trans-acetoxy analogues **7a,b** (Table II). In the trans isomers these methyl groups are more nearly magnetically equivalent. When this ring juncture is cis, one of these methyl groups is forced into a more shielding region over the aromatic nucleus and a significantly greater difference in the chemical shifts of the two methyl groups results.

An additional source of instability in the methoxy analogue **7b** is the hydrolytic cleavage of the epoxide ring upon exposure to silica gel to form the diketone **9** (Scheme II). The structure of **9** is based upon the following considerations: (1) the NMR data indicate the loss of the methoxy group and the presence of three carbonyl groups (^{13}C NMR ($CDCl_3$) δ 170.59, 180.56, 183.24);

(9) See paragraph at end of paper regarding supplementary material; this includes all tables designated by an alphabetic character.

Table II. Correlation of the *gem*-Dimethyl Chemical Shifts of 8a and 8b with Their Stereochemistry

	δ		Δδ, ppm
7a (trans)	1.45	1.60	0.15
7b (trans)	1.50	1.60	0.10
trans-**8a**	1.40	1.50	0.10
trans-**8b**	1.45	1.55	0.10
cis-**8a**	1.25	1.60	0.35
cis-**8b**	1.30	1.65	0.35

(2) the IR bands indicate the presence of carbonyl groups and a hydroxy group (3480, 1740 (br), and 1700 cm^{-1}); (3) the large difference in the chemical shifts of gem-dimethyl groups (δ 1.05 and 1.45, Δδ = 0.40 ppm) indicates a cis ring juncture; and (4) the hydrolytic stability of **9** relative to **7b** indicates that the acetoxy group is adjacent to the carbonyl rather than adjacent to the aromatic nucleus. Finally, the structure of **9** is consistent with mechanistic considerations involving the cleavage of the epoxide ring (vide infra).

The chromanol acetate **10** also has been subjected to photooxidation conditions similar to those used for the chromenol acetates **7a,b**. Here again it was possible to isolate a rearranged acetate **11** (mp 91–93 °C): IR ($CDCl_3$) 1735, 1685 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.40 (3 H, s), 1.50 (3 H, s), 1.65 (3 H, s), 1.85 (3 H, s). Upon exposure to water **11** undergoes hydrolytic ring cleavage to the epoxyquinone **13**: IR ($CHCl_3$) 3600–3500, 1675 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.25 (6 H, s), 1.75 (3 H, s); m/e M^+ = 274.

Discussion

Theoretical arguments have been presented[10,11] which suggest that the initial adduct between singlet oxygen and naphthohydroquinone derivatives might be 1,4-endoperoxides analogous to **4** in Scheme I. In the vitamin K chromenol system when R = H, such an endoperoxide (**4a**) would be expected to undergo fragmentation to the hydroperoxide **5**.[12-14] It is also possible that **5** is formed directly from the phenol **2a** without passing through the endoperoxide **4a**. Base-[15] and light-catalyzed[12] oxygenation of hindered phenols frequently afford related hydroperoxides. Low-temperature photooxidation of tocopherol also has been observed to yield an analogous hydroperoxy-*p*-quinol.[13]

When hydroperoxide formation is blocked through esterification of the phenolic hydroxy (**4a** and **4b**, R = Ac), the 1,4-endoperoxide might rearrange to the dioxetane **6** (Scheme I).[16] Intramolecular cleavage of this dioxetane by the nucleophilic enol ether double

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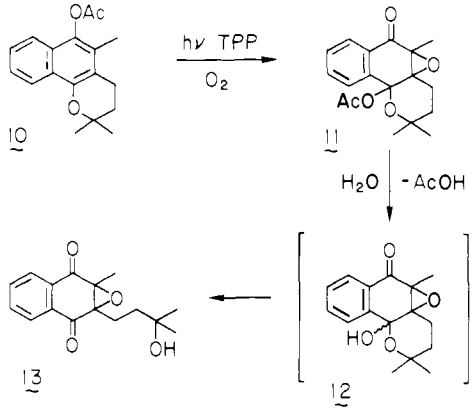
(16) Schaap, A. P; Burns, P. A.; Zaklika, K. A. *J. Am. Chem. Soc.* **1977**, *99*, 1270. In this work the endoperoxide **4b** could not be detected by NMR in the crude reaction mixture at room temperature. No effort was made to observe this intermediate at low temperature.

Scheme III



bond in **6** then could trigger the rearrangement to **7**. As illustrated in Scheme I, such a 1,4-acetoxy migration dictates that the acetoxy group be delivered to the opposite side of the ring from that of the epoxy oxygen. Thus, the exclusive formation of the trans isomer of **7** is nicely rationalized by this mechanism. This type of 1,4 migration may not be restricted to the acetoxy analogue, as an apparently related 1,4-methoxy shift recently has been observed in the photooxidation of naphthohydroquinone dimethyl ethers.[10]

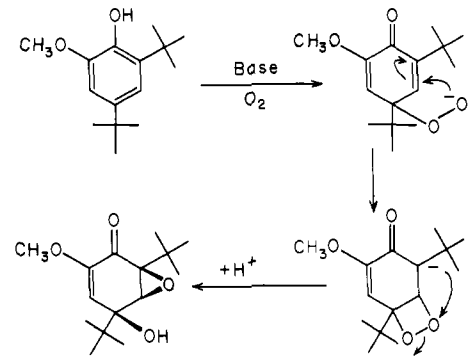
The solvolyses of the acetates **7** to the alcohols **8** are not particularly surprising as this process can proceed through a highly stabilized carbocation as depicted in Scheme II. The formation of the two epimeric alcohols indicates that there is not a strong steric or electronic preference for one epimer over the other. This observation supports a concerted or tight-ion pair mechanism for the aforementioned 1,4-acetoxy migration, since any mechanism which proceeds through the free carbocation intermediate in Scheme II would be expected to afford epimeric mixtures of acetates.

It is interesting to contrast this 1,4-migration mechanism with other mechanisms for forming α-epoxy alcohols by the oxidation of phenols. The best documented of these is the base-catalyzed mechanism outlined in Scheme IV.[15,17] This route can afford analogous epoxy alcohols, but the epoxy and alcohol functional groups bear a cis relationship to each other. The correlation of basic oxygenation leading to cis epoxy alcohols and photooxygenation leading to trans epoxy alcohol derivatives or epimeric epoxy alcohols may be of use in determining the origins of related molecules formed in biological systems.[18]

The formation of the novel diketone **9** can be rationalized through an acetoxy-assisted cleavage of the epoxide ring (Scheme II). Such an assisted cleavage accounts for the cis ring juncture observed in the product. The cyclic carbocation intermediate formed in the cleavage step might solvolyze in either of two directions to form **9** or the isomer of **9** in which the hydroxy and acetoxy groups are interchanged. The latter isomer would be unstable on silica gel and, presumably, would not be isolated.

The stability of the hemiketal units in the isomers of **8** and **9** is worthy of note. In no instance have these functional groups been observed to open to the ketones. It was felt that this stability may be due to the geometric constraints imposed by the cis double bond. This hypothesis has been confirmed by the photooxidation of the chromanol **10** (Scheme III). Hydrolysis of the resulting epoxy ketone **11** affords no detectable hemiketal **12**. Apparently, **12** rapidly opens to the epoxy quinone **13**. It is interesting to note that epoxy quinones analogous to **13** are formed in the photooxidation of tocopherol which also lacks this stabilizing double bond.[13]

Scheme IV



In conclusion, this work has demonstrated that the chromenols of vitamin K and their derivatives are extremely susceptible to photooxidation. The photoproducts which result appear to be more stable than the analogous photooxidation products formed from vitamin E. The biological significance of these unusual photooxidation products and the associated chemistry described here is not clear at present. However, these observations do add a significant dimension to vitamin K chemistry which must be considered in future work in this area.

Experimental Section

General Procedures. Melting points were determined with a Mettler FP-2 hot-stage apparatus equipped with a polarizing microscope and are uncorrected. Proton magnetic resonance spectra were recorded with a Varian Associates T-60. Carbon magnetic resonance spectra were recorded on a Varian Associates CFT-20, FT-80A, or JEOL FX 90-Q spectrometer. Chemical shifts are reported in parts per million (δ) downfield from tetramethylsilane as an internal standard, and apparent coupling constants (J) are in hertz. Infrared spectra were recorded with a Perkin-Elmer Model 599 grating spectrophotometer. Mass spectra were determined with a Hitachi (Perkin-Elmer) RMU-7 spectrometer at 70 eV. Electronic spectra were recorded on a Cary Model 14 spectrophotometer. Dye-sensitized photooxidations were conducted in Griffin-Worden pressure vessels (Kontes) fitted with gas inlet and pressure safety relief valves. The tubes were suspended in an ice-water bath approximately 25 cm below a 400-W sodium vapor lamp (G.E. Lucalox bulb LU400). Analytical and preparative thin-layer chromatography was done with E. Merck silica gel 60 F_{254} precoated plates. Column chromatography was done with E. Merck silica gel 60 (230–400 mesh). Flash chromatography was performed according to Still, Kahn, and Mitra.[19] Microanalyses were determined by Galbraith laboratories, Inc., Knoxville, TN. Removal of solvents under reduced pressure was conducted by using a Büchi rotary evaporator with a water aspirator vacuum. Magnesium sulfate was used as a drying agent.

Dye-Sensitized Photooxidation of Menaquinone 1 Chromenol (2a). Preparation of Hydroperoxy Dienone 5. A solution of 0.204 g (0.85 mmol) of menaquinone 1 (**1a**)[20] was refluxed under nitrogen in 25 mL of pyridine[21] for 3 h. When the solution was cooled, the pyridine was evaporated in vacuo to afford a brown oil which was purified on a silica gel flash chromatography column to afford menaquinone 1 chromenol (**2a**) (0.173 g, 0.72 mmol, 84%) as a light brown oil[22] which was used directly in the next step.

A solution containing 0.173 g (0.72 mmol) of the chromenol **2a** and 0.001 g of *meso*-tetraphenylporphine in 30 mL of acetone was placed in a Griffin-Worden pressure tube, pressurized to 50 psi with oxygen, chilled to 5 °C with a ice-water bath, and irradiated with a 400-W sodium vapor lamp for 3.5 h. The reaction mixture was concentrated to an oil which solidified upon standing. The product was then recrystallized from chloroform–pentane to afford the hydroperoxy dienone **5** (0.167 g, 0.62 mmol, 86%) as white crystals: mp 140–141 °C dec; IR ($CHCl_3$) 3520, 3020, 1655, 1600, 1295 cm^{-1}; ^1H NMR ($CDCl_3$) δ 10.45 (1 H, br s), 8.25–7.35 (4 H, m), 6.72 (1 H, d, J = 10 Hz), 6.30 (1 H, d, J = 10 Hz), 2.10 (3 H, s), 1.70 (3 H, s), 1.40 (3 H, s); ^{13}C NMR (Me_2SO-d_6) δ

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(18) A third mechanism involving diepoxides has been proposed for the photooxygenation of phenolic ethers,[12] but since neither the structure nor the stereochemistry of the epoxy alcohol product has been established with certainty, it is not possible to assess the significance of this mechanism.

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184.19, 143.55, 143.35, 142.56, 132.50, 128.50, 128.11, 125.46, 125.19, 124.98, 118.73, 87.77, 73.23, 30.46, 28.60, 9.86; mass spectrum, *m/e* 272 (M^+), 254, 239, 223 (base), 210, 197. Anal. Calcd for $C_{16}H_{16}O_4$: C, 70.58; H, 5.92. Found: C, 70.72; H, 6.03.

Preparation of 2,2,5-Trimethyl-2*H*-naphtho[1,2-*b*]pyran-6-yl Acetate (3a). A solution of 0.918 g (3.82 mmol) of menaquinone 1 (**1a**)[20] in 20 mL of pyridine was stirred and refluxed under nitrogen for 3.5 h. Acetic anhydride (3.0 mL, 3.25 g, 31.8 mmol) was added and the mixture stirred at reflux for an additional 30 min. When the solution was cooled, most of the pyridine and excess acetic anhydride were removed under reduced pressure to yield a viscous brown oil. The residual oil was then purified on a silica gel flash chromatography column eluted with ethyl acetate–pentane (10:90) to afford 0.873 g (3.1 mmol, 81%) of **3a**. Recrystallization from chloroform–pentane gave white crystals with a melting point of 120–121 °C (lit.[23] mp 122 °C).

Preparation of 2,2-Dimethyl-5-methoxy-2*H*-naphtho[1,2-*b*]pyran-6-yl Acetate (3b). A solution of 1.774 g (6.92 mmol) of *O*-methyllapachol (**1b**) in 20 mL of pyridine was stirred and refluxed under nitrogen for 3.5 h. Acetic anhydride (5.0 mL, 5.41 g, 53.0 mmol) was then added, and the mixture was stirred at reflux for an additional 30 min. The product was obtained as described for **3a**: 1.735 g (5.81 mmol, 84%) of **3b** as white crystals. An analytical sample was prepared by Kugelrohr distillation at 75 °C (0.005 mm): mp 108–108.5 °C; IR ($CHCl_3$) 2965, 1740, 1455, 1345, 1045 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.32–8.00 (1 H, m), 7.80–7.20 (3 H, m), 6.70 (1 H, d, J = 10 Hz), 5.65 (1 H, d, J = 10 Hz), 3.88 (3H, s), 2.40 (3 H, s), 1.50 (6 H, s); ^{13}C NMR ($CDCl_3$) δ 169.29, 147.22, 145.02, 130.96, 129.29, 127.75, 127.10, 124.56, 122.60, 122.29, 120.42, 117.39, 111.08, 61.66, 27.80, 20.56; mass spectrum, *m/e* 298 (M^+), 256, 241 (base), 236. Anal. Calcd for $C_{18}H_{18}O_4$: C, 72.47; H, 6.08. Found: C, 72.34; H, 6.17.

Dye-Sensitized Photooxidation of 2,2,5-Trimethyl-2*H*-naphtho[1,2-*b*]pyran-6-yl Acetate (7a). A solution containing 0.154 g (0.55 mmol) of the chromenol acetate **3a** and 0.001 g (0.0016 mmol) of *meso*-tetraphenylporphine in 30 mL of acetone was placed in a Griffin-Worden pressure tube, pressurized to 50 psi with oxygen, chilled to 5 °C with an ice-water bath, and irradiated with a 400-W sodium vapor lamp for 2 h. The reaction mixture was then concentrated in vacuo to afford in quantitative yield a viscous unstable hygroscopic oil: IR ($CHCl_3$) 3030, 1740, 1710, 1610, 1370, 1240 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.35–8.00 (4 H, m), 6.45 (1 H, d, J = 10 Hz), 5.80 (1 H, d, J = 10 Hz), 1.80 (3 H, s), 1.75 (3 H, s), 1.60 (3 H, s), 1.45 (3 H, s); mass spectrum, *m/e* 314 (M^+), 299, 271, 256, 239, 229, 212 (base), 196.

Dye-Sensitized Photooxidation of 2,2-Dimethyl-5-methoxy-2*H*-naphtho[1,2-*b*]pyran-6-yl Acetate (7b). A solution containing 0.175 g (0.59 mmol) of the chromenol acetate **3b** and 0.001 g (0.0016 mmol) of *meso*-tetraphenylporphine in 30 mL of acetone was irradiated in the same manner as **3a** for 4 h. The reaction mixture was concentrated in vacuo, and the product was recrystallized from ethyl acetate–pentane to give 0.189 g (0.57 mmol, 98%) of **7b** as pale yellow crystals: mp 122–123 °C; IR ($CHCl_3$) 2970, 1730, 1710, 1325, 1260 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.35–8.15 (4 H, m), 6.45 (*1* H, d, J = 10 Hz), 5.95 (*1* H, d, J = 10 Hz), 3.85 (3 H, s), 1.80 (3 H, s), 1.60 (3 H, s), 1.50 (3 H, s); ^{13}C NMR ($CDCl_3$) δ 182.85, 168.39, 144.03, 135.95, 133.34, 130.41, 129.78, 126.41 (2 C), 113.86, 97.84, 86.75, 77.19, 61.33, 56.24, 30.45, 28.80, 21.84; mass spectrum, *m/e* 330 (M^+), 288, 273, 229, 213, 192, 163, 149, 83 (base). Anal. Calcd for $C_{18}H_{18}O_6$: C, 65.45; H, 5.49. Found: C, 65.50; H, 5.61.

X-ray Characterization of (4a*R*,5a*R*,10b*S*)-10b-Hydroxy-5a-methoxy-2,2-dimethyl-2*H*,5a*H*-oxireno[2,3]naphtho[1,2-*b*]pyran-6(10b*H*)-one Acetate (7b). A lemon yellow crystal of **7b** ($C_{18}H_{18}O_6$) of approximate dimensions (0.34 × 0.46 × 0.57 mm) was mounted on a glass fiber and examined by precession photographs (*h0l*, *h1l*, *0kl*, *1kl*, *2kl*). The crystal exhibited *mmm* Laue symmetry and absences of *h0l* and *h* odd and *0kl* for $k + l$ odd, consistent with the orthorhombic space group $Pna2_1$ (no. 33, C_{2v}^9).[24] Intensity data were measured for 3693 reflections ($2.5 < 2\theta < 63.0°$) with Mo Kα radiation (λ = 0.71073 Å) on a Syntex P$\bar{1}$ diffractometer equipped with a graphite single-crystal monochromator. From these, 3169 unique reflections were obtained by averaging (mean discrepancy for multiply measured reflections, 0.010). Of the unique reflections 1834 had $I > 2\sigma(I)$, where ρ, the ignorance factor used to calculate[25] $\sigma(I)$, was set equal to 0.04. Other conditions of data collection were as follows: scan range 2.0° in 2θ; scan rate 4.0–8.0° min^{-1}; four standard reflections measured after every 56 reflections; drift correction (from standards) 1.038–0.994. Empirical absorption corrections were applied[26] (μ = 0.940 cm^{-1}). The cell constants were determined to be a = 17.261 (10) Å, b = 8.680 (7) Å, c = 11.087 (4) Å, U = 1661.1 $Å^3$, Z = 4 and the density to be d = 1.324 g cm^{-3} (calcd = 1.335 g cm^{-3}).

All nonhydrogen atoms were located by direct methods (MULTAN 78)[27] and the hydrogen atoms subsequently located from electron density synthesis. In the final cycles of least-squares refinement when a unit weighting scheme was used, 216 parameters were refined including the overall scale factor, positional parameters, and anisotropic thermal parameters for all nonhydrogen atoms. The hydrogen atoms were found on a difference electron density map. They were subsequently placed at ideal positions[28] and distances (C–H = 0.97 Å) and given arbitrary isotropic temperature parameters[29] (B = 5.0 $Å^2$). Convergence was achieved with R_1 = 0.066 and R_2 = 0.059.[30] In the last cycle of refinement the maximum shift per error was 0.011 and the average shift per error was 0.003. The highest peak on a final difference electron density map represented less than 0.27 e $Å^{-3}$. Neutral atom scattering factors were used for O, C,[31] and H[32] and corrected for anomalous dispersion.[33]

Reaction of the Rearranged Epoxy Acetate 7a with Water. Preparation of Cis and Trans Epoxy Alcohol 8a. An acetone solution containing 0.126 g (0.39 mmol) of freshly prepared **7a** was evaporated in vacuo and redissolved in 25 mL of 15% aqueous tetrahydrofuran. The reaction mixture was stirred for 1 h at reflux, cooled to room temperature, extracted with ether (2 × 50 mL), dried, and evaporated to an oil. The residual oil was separated on a silica gel flash chromatography column eluted with ether–petroleum ether (20:80) to afford *cis*-**8a** (0.0286 g, 0.11 mmol, 27%) and *trans*-**8a** (0.0307 g, 0.12 mmol, 29%). Both the cis and trans isomers were obtained as nearly colorless viscous oils which were further purified by Kugelrohr distillation (90 °C, 0.002 mm).

Trans epoxy alcohol 8a (more polar diastereoisomer): IR ($CHCl_3$) 3565, 2975, 1675, 1595, 1310, 1030 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.10–7.30 (4 H, m), 6.45 (1 H, d, J = 10 Hz), 5.80 (1 H, d, J = 10 Hz), 3.90 (1 H, br s), 1.68 (3 H, s), 1.60 (3 H, s), 1.50 (3 H, s); mass spectrum, *m/e* 272 (M^+), 257, 229 (base), 211, 197. Anal. Calcd for $C_{16}H_{16}O_4$: C, 70.58; H, 5.92. Found: C, 70.41; H, 5.94.

Cis epoxy alcohol 8a (less polar diastereoisomer): IR ($CHCl_3$) 3570, 2975, 1675, 1595, 1340, 1060 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.20–7.35 (4 H, m), 6.40 (1 H, d, J = 10 Hz), 5.60 (1 H, d, J = 10 Hz), 3.25 (1 H, br s), 1.68 (6 H, s), 1.28 (3 H, s); mass spectrum, *m/e* 272 (M^+), 257, 229 (base), 211, 197. Anal. Calcd for $C_{16}H_{16}O_4$: C, 70.58; H, 5.92. Found: C, 70.32; H, 6.11.

Reaction of the Rearranged Epoxy Acetate 7b with Water. Preparation of Cis and Trans Epoxy Alcohol 8b. An acetone solution containing 0.187 g (0.57 mmol) of freshly prepared **7b** was evaporated in vacuo and redissolved in 25 mL of 15% aqueous tetrahydrofuran. The reaction mixture was stirred for 1 h at reflux, cooled to room temperature, extracted with ether (2 × 50 mL), dried, and evaporated to an oil. The residual oil was purified on a silica gel flash chromatography column eluted with ethyl acetate–pentane (20:80) to afford a mixture of the diastereoisomers of the epoxy alcohol **8b** (0.109 g, 0.37 mmol, 67%). *trans*-**8b** was crystallized directly from this mixture in ethyl acetate–pentane solutions, and *cis*-**8b** (an oil) was obtained from the mother liquors by silica gel thick-layer chromatography eluting with chloroform.

Trans epoxy alcohol 8b (more polar diastereoisomer, major component): mp 146–147 °C; IR ($CHCl_3$) 3550, 2970, 1700, 1595 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.40–8.00 (4 H, m), 6.45 (1 H, d, J = 10 Hz), 5.95 (1 H, d, J = 10 Hz), 3.75 (3 H, s), 2.80 (1 H, br s), 1.55 (3 H, s), 1.45 (3 H, s); mass spectrum, *m/e* 288 (M^+), 273, 241, 229, 213 (base), 192. Anal. Calcd for $C_{16}H_{16}O_5$: C, 66.66; H, 5.59. Found: C, 66.82; H, 5.76.

Cis epoxy alcohol 8b (less polar diastereoisomer, minor component):

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IR ($CHCl_3$) 3550, 2970, 1700, 1595 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.20–8.05 (4 H, m), 6.30 (1 H, d, J = 10 Hz), 5.60 (1 H, d, J = 10 Hz), 3.75 (3 H, s), 3.20 (1 H, br s), 1.65 (3 H, s), 1.30 (3 H, s).

Reaction of the Rearranged Epoxy Acetate 7b with Methanol. Preparation of the Cis and Trans Methyl Ether Derivatives of 8b. An acetone solution containing 0.166 g (0.50 mmol) of freshly prepared **7b** was evaporated in vacuo and redissolved in 25 mL of methanol. The reaction mixture was stirred for 1 h at reflux, cooled to room temperature, filtered to remove suspended *meso*-tetraphenylporphine, and evaporated to an oil. The residual oil was separated on a silica gel flash chromatography column eluted with ethyl acetate–pentane (10:90) to afford the *cis*-epoxy methyl ether (0.041 g, 0.14 mmol, 27%) as a colorless oil and the trans epoxy methyl ether (0.053 g, 0.18 mmol, 35%) as colorless crystals with a melting point of 124–125 °C. Analytical samples were prepared by Kugelrohr distillation of the cis isomer (80 °C, 0.003 mm) and recrystallization of the trans isomer from ethyl acetate–pentane.

Trans epoxy methyl ether derivative of 8b (more polar diastereoisomer): IR ($CHCl_3$) 2960, 1710, 1605, 1240, 1325, 1060 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.25–7.95 (4 H, m), 6.30 (1 H, d, J = 10 Hz), 5.85 (1 H, d, J = 10 Hz), 3.80 (3 H, s), 2.70 (3 H, s), 1.50 (3 H, s), 1.45 (3 H, s); mass spectrum, m/e 302 (M^+), 287, 228, 213 (base), 206. Anal. Calcd for $C_{17}H_{18}O_5$: C, 67.54; H, 6.00. Found: C, 67.73; H, 6.07.

Cis epoxy methyl ether derivative of 8b (less polar diastereoisomer): IR ($CHCl_3$) 2990, 1705, 1605, 1360, 1245 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.35–8.20 (4 H, m), 6.25 (1 H, d, J = 10 Hz), 5.70 (1 H, d, J = 10 Hz), 3.75 (3 H, s), 3.20 (3 H, s), 1.55 (3 H, s), 1.25 (3 H, s); mass spectrum, m/e 302 (M^+), 287, 228, 225, 213 (base), 206. Anal. Calcd for $C_{17}H_{18}O_5$: C, 67.54; H, 6.00. Found: C, 67.80; H, 6.19.

Hydrolysis of Epoxy Acetate 7b on Silica Gel; Preparation of Diketone 9. Attempted chromatography of the epoxy acetate **7b** on a silica gel flash chromatography column eluted with 10–20% ethyl acetate–pentane led to varying amounts (35–60%) of the diketone **9** as a colorless crystalline solid. Recrystallization of this material from chloroform–pentane afforded colorless plates which had the following properties: mp 178–179.5 °C; IR ($CHCl_3$) 3480, 3040, 1740 (w), 1700, 1605, 1255, 1045 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.60–8.35 (4 H, m), 6.30 (1 H, d, J = 10 Hz), 6.05 (1 H, d, J = 10 Hz), 4.90 (1 H, s), 2.05 (3 H, s), 1.45 (3 H, s), 1.05 (3 H, s); ^{13}C NMR ($CDCl_3$) δ 183.24, 180.56, 170.59, 137.93, 134.18, 133.99, 132.90, 127.57, 127.04, 119.57, 92.58, 76.79, 74.60, 30.04, 28.26, 20,17; mass spectrum, m/e 316 (M^+), 274, 259, 256, 242, 241 (base), 229, 213. Anal. Calcd for $C_{17}H_{16}O_6$: C, 64.55; H, 5.10. Found: C, 64.49; H, 5.05.

Preparation of Methylchromanol Acetate 10. To a solution of 0.465 g (1.65 mmol) of the methylchromanol acetate **3a** in 100 mL of methanol was added 0.200 g of 10% palladium on charcoal. The reaction mixture was placed in a Parr hydrogenation apparatus, pressurized to 50 psi with hydrogen, and agitated for 3 h. Then the reaction mixture was filtered to remove the catalyst and evaporated to a viscous oil. The product was purified on a silica gel flash chromatography column eluted with ethyl acetate–pentane (10:90) to afford 0.430 g (1.52 mmol, 92%) of the methylchromanol acetate **10** as a colorless crystalline solid. Recrystallization of **10** from pentane afforded crystals which had the following properties: mp 100–102 °C (lit.[34] mp 103–104 °C); IR ($CHCl_3$) 2960, 1735, 1565, 1355, 1155 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.40–8.08 (1 H, m), 7.80–7.10 (3 H, m), 2.65 (2 H, t, J = 8 Hz), 2.35 (3 H, s), 2.14 (3 H, s), 1.80 (2 H, t, J = 8 Hz), 1.35 (6 H, s); mass spectrum, m/e 284 (M^+), 242, 186.

Dye-Sensitized Photooxidation of Methylchromanol Acetate 10. A solution of 0.144 g (0.51 mmol) of methylchromanol acetate **10** and 0.001 g (0.0016 mmol) of *meso*-tetraphenylporphine in 30 mL of acetone in a Griffin-Worden tube, pressurized to 50 psi with oxygen and chilled to 0–5 °C with an ice-water bath, was irradiated with a 400-W sodium vapor lamp for 2.5 h. The reaction mixture was concentrated in vacuo to afford a viscous moisture sensitive oil which solidified upon standing. This solid upon recrystallization from chloroform–pentane afforded 0.119 g (0.38 mmol, 74%) of the saturated epoxy acetate **11** as colorless crystals which had the following properties: mp 91–93 °C; IR ($CHCl_3$) 2960, 1735, 1685, 1590, 1360, 1240 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.15–7.25 (4 H, m), 2.60 (2 H, t, J = 8 Hz), 1.85 (3 H, s), 1.65 (3 H, s), 1.50 (3 H, s), 1.40 (3 H, s), 2.6–3.0 (2 H, complex). Anal. Calcd for $C_{18}H_{20}O_5$: C, 68.34; H, 6.37. Found: C, 68.47; H, 6.40.

Hydrolysis of the Saturated Epoxy Acetate 11. Preparation of the Acyclic Epoxy Ketol 13. An acetone solution of 0.128 g (0.45 mmol) of freshly prepared saturated epoxy acetate **11** was evaporated in vacuo and redissolved in 25 mL of 15% aqueous tetrahydrofuran. The reaction mixture was stirred for 1 h at reflux, cooled to room temperature, extracted with ether (2 × 50 mL), dried, and evaporated to an oil. This oil was purified on a silica gel flash chromatography column eluted with ethyl acetate–pentane (30:70) to afford the epoxy ketol **13** (0.071 g, 0.25 mmol, 58%) as an oil. An analytical sample of **13** was prepared by Kugelrohr distillation at 110 °C (0.007 mm) and had the following properties: IR ($CHCl_3$) 3500–3600, 2965, 1675, 1595, 1295 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.15–7.55 (4 H, m), 2.85–2.00 (4 H, m), 1.90 (1 H, br s), 1.75 (3 H, s), 1.25 (6 H, s). Anal. Calcd for $C_{16}H_{18}O_4$: C, 70.05; H, 6.61. Found: C, 69.99; H, 6.79.

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Registry No. 1a, 957-78-8; **1b**, 17241-45-1; **2a**, 34638-52-3; **3a**, 16511-15-2; **3b**, 81671-30-9; **5**, 81671-31-0; **7a**, 81671-32-1; **7b**, 81687-71-0; *cis*-**8a**, 81671-33-2; *trans*-**8a**, 81737-78-2; *cis*-**8b**, 81671-34-3; *cis*-**8b** methyl ether, 81671-35-4; *trans*-**8b**, 81737-79-3; *trans*-**8b** methyl ether, 81737-80-6; **9**, 81671-36-5; **10**, 4197-93-7; **11**, 81671-37-6; **13**, 81671-38-7.

Supplementary Material Available: Tables A–H giving fractional atomic positional parameters, bond lengths, bond angles, root-mean-square displacements, anisotropic thermal parameters, hydrogen fractional atomic positions, least-squares planes, and calculated and observed structure factors (19 pages). Ordering information is given on any current masthead page.