(shown in Figure 2), the N2–H2 bend is 54° endo, and the three others are exo with 51–54° bend angles. All of the amino hydrogens were prominent in a difference map with densities from 0.5 to 0.7 e Å^{-3}, well above background, 0.26 e Å^{-3}; the "anomalous" endo H atom was one of the strongest of these peaks. The only hydrogen bonding in the crystal involves the endo-bent N2 as an acceptor; a centrosymmetric dimer results, which is shown in Figure 2. The N···N and H···N distances are 3.25 Å and 2.55 Å, and the N–H···N angle is 139°.

Compound 6b: $C_8H_4F_{12}N_6O_4$, fw = 476.14. Clear, colorless prism (0.10 × 0.15 × 0.65 mm) crystallized from CH_2Cl_2/hexane. Unit cell: a = 20.073 (4) Å, β = 7.353 (1) Å, c = 10.832 (2) Å, V = 1598.7 (4) Å^3. Space group: $Pna2_1$, Z = 4 (1 molecule/asymmetric unit), D(X-ray, calcd) = 1.978 mg mm^{-3}. Least-squares refinement of 283 structural parameters gave agreement factors of R = 0.064, R_w = 0.089 for 1205 unique observed reflections. (Another 58 reflections, with $F_o < 3\sigma(F_o)$, were considered unobserved.) No significant features, only ripples from −0.28 to 0.34 e Å^{-3}, were observed in the final difference map. The two N–H groups each donate in H-bonds to nitro oxygen acceptors. One, N4–H4···O2a (x,y−1,z), has H···O and N···O distances of 2.28 Å and 3.06 Å, and an N–H···O angle of 165°. The other, O6a···H8–N8 (x,y−1,z), has H···O, N···O, and N–H···O values of 2.51 Å and 126°. The latter should be the weaker, due to its nonlinearity; both H-bonds go to the same neighboring molecule and are repeated by the lattice ad infinitum along the b axis.

Compound 6c: $C_8H_3F_{12}N_7O_6$, fw = 521.13. Clear, colorless prism (0.62 × 0.23 × 0.35 mm) crystallized from CH_2Cl_2/hexane. Unit cell: a = 6.990 (6) Å, b = 19.090 (2) Å, c = 12.347 (1) Å, β = 95.38 (1)°, V = 1640.1 (3) Å^3. Space group: $P2_1/c$, Z = 4 (1 molecule/asymmetric unit), D(X-ray, calcd) = 2.110 mg mm^{-3}. Least-squares refinement of 367 structural parameters gave agreement factors of R = 0.049, R_w = 0.074 for 2168 unique observed reflections. (Another 91 reflections, with $F_o < 3\sigma(F_o)$, were considered unobserved.) No significant features, only ripples from −0.19 to 0.27 e Å^{-3}, were observed in the final difference map. There is one amino hydrogen that H-bonds to a nitro oxygen on a neighboring molecule at (x−1,y,z); the N···O, H···O, and N–H···O values are 3.18 Å, 2.39 Å, and 140°.

Compound 6d: $C_8H_2F_{12}N_8O_8$, fw = 566.13. Clear, colorless crystal (0.50 × 0.35 × 0.12 mm) crystallized from CH_2Cl_2/hexane. Unit cell: a = 34.074 (5) Å, b = 7.456 (1) Å, c = 13.877 (2) Å, β = 102.41 (1)°, V = 3443.1 (8) Å^3. Space group: $C2/c$, Z = 8 (1 molecule/asymmetric unit), D(X-ray, calcd) = 2.184 mg mm^{-3}. Least-squares refinement of 333 structural parameters gave agreement factors of R = 0.041, R_w = 0.068 for 2799 unique observed reflections. (Another 31 reflections, with $F_o < 3\sigma(F_o)$, were considered unobserved.) No significant features, only ripples from −0.24 to 0.23 e Å^{-3}, were observed in the final difference map.

Compound 8: $C_5H_3F_6N_3O_2$, fw = 251.09. Clear, colorless, needle-shaped crystal (0.10 × 0.20 × 0.70 mm) grown by sublimation at 90 °C (200 mmHg). Unit cell: a = 10.214 (2) Å, b = 10.986 (3) Å, c = 7.614 (2) Å, V = 854.4 (3) Å^3. Space group: $Pna2_1$, Z = 4 (1 molecule/asymmetric unit), D(X-ray, calcd) = 1.952 mg mm^{-3}. Least-squares refinement of 150 structural parameters gave agreement factors of R = 0.051, R_w = 0.061 for 524 unique observed reflections. (Another 59 reflections, with $F_o < 3\sigma(F_o)$, were considered unobserved.) No significant features, only ripples from −0.25 to 0.28 e Å^{-3}, were observed in the final difference map.

Crystals of **8** are volatile and sublime completely at room temperature in 24 h. Rapid data collection was used to obtain a data set in 3 h; all peaks were scanned at a rate of 30° min^{-1}. Three monitor reflections, remeasured after every 60 observations, decreased uniformly from 100% to 87% in intensity, presumably because of sublimation; a smoothed curve of the monitor decrement ratios was used to correct all data.

Acknowledgment. This work was supported by the Office of the Chief of Naval Research, Mechanics Division (Code 1132P).

Supplementary Material Available: Tables of atomic coordinates, temperature parameters, and bond distances and angles for compounds **1c**, **5b**, **6a–d**, and **8** (22 pages). Ordering information is given on any current masthead page.

A Photochemical Approach to the Taxanes

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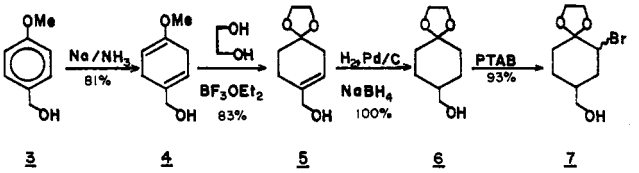
The de Mayo sequence has been applied to the inter- and intramolecular photocycloaddition of various cycloalkenes with homocamphorquinone derivatives to generate a model for the A, B, and C rings of the taxanes. A model sequence of reactions applicable to the construction of the oxetane (D-ring)–tertiary acetate grouping of baccatin III (taxol, cephalomannine) has also been accomplished.

The de Mayo sequence,[1a] photocycloaddition of the enol of a β-diketone and an alkene, followed by retroaldol or other cyclobutane ring fragmentation has been employed extensively for the synthesis of natural products.[1b–l] Its application[2] to the synthesis of the taxane[3] skeleton **1** is

Scheme I



(1) (a) de Mayo, P.; Takeshita, H.; Sattar, A. B. M. A. *Proc. Chem. Soc.* **1962**, 119. Challand, B. D.; Hikino, H.; Kornis, G.; Lang, G.; de Mayo, P. *J. Org. Chem.* **1969**, *34(4)*, 794. de Mayo, P.; *Acc. Chem. Res.* **1970**, *4*, 41. (b) Sammes, P. G. *Q. Rev. Chem. Soc.* **1970**, *24*, 37. (c) Bauslaugh, P. G. *Synthesis* **1970**, 287. (d) Dilling, W. L. *Photochem. Photobiol.* **1977**, *25*, 605. (e) Kossanyi, J. *Pure Appl. Chem.* **1979**, *51*, 181. (f) Baldwin, S. W. *Org. Photochem.* **1981**, *5*, 123. (g) Lenz, G. *Rev. Chem. Intermed.* **1981**, *4*, 369. (h) Oppolzer, W. *Acc. Chem. Res.* **1982**, *15*, 135. (i) Weedon, A. C.; In *Synthetic Organic Photochemistry*; Horspool, W. M., Ed.; Plenum Press: New York, 1984.

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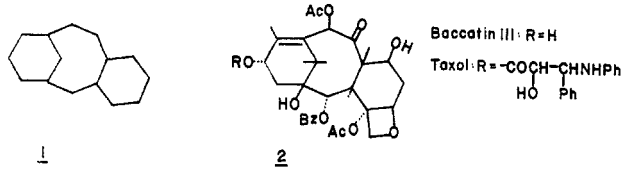
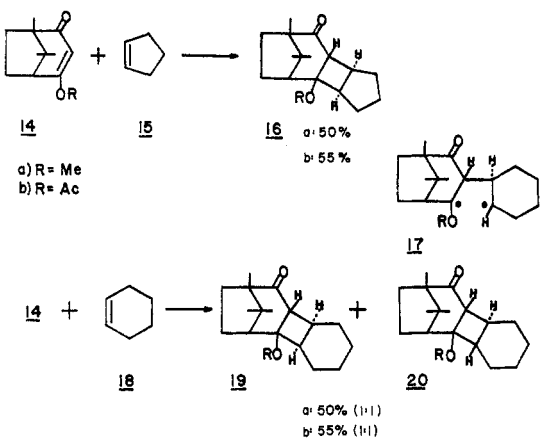
primarily noteworthy because it so readily incorporates a convergent strategy. Prior to[2a-c] and concurrent with[2d]



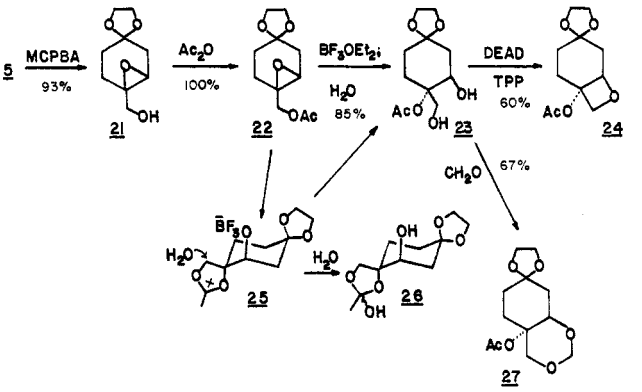
1 2

our own work,[2e,f] four groups have reported model studies that detail the success of this approach, giving a clear picture of the stereochemical constraints on the photocycloaddition step caused by the *gem*-dimethyl group at C-15.

Scheme II

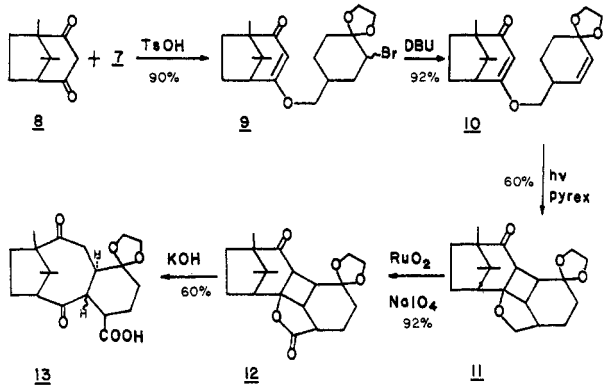


Scheme III



In order to sidestep the apparently lengthy work in constructing an appropriate bicyclo[3.3.1]nonane-2,4-dione (so elegantly accomplished by Blechert[2a]) we devoted our attention to the readily available octane analogue homocamphorquinone 8.[4] A model study employing dimedone and bromo alcohol 7 (see Experimental Section) led to the protocol outlined in Scheme I.

Bromo alcohol 7 was coupled with 8 and then dehydrohalogenated to give the desired de Mayo precursor 10.



Photocycloaddition followed by oxidation gave lactone 12, which was cleaved by base to the taxane model 13. The geometries at positions 3, 4, and 8 are presumed to concur with those found in our preliminary, intermolecular studies (vide infra) and illustrate a strong bias in favor of endo addition.

On the contrary, Inouye[2c] in a very similar study just prior to our own showed that in the absence of the *gem*-

(2) (a) Neh, H.; Blechert, S.; Schnick, W.; Jansen, M. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 905. (b) Swindell, C. S.; de Solms, S. J.; Springer, J. P. *Tetrahedron Lett.* **1984**, *25*, 3797, 3801; **1985**, *26*, 289. Swindell, C. S.; Britscher, S. F. *J. Org. Chem.* **1986**, *51*, 793. (c) Kojima, T.; Inouye, Y.; Kakisawa, H. *Chem. Lett.* **1985**, 323. (d) Cervantes, H.; Do Khac, D.; Fetizon, M.; Guir, F.; Beloeil, J.-C.; Lallemand, J.-Y.; Prange, T. *Tetrahedron* **1986**, *42*, 3491. (e) Berkowitz, W. F.; Perumattam, J.; Amarasekara, A. S. *Tetrahedron Lett.* **1985**, *26*, 3665. (f) Berkowitz, W. F.; Amarasekara, A. S. *Ibid.* **1985**, *26*, 3663.

(3) (1) Lythgoe, B. *The Taxus Alkaloids*, In Manske, R. F. H., Ed.; *The Alkaloids, Chemistry and Physiology* Academic Press, New York, 1968. (2) Wani, M. C.; Taylor, H. L.; Wall, M. E.; Coggon, P.; McPhail, A. T. M. *J. Am. Chem. Soc.* **1971**, *93*, 2325. (3) Nakanishi, K. *Natural Products Chemistry*; Kodansha-Academic Press: Tokyo, 1974; Vol. I, p 281. (4) Miller, R. W.; Powell, R. G.; Smith, C. R., Jr.; Arnold, E.; Clardy, J. *J. Org. Chem.* **1981**, *46*, 1469. (5) Miller, R. W. *J. Nat. Prod.* **1980**, *43*, 425; **1981**, *44*, 312. (6) McLaughlin, J. L.; Miller, R. W.; Powell, R. G.; Smith, C. R., Jr. *J. Nat. Prod.* **1981**, *44*, 314. (7) Rojas, A.; de Marcano, D.; Mendez, B.; de Mendez, J. *Org. Magn. Reson.* **1983**, *21*, 257. (8) De Marcano, D.; Mendez, B.; de Mendez, J.; Monasterios, J.; Rojas, A. C.; Halsall, T. G. *Ibid.* **1983**, 525. (9) Manfredi, J. J.; Horwitz, S. B. *Pharmac. Ther.* **1984**, *25*, 83, a review with 193 references. (10) Senilh, V. Dissertation, Universite de Paris-Sud, Centre D'Orsay, 1984. (11) Senilh, V.; Blechert, S.; Colin, M.; Guenard, D.; Picot, F.; Potier, P.; Varenna, P. *J. Nat. Prod.* **1984**, *47*, 131. Senilh, V.; Gueritte, F.; Guenard, D.; Colin, M.; Potter, P. *C.R. Acad. Sci. Ser. II-Mec. Phys.* **1984**, *299* (15), 1039. (12) Andriamialisoa, R. Z.; Fetizon, M.; Hanna, I.; Pascard, C.; Prange, T. *Tetrahedron* **1984**, *40*, 4285. Synthesis: (13) Ueda, K.; Uyeo, S.; Yamamoto, Y.; Maki, Y. *Tetrahedron Lett.* **1963**, 2167. (14) Kumzawa, S.; Nakno, Y.; Kato, T.; Kitahra, Y. *Tetrahedron Lett.* **1974**, *19*, 1757. (15) Kato, T.; Takayanagi, H.; Suzuki, T.; Uyehara, T. *Tetrahedron Lett.* **1978**, *14*, 1201. (16) Kende, A. S.; Benechie, M.; Curran, D. P.; Fludzinski, P. *Tetrahedron Lett.* **1979**, 4513. (17) Chapman, R. C.; Ph.D. Thesis, Florida State University, 1980. (18) Kitagawa, I.; Shibuya, H.; Fujioka, H.; Kajiwara, A.; Tsujii, S.; Yamamoto, Y.; Takagi, A. *Chem. Lett.* **1980**, 1001. (19) Khan, M. *Tetrahedron Lett.* **1980**, 4547. (20) Inouye, Y.; Fukaya, C.; Kakisawa, H. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 1117. (21) Shibuya, H.; et al. *24th Symp. Chem. Nat. Prod.* **1981**, *24*, 340. (22) Gadwood, R. C.; Lett, R. M. *J. Org. Chem.* **1982**, *47*, 2268. (23) Martin, S. F.; White, J. B.; Wagner, R. *Ibid.* **1982**, *47*, 3190. (24) Trost, B. M.; Hiemstra, H. *J. Am. Chem. Soc.* **1982**, *104*, 886. (25) Shea, K. J.; Gilman, J. W. *Tetrahedron Lett.* **1983**, *24*, 657. (26) Shea, K. J.; Davis, P. D. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 419. (27) Satish, A. V.; Huffman, J. W. *Abstr. 35th South-eastern Regional ACS Meeting*, ORGN-155 (Charlotte, NC) Nov. 9–11, 1983. (28) Sakan, K.; Craven, B. M. *J. Am. Chem. Soc.* **1983**, *105*, 3732. (29) Holton, R. A. *J. Am. Chem. Soc.* **1984**, *106*, 5731. (30) Brown, P. A.; Jenkins, P. R.; Fawcett, J.; Russel, D. R. *J. Chem. Soc., Chem. Commun.* **1984**, 253. (31) Trost, B. M.; Fray, M. J. *Tetrahedron Lett.* **1984**, *25*, 4605. (32) Clark, G. R.; Lin, J.; Nikaido, M. *Tetrahedron Lett.* **1984**, *25*, 2645. (33) Ohtsuka, Y.; Oishi, T. *Heterocycles* **1984**, *21*, 371. (34) Nagaoka, H.; Ohsawa, K.; Takata, T.; Yamada, Y. *Tetrahedron Lett.* **1984**, *25*, 5389. (35) Jackson, C. B.; Pattenden, G. *Tetrahedron Lett.* **1985**, *26*, 3393. (36) Begley, M. J.; Jackson, C. B.; Pattenden, G. *Tetrahedron Lett.* **1985**, *26*, 3397. (37) Clark, G. R.; Lin, J. *Abstr. ACS Meeting 190*, 1985, ORGN-103. Lin, J. MS Thesis, University of Missouri (Columbia), 1985. (38) Ohtsuka, Y.; Oishi, T. *Tetrahedron Lett.* **1986**, *27*, 203. (39) Dnis, J.-N.; Greene, A. E.; Serra, A. A.; Luche, M.-J. *J. Org. Chem.* **1986**, *51*, 46. (40) Abelman, M. M.; Daily, W. J.; Funk, R. L.; Munger, J. D., Jr. *Abstr. ACS Meeting 191*, 1986, ORGN-107. (41) Kende, A. S.; Johnson, S.; Sanfilippo, P.; Hodges, J. C.; Junghein, L. N. *Abstr. ACS Meeting 191*, 1986, ORGN-109. (42) Fetizon, M.; Hanna, I.; Zeghdoudi, R. *Synth. Commun.* **1986**, *16*, 1. (43) Kaczmarek, R.; Blechert, S. *Tetrahedron Lett.* **1986**, *27*, 2845. (44) Trost, B. M.; Hiemstra, H. *Tetrahedron* **1986**, *42*, 3323. (45) Brown, P. A.; Jenkins, P. R. *J. Chem. Soc., Perkin, Trans. 1* **1986**, 1303. (46) Magri, N. F.; Kingston, D. G. I.; Jitrangsri, C.; Piccariello, T. *J. Org. Chem.* **1986**, *51*, 3239. (47) Hayakawa, K.; Ohsuki, S.; Kanematsu, K. *Tetrahedron Lett.* **1986**, *27*, 4205.

(4) (a) Favre, H.; Marinier, B.; Richer, J. C. *Can. J. Chem.* **1956**, *34*, 1329. (b) Eistert, G. B.; Grieber, D.; Caspri, I. *Leibigs Ann. Chem.* **1962**, *64*, 659. (c) Baker, K. M.; Davis, B. R. *Tetrahedron* **1968**, 1655.

dimethyl group the cycloaddition occurred from the exo side, reinforcing even more pointedly Blechert's incisive analysis of the effect of a ketal at C-13, which wholly offset the effect of the *gem*-dimethyl group, and again forced cycloaddition to the exo side.

Intermolecular photoaddition of cyclopentene and cyclohexene to homocamphorquinone derivatives **14a,b** gave the following results (Scheme II).

X-ray analysis of the products (**16a, 19a, 20a**),[5] most graciously performed by Dr. J. F. Blount (Hoffman La Roche, Nutley NJ), first highlighted the effect of the *gem*-dimethyl group, as all additions proved to be endo-directed. Whereas cyclopentene gave only the cis,syn,cis product **16a**, cyclohexene gave two endo addition products, *cis,syn,cis*-**19a** and *cis,anti,trans*-**20a**. The latter product most reasonably arose via a two-step process involving β diradical **17**, the more flexible cyclohexane ring allowing trans ring closure as well. In contrast, intramolecular ring closures follow the "rule of five"[6] and may result in either α[7] or β[2b,d] diradical intermediates.

The Oxetane (D-Ring)–Tertiary Acetate Model. The following sequence of reactions (Scheme III) should be applicable to the construction of the oxetane–tertiary acetate grouping found in baccatin III and related taxanes.[2b,e,3,35]

Treatment of epoxy acetate **22** with $BF_3{\cdot}Et_2O$ as specified by Coxon[8] gave rearranged tertiary acetoxy diol **23**. We suppose that neighboring group participation of the acetate resulted in acetoxonium ion[9] **25** (which precipitated from the mixture). Ring-opening attack of water at the primary carbon then gave **23**, with inversion at the tertiary position. The alternative, regiospecific fragmentation of hemi ortho ester[9] **26**, would be difficult to rationalize.

Ring-closure of cis diol **23** was accomplished by a variation of the Mitsunobu[10] procedure. Diisopropyl diazodicarboxylate was used instead of the more usual diethyl ester, as the hydrazine byproduct of the latter proved difficult to remove from the oxetane. The diol was also converted to dioxane **27**.

Experimental Section

Melting points (uncorrected) were determined in open capillaries in a Thomas-Hoover Uni-melt apparatus. Routine proton spectra were obtained in the indicated solvent on a Varian EM 360 nuclear magnetic resonance (NMR) spectrometer. High field proton and ^{13}C spectra were determined on a IBM Bruker WP-200-SY (200 MHz) instrument. Chemical shifts are reported in ppm downfield from tetramethylsilane. Splitting patterns are designated as s (singlet), d (doublet), t (triplet), q (quartet), and m (multiplet). Coupling constants are given in hertz. Infrared spectra (IR) were recorded on a Perkin-Elmer IR 598 instrument. Ultraviolet (UV) spectra were obtained from solutions in the indicated solvent on a Varian Model 635 LC spectrophotometer. Gas–liquid chromatography (GLC) was performed with a Varian Aerograph 920 thermal conductivity instrument on either a 10 ft by $^1/_4$ in. column packed with 20% silicone oil DC 710 on Chromosorb W (60–80 mesh) or a 10 ft by $^1/_4$ in. column packed with 20% Apiezon L on Chromosorb W. High performance liquid chromatography (HPLC) was conducted with a Waters Associates (Milford, MS) system consisting of two 4-mm by 30-cm μ-Porasil silica columns in series, a 6000 SDS pump, U6K injector, and Model 401 differential refractometer. Flash chromatography was carried out on E. Merck silica gel (230–400 mesh) according to the Still procedure. Preparative column chromatography was performed on E. Merck Art. 7747 silica gel. Some separations were efficiently carried out on a Chromatotron (Harrison) apparatus with rotating plates coated with E. Merck Art. 7749 silica gel. Thin layer chromatography (TLC) was carried out on Machery-Nagel (MN) precoated Polygram Sil N/HR UV silica plates. All photochemical reactions were performed under nitrogen in Pyrex tubes in a Rayonet RPR-100 photoreactor with 3000-Å lamps. X-ray crystallographic analyses of the photoadducts were performed at Hoffmann La Roche by Dr. J. F. Blount.

Dry solvents were used where required. Tetrahydrofuran was distilled from sodium benzophenone ketyl. Ether and dimethoxyethane were distilled from lithium aluminium hydride. Methylene chloride, acetonitrile, triethylamine, *N,N*-dimethylformamide, diglyme, and dimethyl sulfoxide (Me_2SO) were distilled from calcium hydride with distillation of DMF and Me_2SO carried out at reduced pressure. Chloroform was distilled from phosphorous pentoxide and stored over molecular sieves. Benzene distilled from sodium and spectroscopic grade cyclohexane distilled over calcium hydride were used for the photoreactions. Triethylamine, acetic anhydride, boron trifluoride etherate, cyclohexene, and cyclopentene were distilled before use. Solutions were dried during workup over anhydrous Na_2SO_4 and concentrated on a Buchi rotavapor. Microanalyses were performed by Galbraith Laboratories, Knoxville, TN.

4. Birch Reduction of *p*-Methoxybenzyl Alcohol. This compound was prepared by the procedure of Isobe[11] for the Birch reduction of 4-methoxybenzyl alcohol (**3**). Product **4** was obtained in 81% yield, bp 110 °C/0.1 mmHg (lit.[11] bp 120 °C/0.1 mmHg). This product was shown to be pure by GLPC analyses. IR (CCl_4): 3600, 2808, 1690, 1658, 1380 cm^{-1}. ^1H NMR (60 MHz, $CDCl_3$): 5.53 (br s, C-5, 1 H), 4.55 (br s, C-2, 1 H), 4.25 (t, J = 5.0, D_2O exchangeable, OH, 1 H), 3.90 (t, J = 5.0, CH_2OH, 2 H), 3.50 (s, OMe, 3 H), 2.69 (s, C-3 and C-6, 4 H).

5. Direct Ketalization of 4. The Birch reduction product was ketalized directly by Isobe's procedure.[11] The crude product was purified by vacuum distillation to give an 83% yield of ketal **5**, bp 115 °C/0.2 mmHg (lit.[11] bp 105 °C/0.15 mmHg), as a thick oil. GLPC showed only one component. IR (CCl_4): 2920, 2860, 1115, 1058 cm^{-1}. ^1H NMR (60 MHz, $CDCl_3$): 5.54 (br s, C-7, 1 H), 3.97 (s, ketal and CH_2OH, 6 H), 2.55 (s, D_2O exchangeable, OH, 1 H), 1.60–2.30 (m, remaining 6 H).

6. Reduction of the Allylic Alcohol 5. Allylic alcohol **5** (20.00 g, 0.117 mol) was dissolved in 400 mL of absolute ethanol, and to this was added 2.00 g of 10% Pd–C (Fischer Scientific Co.). The mixture was hydrogenated at 30–40 psi in a Parr apparatus for 10 h. The catalyst was filtered off and the solvent was removed under reduced pressure to give an oil (21.2 g). TLC analysis (silica gel, 1:1 hexane/EtOAc) showed a mixture of two compounds. Flash chromatography (silica gel, 1:1 hexane/EtOAc) of 200 mg of the mixture gave two compounds identified as alcohol **6** and an aldehyde on the basis of IR and ^1H NMR.

6. Alcohol. IR (CCl_4): 3642, 3450, 2940, 2928, 2874, 1444, 1373 s, 1357, 1332, 1107, 1085, 1033, 944, 930 cm^{-1}. ^1H NMR (60 MHz, $CDCl_3$): 3.96 (s, ketal and CH_2O, 6 H), 3.50 (br s, exchangeable with D_2O, OH, 1 H), 1.20–2.25 (m, remaining 9 H). ^{13}C NMR ($CDCl_3$): 108.2, 66.1, 63.2, 38.2, 33.3, 25.8. Anal. Calcd for $C_9H_{16}O_3$: C, 62.76; H, 9.36. Found: C, 62.53; H, 9.37. **Aldehyde.** IR (CCl_4): 2890, 1732, 2940, 2870 cm^{-1}. ^1H NMR (60 MHz, $CDCl_3$): 9.67 (s, CHO, 1 H), 3.95 (s, ketal, 4 H), 1.05–2.32 (m, remaining 9 H).

The alcohol/aldehyde mixture (20.00 g) was dissolved in 300 mL of methanol and cooled to 0 °C. To this was added a solution of sodium borohydride (2.50 g, 0.0660 mol) in 100 mL of methanol during a period of 15 min, and stirring was continued for 2 h. The mixture was poured into 400 mL of water and extracted with methylene chloride (5 × 200 mL). The combined organic layers were dried and concentrated to give alcohol **6** as a colorless oil (20.05 g, 100%), which showed only one component on TLC (silica

(5) X-ray data is available as supplementary material.

(6) (a) Srinivasan, R.; Carlough, K. H. *J. Am. Chem. Soc.* **1967**, *89*, 4933. (b) Liu, R. S. H.; Hammond, G. S. *J. Am. Chem. Soc.* **1967**, *89*, 4936. (c) Agosta, W. C.; Wolf, S. *J. Org. Chem.* **1980**, *45*, 4936. (d) Turro, N. J. *Modern Molecular Photochemistry*; Benjamin/Cummings: Menlo Park, CA, 1978; pp 429–432.

(7) Becker, D.; Nagler, M.; Hirsh, S.; Ramun, J. J. *J. Chem. Soc., Chem. Commun.* **1983**, 371.

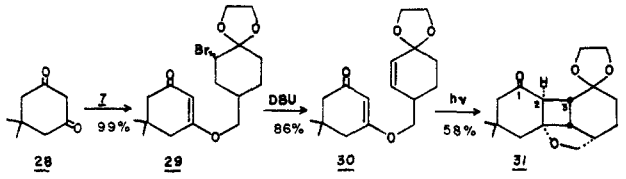
(8) Coxon, J. M.; Hartshorn, M. P.; Kirk, D. N. *Tetrahedron* **1964**, *20*, 2547.

(9) Roberts, R. M.; Rose, J.; Boschan, R.; Seymor, D.; Winstein, S. *J. Am. Chem. Soc.* **1958**, *80*, 1247.

(10) Carlock, J. T.; Mack, M. P. *Tetrahedron Lett.* **1978**, *52*, 5153.

(11) Ito, H.; Isobe, M.; Kawai, T.; Goto, T. *Tetrahedron* **1979**, *35*, 941.

Scheme IV



gel, 3:2 hexane/EtOAc) and GLPC.

7. Bromination of Alcohol 6. The ketal was brominated by the procedure of Marquet.[12] Ketal alcohol **6** (4.00 g, 23.3 mmol) was dissolved in 150 mL of dry methylene chloride and to this was added phenyltrimethylammonium perbromide (PTAB) (8.74 g, 23.3 mmol) during a period of 1 h. The mixture was stirred under nitrogen for 2 days and then poured into 100 mL of 10% aqueous $NaHCO_3$ and separated. The sodium bicarbonate layer was extracted with methylene chloride (2 × 50 mL) and the combined organic layers were washed with water (50 mL), dried, and concentrated to give a thick, pale yellow liquid of crude bromide **7**, 5.43 g (93%). TLC (silica gel, 3:2 hexane/EtOAc) and HPLC analysis showed a mixture of two compounds. The major component was separated for analysis by flash chromatography on silica (3:2 hexane/EtOAc). IR (CCl_4): 3660, 2955, 2900, 2872, 1435, 1332, 1173, 1053 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): 4.22 (m, ketal and C-2, 5 H), 3.515 (AB q, J_1 = 5.0, J_2 = 5.0, CH_2O, 2 H), 2.41–1.20 (m, remaining 7 H). Anal. Calcd for $C_9H_{15}O_3Br$: C, 43.05; H, 6.02; Br, 31.82. Found: C, 43.06; H, 6.20; Br, 31.66.

On the basis of 200-MHz ^1H NMR of the mixture, it was concluded that the product was a mixture of epimeric bromo ketals. The crude mixture was used for further reactions.

Model Photoadduct of 7 and Dimedone (See Scheme IV, Below). Bromo ketal **7** (410 mg, 1.63 mmol) and dimedone (**28**, 228 mg, 1.63 mmol) were dissolved in 50 mL of dry benzene and to this was added 10 mg of *p*-toluenesulfonic acid monohydrate. The mixture was refluxed with a Dean–Stark water separator for 24 h, then washed with 50 mL of 10% aqueous $NaHCO_3$, dried, and concentrated to give thick brown liquid enol ether **29**, 602 mg (99%). ^1H NMR (60 MHz, $CDCl_3$): 5.27 (s, C-2, 1 H), 4.25–3.20 (m, ketal, CH_2O and CHBr, 7 H), 1.04 (s, 2-Me, 6 H), 2.30–0.92 (m, remaining 11 H).

This enol ether (602 mg, 1.61 mmol) was dissolved in diazabicycloundecane (DBU) (1.00 mL, 6.69 mmol) and heated at 100–110 °C under a nitrogen atmosphere for 20 h, then cooled, dissolved in 50 mL of water, and extracted with chloroform (4 × 20 mL). The combined organic layers were dried and concentrated to give a thick brown oil that was dissolved again in chloroform (50 mL) and passed through a short column of basic alumina to remove any unreacted DBU. The alkene-enone **30** thus obtained was a pale yellow oil (406 mg, 86%). ^1H NMR (60 MHz, $CDCl_3$): 5.90 (d, J = 10.0, C-3′, 1 H), 5.63 (d, J = 10.0, C-2′, 1 H), 5.25 (s, C-2, 1 H), 4.20–3.65 (m, ketal and CH_2O, 6 H), 1.03 (s, 2-Me, 6 H), 2.40–0.95 (m, remaining 9 H).

An elemental analysis was not obtained as the material was too unstable. It was therefore used without further purification.

The alkene-enone (100 mg, 0.342 mmol) was dissolved in dry cyclohexane (8.0 mL), degassed with dry nitrogen for 45 min, and then irradiated in a Pyrex tube at 300 nm on a Rayonet apparatus. The reaction was monitored by HPLC and stopped after 3 days. The solvent was removed under vacuum and the residue was flash chromatographed on silica. Elution with 2:3 hexane/EtOAc gave 58 mg (58%) of the photoadduct **31**, mp 145–147 °C. IR (CCl_4): 2957, 2864, 1707, 1465, 1449, 1368, 1255, 1236, 1214 m, 1122, 1105, 1031 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): 4.268 (AB q, J_1 = 7.1, J_2 = 1.0, C-13, 1 H), 4.100 (AB q, J_1 = 7.1, J_2 = 1.0, C-13, 1 H), 4.02–3.65 (m, ketal, 4 H), 2.850 (d, J = 9.2, C-2, 1 H), 2.551 (d br, J = 9.1, C-3, 1 H), 2.243 (s, C-11, 2 H), 2.047 (s, C-7, 1 H), 1.902 (s, C-9, 2 H), 1.643 (s, C-4, 2 H), 1.261 (t, J = 7.2, C-6, 1 H), 1.045 (s, 3 H), and 0.984 (s, *gem*-dimethyl, 6 H), 0.88–0.94 m, C-5, 2 H). Anal. Calcd for $C_{17}H_{24}O_4$: C, 69.84; H, 8.27. Found: C, 69.75; H, 7.82.

The careful work of the French group[2d] has correlated splitting constants of 9.75 and 10.5 Hz with trans-fused cyclobutyl protons, the cis coupling constant being much smaller. Consequently, if the peaks at 2.85 (J = 9.2 Hz) and 2.55 (J = 9.1 Hz) of **31** may be assigned to the protons at C-2 and C-3, respectively, we may posit the cis,anti,trans structure shown for the photoadduct.

8. Homocamphorquinone was prepared by the method of Favre[4a] and Gleiter.[4b] Workup gave a 93% yield of the 1,3-diketone. Recrystallization from benzene gave white solid **8**, mp 218–220 °C (lit.[4b] mp 223–224 °C). IR ($CHCl_3$): 1720, 1700, 1450, 1370 cm^{-1}. ^1H NMR ($CDCl_3$): 0.80 (s, 3 H), 0.95 (s, 3 H), 1.10 (s, 3 H), 1.8–2.1 (m, 4 H), 2.5–2.7 (m, 1 H), 3.25 (dd, 2 H, J = 23 and 18).

9. Homocamphorquinone (1.036 g, 5.756 mmol) and bromo ketal **7** (1.445 g, 5.756 mmol) were dissolved in 100 mL of dry benzene, and to this was added 20 mg of *p*-toluenesulfonic acid monohydrate. The mixture was refluxed with a Dean–Stark water separator for 24 h (monitoring by TLC on silica gel; 8:92 MeOH/$CHCl_3$) and then washed with 100 mL of 10% aqueous $NaHCO_3$. The aqueous layer was back-extracted with ethyl acetate (4 × 100 mL), and the combined organic layers were dried and concentrated to give a yellow, gummy product, 2.40 g (90%). This was flash chromatographed on silica gel, eluting with 5:95 MeOH/$CHCl_3$, and gave two compounds.

9 (Major Isomer). 1.70 g, (72%). ^1H NMR (200 MHz, $CDCl_3$): 5.113 (s, C-3, 1 H), 4.42–3.56 (m, ketal, C-2′ and C-7′, 7 H), 2.46–1.20 (m, remaining 9 H), 1.060 (s, 3 H), 0.940 (s, 3 H), and 0.931 (s, 3 H) C-1 and C-8 methyl groups.

Minor Isomer. 0.090 g, (4%). ^1H NMR (200 MHz, $CDCl_3$): 5.224 (s, C-3, 1 H), 4.40–3.55 (m, ketal, C-2′ and C-7′, 7 H), 2.48–1.25 (m, remaining 9 H), 1.060 (s, 3 H), 1.162 (s, 3 H), 1.211 (s, 3 H), C-1 and C-8 methyl groups.

10. The major compound **9** (1.70 g, 4.11 mmol) was dissolved in DBU (1.80 mL, 12.3 mmol) and heated in an oil bath at 100–110 °C under nitrogen for 16 h. The mixture was then cooled, diluted with 100 mL of water, and extracted with chloroform (5 × 60 mL). The combined organic layers were dried and concentrated to a thick brown oil. Excess DBU was removed by chromatography on a short basic alumina column: eluting with 500 mL of $CHCl_3$ gave pure alkene-enone **10**, 1.26 g (92%). ^1H NMR (200 MHz, $CDCl_3$): 5.858 (d, J = 1.6, C-3′, 1 H), 5.730 (d, J = 1.6, C-2′, 1 H), 4.144 (s, C-3′, 1 H), 4.40–3.65 (m, ketal and C-7′, 6 H), 2.70–1.10 (m, remaining 8 H), 1.063 (s, C-9, 3 H), 1.037 (s, C-10 and C-11, 6 H).

11. Alkene-enone **10** (1.20 g, 3.61 mmol) was dissolved in 85 mL of dry cyclohexane and degassed with dry nitrogen for 45 m and then irradiated in a Pyrex tube at 300 nm in a Rayonet apparatus. The reaction was monitored by HPLC and was stopped after 15 h. The solvent was removed under reduced pressure, leaving a thick oil which was flash chromatographed on silica gel. Elution with 1:1 hexane/EtOAc gave two compounds that were recrystallized from hexane/ethyl acetate.

11 (Major Isomer). 720 mg (60%), mp 132–133 °C. IR (CCl_4): 2965, 2932, 2872, 1703, 1391, 1373, 1250, 1115, 1102, 1085, 1030, 954 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): 4.287 (m, C-15, 2 H), 4.712–4.062 (m, ketal, 4 H), 3.087 (t, J = 9.0, C-3, 1 H), 2.662 (d, J = 6.5, C-4, 1 H), 2.55–1.50 (m, remaining 11 H), 1.000 (s, C-16, C-17, and C-18 methyls, 9 H). ^{13}C NMR ($CDCl_3$): 225.6, 107.8, 74.4, 63.9, 63.6, 50.1, 48.2, 45.5, 41.4, 38.8, 36.0, 31.7, 28.3, 26.6, 25.7, 24.4, 20.9, 13.6. Anal. Calcd for $C_{20}H_{28}O_4$: C, 72.26; H, 8.49. Found: C, 72.49; H, 8.55.

Minor Isomer. 143 mg, (12%), mp 161–161.5 °C. IR (CCl_4): 2965, 2940, 2870, 1701, 1373, 1256, 1132, 1112, 1050, 1034 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): 4.018 (t, J = 9.2, C-15, 1 H), 4.08–3.92 (m, ketal, 4 H), 3.737 (t, J = 9.8, C-15, 1 H), 2.860 (t, J = 10.4, C-3, 1 H), 2.52–1.50 (m, remaining 12 H), 1.019 (s, 3 H), 0.955 (s, 3 H), 0.913 (s, 3 H), C-16, 17, and 18 methyls. ^{13}C NMR ($CDCl_3$): 212.8, 107.4, 98.5, 86.7, 70.3, 64.1, 57.9, 50.8, 48.0, 43.3, 36.4, 34.2, 31.7, 27.6, 24.0, 23.8, 21.0, 20.5, 13.1. Anal. Calcd for $C_{20}H_{28}O_4$: C, 72.26; H, 8.49. Found: C, 72.50; H, 8.48.

12. Sodium metaperiodate (582 mg, 2.72 mmol) and H_2O[13] (9.1 mg) were dissolved in a mixture of 7 mL of water, 2 mL of ace-

(12) (a) Marquet, A.; Jacques, J. *Tetrahedron Lett.* **1959**, *24*. (b) Marquet, A., et al. *Bull. Soc. Chim. Fr.* **1961**, 1822. (c) Mondon, A., et al. *Chem. Ber.* **1979**, *112*, 1110. (d) Dailey, O. D.; Fuchs, P. L. *J. Org. Chem.* **1980**, *45*, 216.

(13) (a) Berkowitz, L. M.; Rylander, P. N. *J. Am. Chem. Soc.* **1958**, *80*, 6682. (b) Smith, A. B., III.; Scarborough, R. M., Jr. *Synth. Commun.* **1980**, *10*, 205. (c) Calsen, P. H. J.; Katsuki, T.; Martin, V. S.; Sharpless, K. B. *J. Org. Chem.* **1981**, *46*, 3936.

tonitrile,[13c] and 7 mL of carbon tetrachloride. The mixture was stirred for 10 min, and a deep green color appeared. The photoadduct **11** (225.7 mg, 0.6790 mmol) in 10 mL of acetonitrile was then added slowly (in 15 min), and the color changed to black. Stirring was continued for 20 h at room temperature; then the aqueous layer was separated and extracted with ethyl acetate (4 × 10 mL). The combined organic layers were dried and concentrated to give a thick brown oil. This was flash chromatographed on silica gel, eluting with 3:2 hexane/EtOAc, and yielded 216 mg of lactone **12** (92%), mp 192–193 °C. IR (CCl_4): 2970, 2870, 2760, 1767, 1729, 1380, 1370, 1232, 1092, 1050, 1010 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): 4.434–3.816 (m, ketal, 4 H), 3.348 (t, J = 9.4, C-3, 1 H), 2.992 (d, d, J_1 = 9.5, J_2 = 1.3, C-4, 1 H), 2.638 (d, d, J_1 = 6.6, J_2 = 4.0, C-8, 1 H), 2.90–1.10 (m, remaining 10 H), 1.079 (s, 3 H), 1.062 (s, 3 H), 1.046 (s, 3 H), C-16, C-17, and C-18 methyls. Anal. Calcd for $C_{20}H_{26}O_5$: C, 69.34; H, 7.57. Found: C, 69.37; H, 7.65.

13. Lactone **12** (124.4 mg, 0.3590 mmol) was dissolved in 8.0 mL of absolute ethanol, and to this potassium hydroxide (250 mg, 4.46 mmol) was added. The mixture was refluxed for 2.0 h and then cooled and diluted with 50 mL of water. The solution was extracted with ether (10 mL), and the aqueous layer was acidified with concentrated HCl to pH 2 and again extracted with ether (4 × 20 mL). The acidic organic extracts were combined, dried, and concentrated to give a white solid, which was recrystallized from ethyl acetate to give **13** as white needles, 78 mg (60%), mp 225–226 °C. ^1H NMR (200 MHz, $CDCl_3$): 8.368 (br s, carboxylic acid 1 H), 4.395–3.579 (m, ketal, 4 H), 3.456 (d, d, J_1 = 8.8, J_2 = 7.3, C-3, 1 H), 2.90–1.10 (m, remaining 13 H), 1.263 (s, 6 H), 0.868 (s, 3 H), C-16, C-17, and C-18 methyls. Anal. Calcd for $C_{20}H_{28}O_6$: C, 65.92; H, 7.74. Found: C, 66.12; H, 7.76.

14a. Methyl Enol Ether of Homocamphorquinone. The methyl enol ether was prepared by using a variation of the Favre[4a] and Baker[4c] procedures. Workup provided a 94% yield of product as a yellowish oil. Distillation of this product (bp 146–147 °C, 8 mm) yielded 1.54 g of colorless oil as a mixture of two regioisomers (8:1) which were separated by column chromatography using hexane/ethyl acetate (2:1) as the solvent. Both isomers were purified by crystallization from hexane and were obtained as fine crystals. The structures of these two enol ethers have been distinguished by a combination of chemical and spectral data.[4c]

14a (Major Isomer), mp 68–69 °C (lit.[4c] mp 68–69 °C). IR (CCl_4): 1650, 1600, 1450, 1365, 1275, 1210 cm^{-1}. ^1H NMR (CCl_4) 0.94 (s, 6 H), 0.99 (s, 3 H), 1.2–2.0 (m, 4 H), 2.3–2.5 (m, 1 H), 3.5 (s, 3 H), 5.1 (s, 1 H).

Minor Isomer, mp 52–54 °C (lit.[4c] 54–55 °C). IR (CCl_4): 1650, 1600, 1450, 1365, 1275, 1215 cm^{-1}. ^1H NMR (CCl_4): 0.93 (s, 3 H), 0.95 (s, 3 H), 1.1 (s, 3 H), 1.4–2.2 (m, 4 H), 2.3–2.5 (m, 1 H), 3.65 (s, 3 H), 5.15 (s, 1 H).

14b. Enol Acetate of Homocamphorquinone. The enol acetate was prepared in a straightforward manner by adding pyridine (0.407 mL, 5.72 mmol) and acetyl chloride (0.463 mL, 5.72 mmol) to a solution of homocamphorquinone (859 mg, 4.77 mmol) in 50 mL of dry chloroform and stirring for 3 h. The mixture was washed with 5% aqueous hydrochloric acid (25 mL), dried, and concentrated, to give the crude mixture of two enol acetates (TLC: silica gel, 5:1 hexane/EtOAc) which were separated on a Chromatotron (silica gel plate, 4:1 hexane/EtOAc), to give two isomeres as colorless oils. A second preparation was separated easily by column chromatography (petroleum ether/ethyl acetate, 4:1) with similar results. The major isomer was assumed to have the structure shown in analogy to the (proven) structure of the major enol ether isolated.

14b (Major Isomer): 630 mg (63%). IR (CCl_4): 1762, 1655, 1440, 1360 cm^{-1}. ^1H NMR (60 MHz, $CDCl_3$): 5.68 (s, C-3, 1 H), 2.50–2.72 (m, C-5, 1 H), 2.36 (s, OAc, 3 H), 1.8–2.2 (m, remaining 4 H), 1.03 (s, C-8 methyl groups, 6 H), 1.14 (s, C-1 Me, 3 H).

Minor Isomer. 158 mg (16%). IR (CCl_4): 1764, 1650, 1360 cm^{-1}. ^1H NMR ($CDCl_3$): 5.70 (s, C-3, 1 H), 2.48–2.64 (m, C-5, 1 H), 2.40 (s, OAc, 3 H), 1.8–2.2 (m, remaining 4 H), 1.05 (s, 3 H), 1.15 (s, 3 H), and 1.21 (s, 3 H, C-1 and C-8 methyl groups).

16a. To a solution of methyl enol ether **14a** (320 mg, 1.64 mmol) in 8 mL of dry cyclohexane in a Pyrex photoreaction tube was added 8 g (0.1 mol) of freshly distilled cyclopentene. Dry nitrogen gas was bubbled through the solution with ice cooling to avoid excessive evaporation of the cyclopentene. This reaction mixture was irradiated in a Rayonet apparatus at 300 nm. Progress of the reaction was monitored by UV spectroscopy. Absorption at 254 nm decreased by 95% during 19 h. The solvent and excess cyclopentene were removed in vacuo and the crude product, contaminated with cyclopentene dimer among other things, gave, upon column chromatography on silica gel (hexane/ethyl acetate, 5:1), 214 mg (50%) of photoadduct **16a** as a white solid. Crystallization from hexane provided pure crystals, mp 90–91 °C. IR ($CHCl_3$): 1680, 1460, 1370, 1160, 1075 cm^{-1}. ^1H NMR ($CDCl_3$): 0.95 (s, 3 H), 1.05 (3, 6 H), 1.6–2.5 (m, 13 H), 2.7–2.9 (m, 1 H), 3.15 (s, 3 H). Anal. Calcd for $C_{17}H_{26}O_2$: C, 69.17; H, 10.96. Found: C, 68.27; H, 10.87.

16b. A solution of enol acetate **14b** (250 mg, 1.13 mmol) and cyclopentene (6 g, 0.075 mmol) in 6 mL of dry cyclohexane was similarly irradiated: UV absorption at 236 nm decreased by 90% within 23 h. Solvent and excess cyclopentene were removed in vacuo, and the residue was chromatographed on silica gel as before, affording 180 mg (55%) of photoadduct **16b** as a white solid. Crystallization from hexane gave fine needles, mp 105–107 °C. IR (CCl_4): 1730, 1695, 1550, 1370, 1230 cm^{-1}. ^1H NMR (CCl_4): 0.95 (s, 3 H), 1.0 (s, 3 H), 1.5–2.6 (m, 13 H), 2.0 (3, 3 H), 3.0–3.2 (m, 1 H). Anal. Calcd for $C_{18}H_{26}O_3$: C, 74.40; H, 8.95. Found: C, 74.58; H, 8.92.

19a, 20a. Similarly, a solution of 300 mg (1.54 mmol) of enol ether **14a** and 6 g (0.073 mmol) of freshly distilled cyclohexene in 6 mL of dry cyclohexane was degassed and irradiated. The carbonyl peak of the starting material at 1650–1600 cm^{-1} diminished by 90% in 32 h. The solution was concentrated in vacuo, and the residue was chromatographed on silica gel (hexane/ethyl acetate, 9:1), giving 210 mg (50%) of mixed photoadducts as a white solid. An NMR spectrum of this mixture showed two OMe peaks of equal intensity at 3.0 and 3.1 ppm. The isomers were separated by preparative LC (hexane/ethyl acetate, 9:1).

19a: mp 117–118 °C. IR ($CHCl_3$): 1675, 1440, 1070 cm^{-1}. ^1H NMR ($CDCl_3$): 0.95 (s, 3 H), 1.05 (s, 6 H), 1.5–2.7 (m, 16 H), 3.0 (s, 3 H). Anal. Calcd for $C_{18}H_{28}O_2$: C, 78.21; H, 10.21. Found: C, 77.91; H, 10.11.

20a, mp 104–105 °C. IR ($CHCl_3$): 1680, 1440, 1075 cm^{-1}. ^1H NMR ($CDCl_3$) 0.95 (s, 3 H), 0.90 (s, 3 H), 0.85 (s, 3 H), 1.5–2.3 (m, 15 H), 2.4–2.6 (m, 1 H), 3.1 (s, 3 H). Anal. Calcd for $C_{18}H_{28}O_2$: C, 78.21; H, 10.21. Found: C, 78.31; H, 10.26.

19b, 20b. A solution of enol acetate **14b** (300 mg, 1.35 mmol) and 8 g (0.09 mmol) of cyclohexene in 6 mL of dry cyclohexane was also degassed and irradiated until the enone peak (IR) had receded by 90% (21 h). Concentration gave a colorless viscous liquid which on chromatographic purification (silica gel, hexane/ethyl acetate, 5:1) gave 255 mg (55%) of a colorless solid. HPLC and GLC showed the presence of two isomers which were partially separated by fractional crystallization (hexane), to give one isomer of 80% purity which gave the following data. IR (CCl_4) 1720, 1680, 1550, 1370, 1230 cm^{-1}. ^1H NMR (CCl_4): 0.9 (s, 3 H), 0.95 (s, 6 H), 2.1 (s, 3 H). Anal. Calcd for $C_{19}H_{28}O_3$: C, 74.97; H, 9.27. Found: C, 75.15; H, 9.37.

21. Epoxy alcohol **5** (22.3 g, 0.113 mol) was dissolved in methylene chloride (100 mL) and cooled to 0 °C. To this was added a solution of 85% *m*-chloroperoxybenzoic acid (MCPBA, 29.3 g, 0.123 mol) in methylene chloride (250 mL) during a period of 20 m, followed by stirring for 1 h. A solution of 10% aqueous NaOH (100 mL) was then added and the mixture was extracted with methylene chloride (3 × 150 mL). The combined organic layers were washed with water (100 mL), dried, and evaporated to give the epoxide **21** as a colorless oil, 22.7 g (93%). IR ($CHCl_3$): 3500 (br), 2240, 2038, 1440, 1360 cm^{-1}. ^1H NMR (60 MHz, $CDCl_3$) 3.85 (s, ketal, 4 H), 3.49 (s, CH_2O-, 2 H), 3.07 (t, J = 3.0, C-6, 1 H), 2.78 (br s, D_2O exchangeable, OH, 1 H), 1.95 (d, J = 3.0, C-5, 2 H), 1.25–1.85 (m, C-2 and C-3, 4 H). Anal. Calcd for $C_9H_{14}O_4$: C, 58.05; H, 7.58. Found: C, 57.98; H, 7.60.

22. Epoxy acetate **21** (20.00 g, 0.1070 mol) was dissolved in ether (300 mL), and to this triethylamine (12.06 g, 0.1170 mol) and acetic anhydride (12.00 g, 0.117 mol) were added. The mixture was stirred at room temperature for 4 days, then poured into 300 mL of water, and extracted with ether (4 × 200 mL). The combined ether layers were dried and concentrated under reduced pressure to give 24.40 g (100%) of **22**. GLPC showed only one compound. IR (CCl_4): 2942, 2880, 1742, 1427, 1364, 1228, 1123, 1068, 1037 cm^{-1}. ^1H NMR (60 MHz, $CDCl_3$): 4.10 (q, J = 11.0,

CH_2OAc, 2 H), 3.92 (s, ketal, 4 H), 3.15 (t, J = 3.0, C-6, 1 H), 2.10 (s, OAc, 3 H), 1.15–2.00 (m, remaining, 6 H). ^{13}C NMR ($CDCl_3$): 169.9, 106.2, 66.5, 64.1, 63.7, 57.2, 55.0, 34.2, 27.3, 22.7, 20.2. Anal. Calcd for $C_{11}H_{16}O_5$: C, 57.88; H, 7.06. Found: C, 57.79; H, 6.99.

23. Acetoxy Diol: Rearrangement of Epoxy Acetate 22. Method A. Epoxy acetate **22** (230 mg, 1.24 mmol) was dissolved in 2.00 mL of methylene chloride and cooled to −10 °C in an ice/salt bath. To this were added boron trifluoride etherate (10 μL) and glacial acetic acid (74 mg, 1.236 mmol), and the solution was stirred under nitrogen for 1.0 h. The mixture was washed with water (5 mL), dried, and evaporated. The residue was flash chromatographed on silica gel, eluting with 5% methanol in chloroform, and gave 70 mg of tertiary acetoxy diol **23** (22%) as a thick oil. IR ($CHCl_3$): 3500 (br), 2950, 2880, 1720, 1235, 1095 cm^{-1}. ^1H NMR (60 MHz, $CDCl_3$) 4.17 (br s, CH_2O, 1 H), 3.97 (s, ketal, 4 H), 3.60 (br s, CH_2O, 1 H), 3.43 (s, D_2O exchangeable, 2 OH, 2 H), 2.10 (s, OAc), 2.03–1.20 (m, remaining, 7 H). Anal. Calcd for $C_{11}H_{18}O_6$: C, 53.65; H, 7.37. Found: C, 54.02; H, 7.39.

Method B. The procedure of Coxon was employed.[8] Epoxy acetate **22** (21.83 g, 0.09600 mol) was suspended in 300 mL of dry benzene, and to this was added boron trifluoride etherate (11.80 g, 0.105 mol). A white gelatinous precipitate was formed instantaneously. The mixture was shaken for 2 min at room temperature, and to it was added a solution of 10% aqueous sodium acetate (250 mL) all at once. The mixture was shaken briefly and the layers were separated. The aqueous layer was extracted with ethyl acetate (4 × 150 mL) and the combined organic layers were washed with 250 mL of water, dried, and then concentrated to give 20.00 g of acetoxy diol **23** (85%). Spectra of this preparation were identical with those obtained in method A.

24. Oxetane. In an oven-dried, three-necked flask was dissolved acetoxy diol **23** (370 mg, 1.50 mmol) in 5 mL of dry chloroform, under a nitrogen atmosphere. To this was added triphenylphosphine (393 mg, 1.50 mmol). The solution was cooled in an ice bath, and then diisopropyl azodicarboxylate[10] (303 mg, 1.50 mmol) was added via a syringe during a 10-min period. The red color of the azo compound disappeared instantaneously during the addition. Stirring was continued for 4 h at 0 °C. The solution was evaporated to dryness, leaving a thick oil which was flash chromatographed on silica gel, eluting with 3:2 hexane/EtOAc. The acetoxyoxetane **24** was obtained as a thick colorless oil, 202 mg (60%). Only one component was evident on TLC (silica gel, 3:2 hexane/EtOAc) and HPLC. IR ($CHCl_3$): 1727, 1225, 1045, 910 cm^{-1}. ^1H NMR: (60 MHz, $CDCl_3$) 4.85 (dd, J_1 = 6.0, J_2 = 4.0, C-6, 1 H), 4.16 (AB q, J = 3.0, C-8, 2 H), 3.93 (s, ketal, 4 H), 2.13 (s, OAc, 3 H), 2.00–1.15 (m, remaining 6 H). Anal. Calcd for $C_{11}H_{16}O_5$: C, 57.89; H, 7.07. Found: C, 57.89; H, 6.88.

27. 1,3-Dioxane. Acetoxy diol **23** (2.00 g, 8.13 mmol) was dissolved in dry methylene chloride (50 mL). To this was added paraformaldehyde (2.00 g, 66.6 mmol) and 2 drops of concentrated sulfuric acid. The mixture was stirred under nitrogen for 4 h and then diluted with 50 mL of methylene chloride and washed with 50 mL of 10% aqueous $NaHCO_3$. The aqueous layer was back-extracted with methylene chloride (3 × 50 mL) and the combined organic layers were washed with water, dried, and concentrated to give 2.20 g of the crude product. This was flash chromatographed on silica gel, eluting with 1:1 hexane/EtOAc, to give pure **27**, 1.40 g (67.0%). IR (CCl_4): 2970, 2940, 2918, 2880, 1740, 1711, 1453, 1380, 1288, 1253, 1230, 1198, 1189, 1085, 1030 cm^{-1}. ^1H NMR (60 MHz, $CDCl_3$): 5.16 (s, C-4, 2 H), 4.85 (s, C-2, 2 H), 4.23 (s, ketal, 4 H), 2.15 (s, OAc, 3 H), 1.25–2.25 (m, remaining 5 H). ^{13}C NMR ($CDCl_3$): 207.6 (C=O), 169.9 (C-1), 97.4 (C-8), 93.1 (C-4), 77.6 (ketal), 76.2 (C-6), 75.7 (ketal), 66.3 (C-2), 40.7 (C-7), 32.9 (C-9), 27.3 (C-10), 20.2 (acetate CH_3). Anal. Calcd for $C_{12}H_{18}O_6$: C, 55.80; H, 7.02. Found: C, 55.59; H, 6.88.

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Supplementary Material Available: X-ray structural data for compounds **16**, **19**, and **20** (20 pages). Ordering information is given on any current masthead page.

Stereochemical Evidence for an Alkylated Perepoxide Intermediate

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Peroxymercuration of (*Z*)-pent-2-ene afforded single stereoisomers of 2-(bromomercurio)-3-(*tert*-butylperoxy)pentane (M1) and 3-(bromomercurio)-2-(*tert*-butylperoxy)pentane (M2), which were separated by medium pressure liquid chromatography. Iodinolysis of each of these gave a pair of epimeric β-iodopentyl *tert*-butyl peroxides (I1A and I1B from M1, and I2A and I2B from M2), which were similarly separated. When treated with silver trifluoroacetate, the regioisomers I1A and I2A each yielded the *same* 5:3 mixture of 3-(*tert*-butylperoxy)-2-(trifluoroacetoxy)pentane (T1) and 2-(*tert*-butylperoxy)-3-(trifluoroacetoxy)pentane (T2). Independent experiments showed that the starting iodides and the product trifluoroacetates were stereochemically stable under the reaction conditions. Hence, the results are taken to provide compelling evidence for the intermediacy of a *tert*-butylated perepoxide (P_A) that is sufficiently long-lived to be attacked at each ring carbon atom. However, the epimeric regioisomers I1B and I2B each reacted with silver trifluoroacetate to afford a single, new, trifluoroacetate with retention of both regio- and stereochemistry. This is taken to provide evidence for a new mechanism of substitution involving a six-centered cyclic transition state. Product correlations for similar substitutions with analogous bromo peroxides for which stereochemistries are identified by assuming trans addition for peroxymercuration and retention of configuration during bromodemercuration indicate that the alkylated perepoxide (P_A) has the structure with *cis*-alkyl groups. This was confirmed by identifying the stereochemistry of T1 and T2 by $LiAlH_4$ reduction to *threo*-pentane-2,3-diol.

The formation of perepoxides **1** as intermediates in chemical reactions has been vigorously disputed in the scientific literature for the past 25 years.[2,3] Perepoxides have been postulated to mediate in the singlet oxygenation of alkenes[4] and in the base-induced reactions of β-hydro-

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(2) Sharp, D. B.; *Abstracts of Papers*, 138th National Meeting of the American Chemical Society, New York; American Chemical Society: Washington, DC; 1960; p 79.

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