Substituent Effects in the Highly Regioselective and Diastereoselective Ene Reaction of Singlet Oxygen with Chiral Cyclohexadienes

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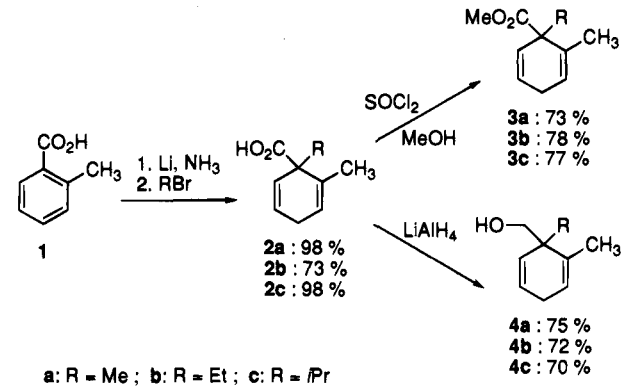
Abstract: The photooxygenation of the cyclohexadienes **3** and **4**, which are readily available through Birch reduction of 2-methylbenzoic acid (**1**), yielded only one regioisomeric hydroperoxide in a remarkable high diastereoselectivity. A strong directing effect on the stereochemical course of this singlet oxygen ene reaction (Schenck reaction) was observed for various functional groups, including esters and homoallylic alcohols which are unprecedented. This control of diastereoselectivity is rationalized in terms of steric and electronic factors, which provide strong support for perepoxide intermediates in the Schenck reaction. An observation important for synthetic applications is the opportunity to steer the attack of $^1O_2$ by the proper choice of functional groups. Thus, both diastereomers of the diacetate **11** were selectively prepared from the ester **3a** or alcohol **4a** of the same starting material **1**. The convenience of the reaction sequence Birch reduction–photooxygenation should provide an attractive route to natural products.

The photooxygenation of olefins with singlet oxygen provides a convenient and effective route to allylic hydroperoxides.[1] Much effort has been invested to achieve regiocontrol in this ene reaction.[2] It was shown that especially functionalized alkenes like α,β-unsaturated ketones,[3] sulfoxides,[4] vinylstannanes,[5] and vinylsilanes[6] exhibit remarkable regioselectivity. The diastereomeric course of the singlet oxygen ene reaction (the Schenck reaction) has been studied less intensively, but high stereoselectivities were recently accomplished.[7]

In connection with the synthesis of dihydroxyvitamin D_3 (calcitriol),[8] we developed the reaction sequence Birch reduction–photooxygenation as an entry to functionalized cyclohexenol derivatives.[9] In the course of this study, remarkably high regio- and stereoselectivities were observed in the singlet oxygen ene reaction of chiral cyclohexadiene carboxylic acids. Such directing effects of carboxyl groups were hitherto unknown for $^1O_2$ reactions. In this paper we report on the influence of different substituents on the stereoselectivity of the photooxygenation of chiral cyclohexadienes. It is shown that appropriate functional groups control diastereoselctivity and, therefore, this methodology can be conveniently extended to other ene substrates.

Scheme 1



Birch reduction[10] and alkylation of 2-methylbenzoic acid (**1**) afforded the racemic 2,5-cyclohexadiene-1-carboxylic acids **2a–c** in high yields. The racemic acids were transformed into the esters **3a–c** or alcohols **4a–c** in one step (Scheme 1). Photooxygenation of esters **3a–c** and alcohols **4a–c** proceeded smoothly with tetraphenylporphin (TPP) as sensitizer. The hydroperoxides **5a–c** and **6a–c** were obtained as sole products as a result of the ene reaction with singlet oxygen (Scheme 2). The observed product ratios, which were determined by ^1H NMR spectroscopy directly on the crude reaction mixture after evaporation of the solvent, are given in Table 1. The diastereomeric assignments are based on NOE experiments and the spectral data correspond to the previously described carboxylic acids.[9]

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(1) (a) Gollnick, K.; Schenck, G. O. *Pure Appl. Chem.* **1964**, *9*, 507–525. (b) Wasserman, H. H.; Ives, J. L. *Tetrahedron* **1981**, *37*, 1825–1852. (c) Frimer, A. A.; Stephenson, L. M. In *Singlet Oxygen*; Frimer, A. A., Ed.; CRC Press Inc.: Boca Raton, 1985; Vol. II, pp 67–92.

(2) (a) Schulte-Elte, K. H.; Rautenstrauch, V. *J. Am. Chem. Soc.* **1980**, *102*, 1738–1740. (b) Clennan, E. L.; Chen, X.; Koola, J. J. *J. Am. Chem. Soc.* **1990**, *112*, 5193–5199. (c) Orfanopoulus, M.; Stratakis, M.; Elemes, Y. *J. Am. Chem. Soc.* **1990**, *112*, 6417–6419.

(3) (a) Ensley, H. E.; Carr, R. V. C.; Martin, R. S.; Pierce, T. E. *J. Am. Chem. Soc.* **1980**, *102*, 2836–2838. (b) Kwon, B.-M.; Kanner, R. C.; Foote, C. S. *Tetrahedron Lett.* **1989**, *30*, 903–906.

(4) Akasaka, T.; Misawa, Y.; Goto, M.; Ando, W. *Tetrahedron* **1989**, *45*, 6657–6666.

(5) (a) Adam, W.; Klug, P. *J. Org. Chem.* **1993**, *58*, 3416–3420. (b) Adam, W.; Klug, P. *J. Org. Chem.* **1994**, *59*, 2695–2699.

(6) (a) Fristad, W. E.; Bailey, T. R.; Paquette, L. A. *J. Org. Chem.* **1980**, *45*, 3028–3037. (b) Adam, W.; Richter, M. J. *J. Org. Chem.* **1994**, *59*, 3335–3340.

(7) (a) Adam, W.; Catalani, L. H.; Griesbeck, A. *J. Org. Chem.* **1986**, *51*, 5494–5496. (b) Adam, W.; Nestler, B. *J. Am. Chem. Soc.* **1993**, *115*, 5041–5049. (c) Dussault, P. H.; Lee, R. J. *J. Am. Chem. Soc.* **1994**, *116*, 4485–4486. (d) Dussault, P. H.; Woller, K. R.; Hillier, M. C. *Tetrahedron* **1994**, *50*, 8929–8940.

(8) Selected examples of calcitriol syntheses: (a) Nagasawa, K.; Zako, Y.; Ishihara, H.; Shimizu, I. *Tetrahedron Lett.* **1991**, *32*, 4937–4940. (b) Posner, G. H.; Carry, J.-C.; Anjeh, T. E. N.; French, A. N. *J. Org. Chem.* **1992**, *57*, 7012–7014. (c) Chen, C.; Crich, D. *Tetrahedron* **1993**, *49*, 7943–7954.

(9) Linker, T.; Fröhlich, L. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1971–1972.

(10) (a) van Bekkum, H.; van den Bosch, C. B.; van Minnen-Pathuis, G.; de Mos, J. C.; van Wijk, A. M. *Recl. Trav. Chim. Pays-Bas* **1971**, *90*, 137–149. (b) Acheson, R. M.; Flowerday, R. F. *J. Chem. Soc., Perkin Trans. 1* **1974**, 2339–2342. (c) Mah, T.; Sirat, H. M.; Thomas E. J. *J. Chem. Soc., Perkin Trans. 1* **1979**, 2255–2260.

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Scheme 2

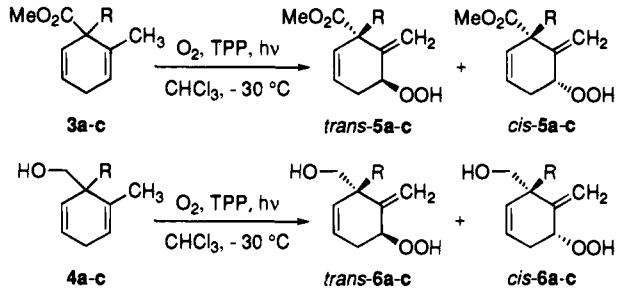
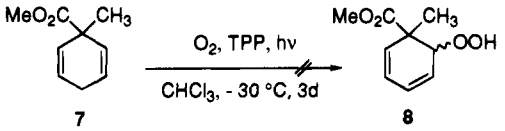


Table 1. Photooxygenation of Cyclohexadienes *rac*-**3** and *rac*-**4**

				yield (%)[b]	
entry no.	cyclohexadiene	R	dr[a] *trans*:*cis*	*trans*-**5** (**6**)	*cis*-**5** (**6**)
1	**3a**	Me	88:12	79	10
2	**3b**	Et	30:70	25	65
3	**3c**	*i*Pr	<4:96		85
4	**4a**	Me	39:61	35	59
5	**4b**	Et	<4:96		86
6	**4c**	*i*Pr	<4:96		93

[a] Diastereomeric ratios (dr) determined by ^1H NMR analysis of the crude product (400 MHz). [b] Isolated product after silica gel column chromatography.

Scheme 3



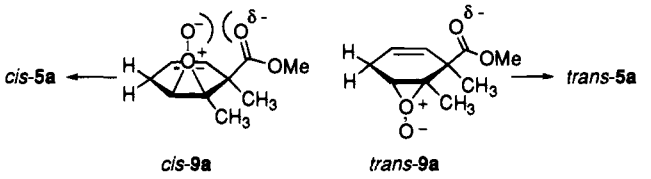
As shown in Scheme 2, the regioisomeric hydroperoxide with an exocyclic double bond is formed exclusively in all photooxygenations. This remarkable result appears to be due to the planar conformation of 1,4-cyclohexadienes,[11] since the Schenck reaction of 1-methylcyclohexenes proceeds with low regioselectivities.[2a,12] The site selection of singlet oxygen for the higher substituted double bond could be rationalized in terms of the electrophilic character of this species. However, if the electrophilic character was the main factor controlling the reaction, then the less substituted double bond would be attacked after elongated reaction times. This is not the case since the hydroperoxides **5** and **6** are stable under the conditions of photooxygenation. For the regioselectivity, the exclusive formation of the secondary hydroperoxides cannot be explained completely by the geminal effect, since related acyclic systems exhibit only moderate selectivities.[2c] Obviously, the planar conformation of 1,4-cyclohexadienes[11] allows hydrogen abstraction from the 2-methyl group only and leads to both the site- and regioselectivity of the ene reaction. To further prove the importance of the 2-methyl group in the Schenck reaction of cyclohexadienes we conducted the photooxygenation of ester **7** (Scheme 3). Indeed, even after 3 days no conversion to the hydroperoxide **8** was observed and the starting material was recovered in quantitative yield.

In addition to the observed high regioselectivities, distinct substituent effects on the diastereomeric course of the photooxygenations are observed (Table 1). Thus, the *cis* selectivity increased drastically by changing the substituents from methyl to ethyl to isopropyl, which can only be rationalized by steric interactions.

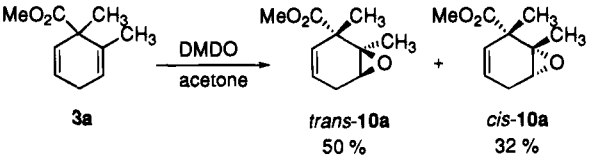
(11) Rabideau, P. W. *The Conformational Analysis of Cyclohexenes, Cyclohexadienes, and Related Hydroaromatic Compounds*; VCH: Weinheim, 1989; Chapter 4.

(12) (a) Dutcher, J. S.; Macmillan, J. G.; Heathcock, C. H. *J. Org. Chem.* **1976**, *41*, 2663–2669. (b) Stephenson L. M. *Acc. Chem. Res.* **1980**, *13*, 419–425.

Scheme 4



Scheme 5



On the other hand, the methyl-substituted ester **3a** (entry 1) shows a strong preference for *trans* attack of $^1O_2$, which must be due to electronic factors, since methyl esters possess nearly the same steric demand as methyl groups.[13] Unfavorable electronic repulsions in the perepoxide *cis*-**9a**[14] (Scheme 4), which are not present in *trans*-**9a**, seem to be responsible for the high *trans* selectivity. Such remarkable directing effects of ester groups are unknown for $^1O_2$ reactions, but are in accordance with our previously reported singlet oxygen ene reactions of carboxylic acids.[9] Furthermore, evidence for the importance of electronic interactions was illustrated in the epoxidation of ester **3a** with dimethyldioxirane (DMDO)[15] as shown in Scheme 5. In the course of this reaction, no zwitterionic species are formed as intermediates, and the diastereoselectivity drops to 61:39 compared to 88:12 in the photooxygenation.

An opposite sense of stereocontrol was observed in the ene reaction of the alcohols **4a–c** (entries 4–6). Even in the case of the sterically less demanding methyl group (entry 4), the major product is *cis*-**6a**. Moreover, the ethyl and isopropyl substituted alcohols **4b** and **4c** exclusively afforded *cis*-configurated hydroperoxides (entries 5 and 6), since steric and electronic factors in these substrates reinforce each other. These results can conveniently be rationalized in terms of attractive interactions between $^1O_2$ and the hydroxy group. Such directing effects were recently described for the photooxygenation of allylic alcohols,[7b] but they were hitherto unknown for homoallylic systems.

Additionally, the herein substantiated reverse directing ability of homoallylic alcohols *versus* esters in the singlet oxygen ene reaction is an important observation for preparative purposes. The simplicity of the transformation of esters into alcohols allows the control of the diastereoselectivity of the photooxygenation starting from the same substrate. Thus, the *trans* and *cis* isomers of the diacetate **11** were obtained diastereomerically pure from the ester **3a** or from the alcohol **4a** of 2-methylbenzoic acid (**1**) (Scheme 6).

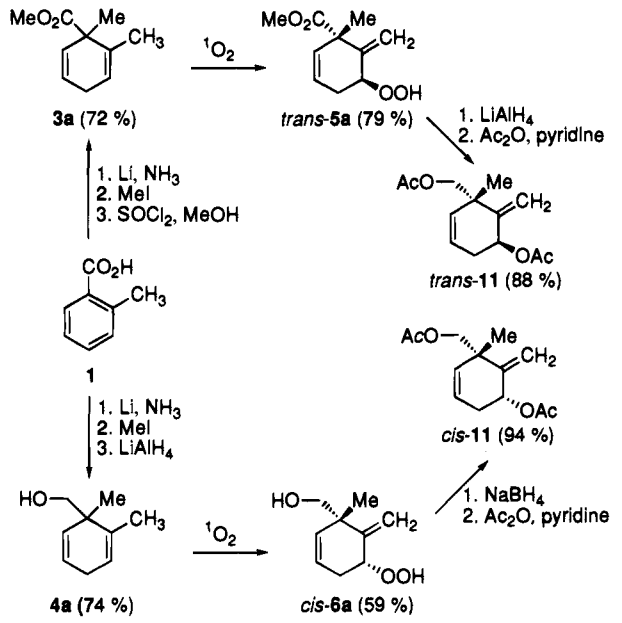
In conclusion, the singlet oxygen ene reaction of chiral cyclohexadienes proceeds in high regio- and diastereoselectivity through control by a combination of electronic and steric interactions. Therefore, strong substituent effects on the photooxygenation were observed, which permit the direct stereo-

(13) Förster, H.; Vögtle, F. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 429–448.

(14) For perepoxides as intermediates in singlet oxygen ene reactions see: (a) Hurst, J. R.; Wilson, S. L.; Schuster, G. B. *Tetrahedron* **1985**, *41*, 2191–2197. (b) Orfanopoulos, M.; Smonou, I.; Foote, C. S. *J. Am. Chem. Soc.* **1990**, *112*, 3607–3614. (c) Luis, J. G.; Andrés, L. S.; Fletcher, W. Q. *Tetrahedron Lett.* **1994**, *35*, 179–182.

(15) Schultz, A. G.; Harrington, R. E.; Tham, F. S. *Tetrahedron Lett.* **1992**, *33*, 6097–6100.

Scheme 6



chemical control of the reaction by the proper choice of functional groups. Since the carboxylic acids **2** can be prepared in enantiomerically pure form,[16] the reaction sequence Birch reduction–photooxygenation should provide a convenient route to optically active, oxyfunctionalized natural products.

Experimental Section

Solvents and commercially available chemicals were purified by standard procedures or used as purchased. Carboxylic acids **2** and methyl esters **3** and **7** were prepared from 2-methylbenzoic acid (**1**) according to literature procedures.[10] TLC was performed on Polygram Sil G UV (40 × 80 mm), Macherey & Nagel. Silica gel (63–200 μm, Woelm, Erlangen) was used for column chromatography. Melting points were measured on a Büchi SMP 20 apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer 1600 FT-IR spectrometer. NMR spectra were recorded on either a Bruker AC 200 or WM 400 with $CDCl_3$ as solvent and TMS as internal standard. Combustion analyses were carried out at the Microanalytical Division of the Institute of Organic Chemistry, University of Giessen, Germany.

1,2-Dimethyl-2,5-cyclohexadiene-1-methanol (4a). To a suspension of 455 mg (12.0 mmol) of $LiAlH_4$ in 30 mL of diethyl ether under argon at 0 °C was added a solution of 1.52 g (10.0 mmol) of acid **2a**[10a] in 25 mL of diethyl ether over a period of 20 min. After the solution was stirred for 18 h at room temperature a mixture of 2.0 mL of H_2O and 7.0 mL of dioxane was added at 0 °C within 10 min. Stirring was continued for 15 min at room temperature and the mixture was filtered and dried (Na_2SO_4). Evaporation of the solvent and distillation of the residual liquid yielded 1.04 g (75%) of **4a** as a colorless oil, bp 93–96 °C (0.1 Torr). ^{1}H NMR δ 1.03 (s, 3H), 1.56 (br s, 1H), 1.71 (s, 3H), 2.60–2.72 (m, 2H), 3.19 (d, J = 10.3 Hz, 1H), 3.60 (d, J = 10.3 Hz, 1H), 5.37 (dt, J = 10.0, 2.0 Hz, 1H), 5.60–5.72 (m, 1H), 5.90 (dtd, J = 10.0, 3.5, 1.6 Hz, 1H). ^{13}C NMR δ 18.2 (q), 22.8 (q), 27.2 (t), 41.5 (s), 66.2 (t), 123.1 (d), 126.4 (d), 132.0 (d), 134.3 (s). IR (neat) ν 3450, 2980, 2920 cm^{-1}. Anal. Calcd for $C_9H_{14}O$: C, 78.21; H, 10.21. Found: C, 78.06; H, 10.40.

1-Ethyl-2-methyl-2,5-cyclohexadiene-1-methanol (4b). By following the above procedure and by using 1.66 g (10.0 mmol) of acid **2b**[10b] there was obtained 1.10 g (72%) of **4b** as a pale yellow oil, bp 104–107 °C (0.1 Torr). ^{1}H NMR δ 0.74 (t, J = 7.6 Hz, 3H), 1.08 (dq, J = 14.1, 7.6 Hz, 1H), 1.38 (dd, J = 6.9, 5.4 Hz, 1H), 1.49 (dq, J = 14.1, 7.6 Hz, 1H), 1.66 (d, J = 1.9 Hz, 3H), 2.64–2.69 (m, 2H), 3.19 (dd, J = 10.5, 5.4 Hz, 1H), 3.62 (dd, J = 10.5, 6.9 Hz, 1H), 5.25 (dt, J = 10.0, 2.0 Hz, 1H), 5.75–5.78 (m, 1H), 5.99 (dtd, J = 10.0, 3.3, 1.6 Hz, 1H). ^{13}C NMR δ 8.3 (q), 18.1 (q), 26.8 (t), 27.4 (t), 46.9 (s), 68.2 (t), 125.4 (d), 128.3 (d), 130.4 (d), 132.2 (s). IR (neat) ν 3430, 2960, 2910 cm^{-1}. Anal. Calcd for $C_{10}H_{16}O$: C, 78.90; H, 10.59. Found: C, 78.65; H, 10.70.

1-Isopropyl-2-methyl-2,5-cyclohexadiene-1-methanol (4c). By following the above procedure and by using 1.80 g (10.0 mmol) of acid **2c**[10a] there was obtained 1.17 g (70%) of **4c** as a pale yellow oil, bp 128–132 °C (0.1 Torr). ^{1}H NMR δ 0.75 (d, J = 6.9 Hz, 3H), 0.89 (d, J = 6.9 Hz, 3H), 1.31 (br s, 1H), 1.68 (d, J = 1.7 Hz, 3H), 1.86 (sept, J = 6.9 Hz, 1H), 2.62–2.67 (m, 2H), 3.48 (dd, J = 10.3, 4.5 Hz, 1H), 3.60 (dd, J = 10.3, 4.5 Hz, 1H), 5.45 (dt, J = 10.2, 2.0 Hz, 1H), 5.74–5.79 (m, 1H), 6.05 (dtd, J = 10.2, 3.3, 1.6 Hz, 1H). ^{13}C NMR δ 16.1 (q), 16.3 (q), 18.6 (q), 27.2 (t), 31.0 (d), 48.8 (s), 66.6 (t), 125.5 (d), 126.5(d), 128.9 (d), 133.3 (s). IR (neat) ν 3417, 3023, 2960 cm^{-1}. Anal. Calcd for $C_{11}H_{18}O$: C, 79.47; H, 10.91. Found: C, 79.18; H, 11.17.

General Procedure for the NMR Scale Photooxygenations. A solution of 0.500 mmol of the corresponding cyclohexadiene and ca. 1 mg of tetraphenylporphin (TPP) as sensitizer in 0.7 mL of $CDCl_3$ was photooxygenated directly in an NMR tube at −30 °C by passing a slow stream of dry oxygen gas through the solution while externally irradiating with two 150-W sodium lamps until complete conversion of the cyclohexadiene (TLC). The product ratios were determined by ^{1}H NMR spectroscopy.

General Procedure for the Preparative Photooxygenations. A solution of 5.00 mmol of the appropriate cyclohexadiene and ca. 2 mg of tetraphenylporphin (TPP) in 70 mL of $CHCl_3$ was photooxygenated by passing a slow stream of dry oxygen gas through the solution at −30 °C. The mixture was externally irradiated with two 150-W sodium lamps until complete conversion of the cyclohexadiene (TLC). The solvent was removed (0 °C (20 Torr)) and the remaining oily residue was purified directly by column chromatography.

Methyl 1-Hydroperoxy-3-methyl-2-methylenecyclohex-4-ene-3-carboxylate (5a). The photooxygenation of 830 mg (5.00 mmol) of ester **3a**[10b] yielded after silica gel column chromatography (petroleum ether–*tert*-butyl methyl ether 9:1) 780 mg (79%) of *trans*-**5a** (R_f = 0.10) and 100 mg (10%) of *cis*-**5a** (R_f = 0.16) as pale yellow oils. *trans*-**5a**: ^{1}H NMR δ 1.48 (s, 3H), 2.22 (dddd, J = 17.0, 8.0, 3.1, 2.2 Hz, 1H), 2.61(dddd, J = 17.0, 5.7, 4.4, 1.6 Hz, 1H), 3.75 (s, 3H), 4.77 (ddt, J = 8.0, 5.7, 1.0 Hz, 1H), 5.16 (s, 1H), 5.34 (s, 1H), 5.55 (ddd, J = 9.8, 2.2, 1.6 Hz, 1H), 5.73 (ddd, J = 9.8, 4.4, 3.1 Hz, 1H), 8.67 (br s, 1H). ^{13}C NMR δ 24.5 (q), 31.0 (t), 50.0 (s), 52.6 (q), 82.3 (d), 110.7 (t), 124.3 (d), 130.8 (d), 145.7 (s), 175.1 (s). IR (neat) ν 3440, 2954, 1734 cm^{-1}. Anal. Calcd for $C_{10}H_{14}O_4$: C, 60.60; H, 7.12. Found: C, 60.68; H, 7.24. *cis*-**5a**: ^{1}H NMR δ 1.51 (s, 3H), 2.30–2.52 (m, 2H), 3.73 (s, 3H), 4.60 (dd, J = 4.9, 1.1 Hz, 1H), 5.34 (s, 1H), 5.45 (s, 1H), 5.60–5.68 (m, 2H). ^{13}C NMR δ 24.7 (q), 30.9 (t), 51.0 (s), 53.8 (q), 84.1 (d), 118.0 (t), 124.0 (d), 129.7 (d), 143.8 (s), 174.1 (s). IR (neat) ν 3430, 2951, 1727 cm^{-1}. Anal. Calcd for $C_{10}H_{14}O_4$: C, 60.60; H, 7.12. Found: C, 60.72; H, 7.31.

Methyl 3-Ethyl-1-hydroperoxy-2-methylenecyclohex-4-ene-3-carboxylate (5b). From the photooxygenation of 900 mg (5.00 mmol) of ester **3b**[10b] were obtained 690 mg (65%) of pure *cis*-**5b** (R_f = 0.20) and 270 mg (25%) of *trans*-**5b** (R_f = 0.15) after silica gel column chromatography (petroleum ether–*tert*-butyl methyl ether 9:1), which contained a small amount of *cis*-**5b**. *cis*-**5b**: ^{1}H NMR δ 0.90 (t, J = 7.5 Hz, 3H), 1.98 (q, J = 7.5 Hz, 2H), 2.32–2.46 (m, 2H), 3.74 (s, 3H), 4.56 (dd, J = 4.7, 1.9 Hz, 1H), 5.30 (s, 1H), 5.55 (s, 1H), 5.63 (dt J = 10.0, 2.2 Hz, 1H), 5.74 (ddd, J = 10.0, 4.5, 2.5 Hz, 1H), 9.64 (s, 1H). ^{13}C NMR δ 8.4 (q), 29.0 (t), 30.1 (t), 50.9 (s), 53.0 (q), 84.4 (d), 119.3 (t), 125.1 (d), 129.7 (d), 140.4 (s), 177.7 (s). IR (neat) ν 3450, 2974, 1705 cm^{-1}. Anal. Calcd for $C_{11}H_{16}O_4$: C, 62.25; H, 7.60. Found: C, 61.84; H, 7.63. *trans*-**5b**: ^{1}H NMR δ 3.68 (s, 3H), 4.69 (dd, J = 8.1, 3.7 Hz, 1H), 5.18 (s, 1H), 5.41 (s, 1H), the signals are partially overlapped by those of the *cis*-**5b** diastereomer and only the separated resonances are given. ^{13}C NMR δ 8.7 (q), 29.2 (t), 30.3 (t), 52.3 (q), 55.2 (s), 82.3 (d), 112.0 (t), 127.5 (d), 128.6 (d), 143.0 (s), 171.7 (s).

Methyl 1-Hydroperoxy-3-isopropyl-2-methylenecyclohex-4-ene-3-carboxylate (5c). The photooxygenation of 970 mg (5.00 mmol) of ester **3c**[10b] afforded after silica gel column chromatography (petro-

(16) (a) Schultz, A. G.; Macielag, M.; Sundararaman, P.; Taveras, A. G.; Welch, M. *J. Am. Chem. Soc.* **1988**, *110*, 7828–7841. (b) Schultz, A. G. *Acc. Chem. Res.* **1990**, *23*, 207–213.

leum ether−*tert*-butyl methyl ether 9:1) 960 mg (85%) of pure *cis*-**5c** (R_f = 0.20) as a colorless oil. ^{1}H NMR δ 0.88 (d, J = 6.8 Hz, 3H), 0.96 (d, J = 6.8 Hz, 3H), 2.38−2.51 (m, 2H), 2.48 (sept, J = 6.8 Hz, 1H), 3.72 (s, 3H), 4.54 (dd, J = 5.0, 2.1 Hz, 1H), 5.39 (s, 1H), 5.51 (s, 1H), 5.65−5.80 (m, 2H), 8.78 (s, 1H). ^{13}C NMR δ 17.7 (q), 18.0 (q), 30.2 (t), 32.2 (d), 52.7 (q), 53.9 (s), 85.3 (d), 118.7 (t), 124.8 (d), 125.0 (d), 141.3 (s), 177.4 (s). IR (neat) ν 3440, 2959, 1722 cm^{-1}. Anal. Calcd for $C_{12}H_{18}O_4$: C, 63.70; H, 8.02. Found: C, 63.42; H, 7.96.

1-Hydroperoxy-3-methyl-2-methylenecyclohex-4-ene-3-methanol (6a). The photooxygenation of 690 mg (5.00 mmol) of alcohol **4a** yielded 300 mg (35%) of pure *trans*-**6a** (R_f = 0.20) and 500 mg (59%) of pure *cis*-**6a** (R_f = 0.25) after silica gel column chromatography (petroleum ether−*tert*-butyl methyl ether 8:2). *trans*-**6a**: ^{1}H NMR δ 1.20 (s, 3H), 2.34−2.42 (m, 2H), 3.15 (br s, 1H), 3.33 (d, J = 11.4 Hz, 1H), 3.49 (d, J = 11.4 Hz, 1H), 4.71 (ddt, J = 6.6, 2.3, 1.1 Hz, 1H), 5.30 (s, 1H), 5.38 (s, 1H), 5.37−5.74 (m, 2H), 9.75 (s, 1H). ^{13}C NMR δ 23.6 (q), 30.8 (t), 44.7 (s), 70.0 (t), 82.5 (d), 110.6 (t), 122.1 (d), 129.7 (d), 148.0 (s). IR (neat) ν 3450, 2965 cm^{-1}. Anal. Calcd for $C_9H_{14}O_3$: C, 63.51; H, 8.29. Found: C, 63.90; H, 8.58. *cis*-**6a**: ^{1}H NMR δ 1.22 (s, 3H), 2.24−2.38 (m, 2H), 3.15 (br s, 1H), 3.41 (d, J = 10.5 Hz, 1H), 3.66 (d, J = 10.5 Hz, 1H), 4.61 (dd, J = 4.3, 2.3 Hz, 1H), 5.32 (s, 1H), 5.53 (s, 1H), 5.65−5.72 (m, 2H), 9.75 (s, 1H). ^{13}C NMR δ 24.6 (q), 29.3 (t), 42.4 (s), 72.0 (t), 83.8 (d), 118.3 (t), 124.5 (d), 132.4 (d), 146.0 (s). IR (neat) ν 3430, 2960 cm^{-1}. Anal. Calcd for $C_9H_{14}O_3$: C, 63.51; H, 8.29. Found: C, 63.82; H, 8.48.

3-Ethyl-1-hydroperoxy-2-methylenecyclohex-4-ene-3-methanol (6b). From the photooxygenation of 760 mg (5.00 mmol) of alcohol **4b** was obtained 790 mg (86%) of pure *cis*-**6b** (R_f = 0.20) as a colorless oil after column chromatography (petroleum ether−*tert*-butyl methyl ether 9:1). ^{1}H NMR δ 0.76 (t, J = 7.3 Hz, 3H), 1.28 (dq, J = 13.8, 7.3 Hz, 1H), 1.71 (dq, J = 13.8, 7.3 Hz, 1H), 2.25−2.33 (m, 2H), 2.35 (br s, 1H), 3.41 (d, J = 10.4 Hz, 1H), 3.62 (d, J = 10.4 Hz, 1H), 4.60 (t, J = 3.3 Hz, 1H), 5.25 (d, J = 10.6 Hz, 1H), 5.30 (s, 1H), 5.49 (s, 1H), 5.90 (dt, J = 10.6, 3.9 Hz, 1H), 9.54 (s, 1H). ^{13}C NMR δ 8.0 (q), 28.6 (t), 29.3 (t), 40.4 (s), 73.8 (t), 84.1 (d), 119.6 (t), 127.4 (d), 130.4 (d), 143.2 (s). IR (neat) ν 3312, 3024, 2965 cm^{-1}. Anal. Calcd for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75. Found: C, 64.94; H, 9.03.

1-Hydroperoxy-3-isopropyl-2-methylenecyclohex-4-ene-3-methanol (6c). The photooxygenation of 830 mg (5.00 mmol) of alcohol **4c** yielded 920 mg (93%) of pure *cis*-**6c** (R_f = 0.20) after silica gel column chromatography (petroleum ether−*tert*-butyl methyl ether 6:4) as a white solid, mp 55−56 °C. ^{1}H NMR δ 0.78 (d, J = 6.8 Hz, 3H), 0.92 (d, J = 6.8 Hz, 3H), 2.10 (sept, J = 6.8 Hz, 1H), 2.29−2.34 (m, 2H), 2.80 (br s, 1H), 3.51 (d, J = 10.4 Hz, 1H), 3.81 (d, J = 10.4 Hz, 1H), 4.59 (t, J = 3.6 Hz, 1H), 5.40 (s, 1H), 5.48 (s, 1H), 5.44 (d, J = 10.3 Hz, 1H), 5.96 (dt, J = 10.3, 4.1 Hz, 1H), 9.56 (s, 1H). ^{13}C NMR δ 17.3 (q), 18.3 (q), 27.9 (t), 34.9 (d), 49.8 (s), 71.4 (t), 84.3 (d), 119.2 (t), 127.31 (d), 128.1 (d), 144.8 (s). IR (neat) ν 3314, 2962 cm^{-1}. Anal. Calcd for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15. Found: C, 66.57; H, 9.27.

The photooxygenation of 761 mg (5.00 mmol) of **methyl 1-methyl-2,5-cyclhexadiene-1-carboxylate (7)** yielded after 3 days no hydroperoxide **8**. After removal of the solvent ester **7** was recovered in quantitative yield.

***trans*-1-Acetoxy-3-methyl-2-methylenecyclohex-4-ene-3-methanol Acetate (*trans*-11).** To a suspension of 265 mg (7.0 mmol) of $LiAlH_4$ in 15 mL of diethyl ether under an argon gas atmosphere was added at 0 °C a solution of 595 mg (3.00 mmol) of the hydroperoxide *trans*-**5a** in 10 mL of diethyl ether over a period of 20 min. After the solution was stirred for 18 h at room temperature, a mixture of 1.0 mL of H_2O and 3.5 mL of dioxane was added at 0 °C within 10 min. Stirring was continued for 15 min at room temperature and the mixture was filtered over Celite and dried (Na_2SO_4). Evaporation of the solvent afforded 530 mg (>98%) crude product, which was directly dissolved in a mixture of 5.00 mL (53.0 mmol) of acetic anhydride and 10.0 mL (124 mmol) of pyridine. After standing for 20 h at room temperature, the solution was concentrated (40 °C, (18 Torr)) and the residue was directly purified by silica gel column chromatography (petroleum ether−*tert*-butyl methyl ether 9:1) to yield 630 mg (88%) of diastereomerically pure *trans*-**8** (R_f = 0.24) as a colorless oil. ^{1}H NMR δ 1.22 (s, 3H), 2.06 (s, 3H), 2.12 (s, 3H), 2.19 (ddd, J = 16.6, 9.2, 2.6 Hz, 1H), 2.52 (ddd, J = 16.6, 5.8, 5.3 Hz, 1H), 3.91 (d, J = 10.8 Hz, 1H), 4.04 (d, J = 10.8 Hz, 1H), 5.01 (s, 1H), 5.18 (s, 1H), 5.39 (dd, J = 9.8, 0.5 Hz, 1H), 5.61 (dd, J = 9.2, 5.8, 0.5 Hz, 1H), 5.70 (ddd, J = 9.8, 5.3, 2.6 Hz, 1H). ^{13}C NMR δ 20.8 (q), 21.1 (q), 23.7 (q), 32.4 (t), 42.8 (s), 70.6 (d), 71.2 (t), 107.9 (t), 124.2 (d), 132.6 (d), 147.6 (s) 169.9 (s), 170.8 (s). Anal. Calcd for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61. Found: C, 65.66; H, 7.30.

***cis*-1-Acetoxy-3-methyl-2-methylenecyclohex-4-ene-3-methanol Acetate (*cis*-11).** To a solution of 340 mg (2.00 mmol) of the hydroperoxide *cis*-**6a** in 10 mL of methanol was added 40.0 mg (1.06 mmol) of sodium borohydride under argon at 0 °C. After the mixture was stirred for 2 h at room temperature, the solvent was evaporated and the crude product was directly dissolved in a mixture of 5.00 mL (53.0 mmol) of acetic anhydride and 10.0 mL (124 mmol) of pyridine. After standing for 20 h at room temperature, the solution was concentrated (40 °C (18 Torr)) and the residue was directly purified by silica gel column chromatography (petroleum ether−*tert*-butyl methyl ether 9:1) to yield 450 mg (94%) of diastereomerically pure *cis*-**8** (R_f = 0.30) as a colorless oil. ^{1}H NMR δ 1.23 (s, 3H), 2.05 (s, 3H), 2.09 (s, 3H), 2.23 (dddd, J = 17.2, 6.7, 3.5, 2.0 Hz, 1H), 2.48 (dddd, J = 17.2, 5.1, 4.2, 1.7 Hz, 1H), 4.06 (d, J = 10.8 Hz, 1H), 4.14 (d, J = 10.8 Hz, 1H), 5.02 (s, 1H), 5.20 (s, 1H), 5.48 (ddd, J = 10.0, 2.0, 1.7 Hz, 1H), 5.54 (ddd, J = 6.7, 5.1, 0.5 Hz, 1H), 5.69 (ddd, J = 10.0, 4.2, 3.5 Hz, 1H). ^{13}C NMR δ 20.9 (q), 21.3 (q), 23.3 (q), 32.2 (t), 41.7 (s), 69.8 (t), 71.2 (d), 110.2 (t), 123.6 (d), 132.2 (d), 146.5 (s) 170.2 (s), 171.9 (s). Anal. Calcd for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61. Found: C, 65.69; H, 7.51.

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