Diastereoselective Addition of Singlet Oxygen to Highly Functionalized *Z*-Allylic Alcohols: Effect of Neighboring Functional Groups

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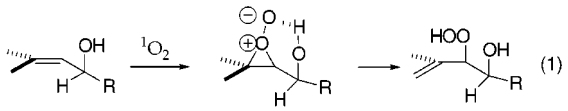
Introduction

As part of a program targeting stereoselective synthesis of hydroperoxide-containing natural products,[1] we became interested in highly functionalized peroxides as precursors to both hydroperoxyeicosatetraenoic acids (HPETEs) and alkoxy dioxins (Scheme 1). A convenient approach to the desired synthons seemed to lie in addition of singlet oxygen ($^1O_2$) to a 3-hydroxy-4*Z*-alkenoate, followed by hydroboration of the resulting alkene and elimination of the original hydroxyl directing group. The key step of this sequence, diastereoselective oxygenation of chiral 2-alkenols, has not been extensively studied other than for relatively simple models.[2,3] In this paper, we describe the diastereoselectivity of hydroxyl-directed $^1O_2$ addition in the presence of nearby Lewis basic functional groups. The reaction diastereoselection, while greatly reduced for alcohols containing a neighboring carbonyl, proves to be remarkably tolerant of nearby ethers, alcohols, and alkenes.

Results and Discussion

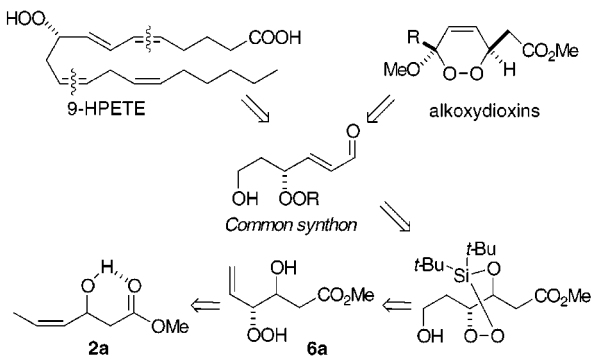
Our initial approach to the desired synthon began with allylic alcohol **2a** (Scheme 1). Addition of $^1O_2$ to the allylic alcohol would introduce the hydroperoxide group while establishing a terminal alkene for necessary synthetic elaboration. On the basis of Adam's studies, oxygenation of **2a** was anticipated to selectively furnish 1,2-hydroperoxy alcohol **6a** as the syn diastereomer. The syn selectivity in these oxygenations has been attributed to hydrogen bonding between the hydroxyl group and either the incoming $^1O_2$ or the developing perepoxide in a ground-state conformation that is limited by allylic strain (eq 1).[2] In fact, photooxygenation of **2a** proceeded in 57% yield but produced the allylic hydroperoxide **6a** as a 60:40 mixture of diastereomers.



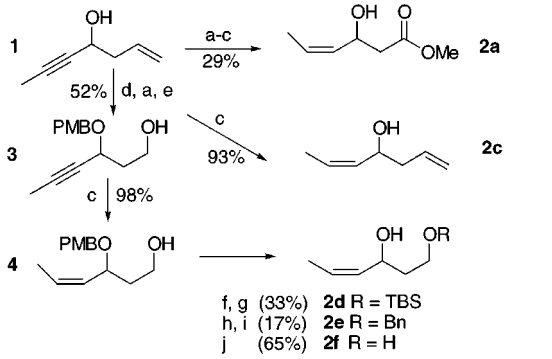
(1)

Suspecting that the disappointing diastereoselectivity reflected disruption of the hydrogen-bonded transition state by an intramolecular hydrogen bond between the hydroxyl and the carbonyl, we investigated a series of *Z*-allylic alcohol derivatives **2a**−**i** to test the impact of neighboring oxygenation on the diastereoselectivity of hydroxyl-directed oxygenation.

Scheme 1



Scheme 2[a]



[a] Key: (a) O_3, −78 °C, CH_2Cl_2/MeOH (85:15); (b) Ac_2O, NEt_3; (c) Pd/$CaCO_3$, H_2, quinoline; (d) PMBBr, NaH, DMF; (e) $NaBH_4$; (f) TBSCl, Imid, DMF; (g) $MgBr_2$·OEt_2, Me_2S, CH_2Cl_2; (h) BnBr, NaH, DMF; (i) DDQ, CH_3CN/H_2O (9:1); (j) Li, NH_3.

Synthesis of 1,3-Functionalized Substrates. Propargyl alcohol **1** was prepared through [2,3] Wittig rearrangement of allyl 2-butynyl ether, itself available from allylation of 2-butynol.[4,5] Ozonolysis of **1** in the presence of methanol, followed by Kornblum elimination of the intermediate hydroperoxy acetal,[6,7] furnished a hydroxyalkynoate that was reduced to hydroxyester **2a** (Scheme 2). A simple alkenol substrate, (*Z*)-2-decen-3-ol (**2b**), was prepared through a reported procedure.[8] Dienol **2c** was obtained from semihydrogenation of **1**. Conversion of **1** as the PMB ether, followed by ozonolysis and reduction, furnished alkynol **3**, which underwent reduction to form alkene **4**, the precursor of three different substrates. Silylation or benzylation of the primary alcohol, followed by removal of the PMB group,[9] furnished diol monoethers **2d** and **2e**, respectively. Alternatively, deprotection of the PMB ether from **4** could be accomplished under dissolving metal conditions to furnish diol **2f**.

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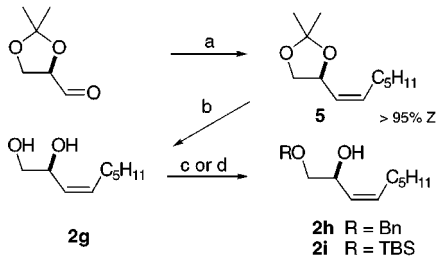
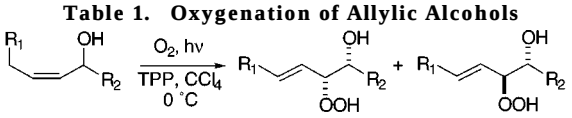
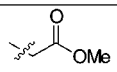
Scheme 3[a]



[a] Key: (a) LiHMDS, hexyl-$PPh_3^+Br^-$, THF, −78 °C, (67%); (b) DOWEX 50 × 8, EtOH, (89%); (c) TBSCl, NEt_3, DMAP, CH_2Cl_2, (55%); (d) (i) $Bu_2Sn(OMe)_2$, Dean−Stark, C_6H_6, Δ; (ii) BnBr, CsF, (33%).

Table 1. Oxygenation of Allylic Alcohols



entry	substrate	R_1	R_2	product	yield(%)[a]	syn:anti[b]
1	**2a**	H		**6a**	57	60:40
2	**2b**	H	C_6H_{13}	**6b**	70	95:5
3	**2c**	H		**6c**	58	90:10
4	**2d**	H		**6d**	50	88:12
5	**2e**	H		**6e**	55	89:11
6[c]	**2f**	H		**6f**	50	88:12
7	**2g**	C_4H_9	CH_2OH	**6g**	33	81:19
8	**2h**	C_4H_9	CH_2OTBS	**6h**	54	70:30
9	**2i**	C_4H_9	CH_2OBn	**6i**	63	68:32

[a] All yields based on isolated materials. [b] Ratio determined by ^1H NMR. [c] Reaction performed in CH_2Cl_2.

Synthesis of 1,2-Functionalized Substrates. The 1,2-diol derivatives were prepared from glyceraldehyde acetonide (Scheme 3).[10,11] Wittig homologation furnished (*Z*)-alkene **5**,[12] which was deprotected to form diol **2g**. Selective protection of the primary alcohol with TBSCl or BnBr furnished diol monoethers **2h** and **2i**, respectively.[12,13]

Diastereoselectivity of Oxygenation. As described above, photooxygenation of 1,3-hydroxy ester **2a** furnished the desired 1,2 peroxy alcohol **6a** in 57% yield as a 60:40 mixture of diastereomers (Table 1, entry 1).[14,15] The disappointing diastereoselectivity was attributed to the presence of an intramolecular hydrogen bond between the hydroxyl group and the ester, preventing effective direction of the incoming $^1O_2$. The presence of an intramolecular hydrogen bond was confirmed by comparison of solution IR spectra for **2a** and methyl 12-hydroxystearate under conditions (0.1 M in CCl_4) similar to those present during the photooxygenations. Under these conditions, the hydroxystearate displayed a single peak centered around 3634 cm^{-1}, indicative of a free OH stretch.[16] In contrast, the solution IR of **2a** displayed a small peak at 3620 cm^{-1} and a much larger peak centered at 3550 cm^{-1}, supporting the predominance of the intramolecular hydrogen bond. The spectrum of **2a** is similar to that reported for methyl 4-methyl-3-hydroxybutanoate, which has a intramolecular H-bond stretch at 3537 cm^{-1}.[17]

On the basis of this result, we were interested in the effect of other functional groups on the diastereoselectivity of hydroxyl-directed oxygenation (Table 1). As would be predicted, oxygenation of dienol **2c** compared favorably with control substrate **2b** (Table 1, entries 2 and 3). We next investigated the oxygenation of the 1-monobenzyl (Bn) and the 1-mono-*tert*-butyldimethylsilyl (TBS) ethers of 4-hexen-1,3-diol, assuming that the presence or absence of an intramolecular hydrogen bond would be manifested in the reaction diastereoselectivity. The choice of TBS and Bn ethers was based upon spectroscopic studies of Lewis acid complexation to 3-alkoxyaldehydes, in which benzyl ethers were found to readily enter into chelates while silyl ethers did not.[18] Our initial hypothesis appeared to be substantiated, with monosilyl ether **2d** reacting to form the 1,2 peroxy alcohol **6d** in 50% yield with diastereoselection of 88:12 (Table 1, entry 4). However, photooxygenation of benzyl ether **2e** produced the 1,2 peroxy alcohol **6e** with remarkably similar diastereoselectivity (89:11), and even the 1,3 diol (**2f**) reacted with good diastereoselectivity. Clearly, the diastereoselectivity of hydroxyl-directed oxygenation is little unaffected by the presence of alcohols, alkenes, or ethers in the 3-position relative to the original directing hydroxyl group.

Surprisingly, solution IR spectra of benzyl ether **2e** under typical reaction conditions (0.1 M in CCl_4) revealed a mixture of free (3622 cm^{-1}) and hydrogen-bonded (3532 cm^{-1}) OH stretches in which the latter was slightly dominant. However, the fraction of free OH stretch in the spectra of **2e** was substantially greater than in hydoxyester **2a**.

Oxygenation Studies of 1,2 Substrates. Several 1,2 functionalized substrates were also examined for the impact of a neighboring Lewis base on diastereoselectivity (Table 1, entries 7−9). Oxygenation of diol **2g** appeared to proceed with moderate diastereoselectivity. However, the limited solubility of the diol and the significant product decomposition observed during the reaction make it dangerous to draw conclusions from this substrate. Both an α-siloxy group (**2h**) and an α-benzyloxy group (**2i**) had a negative effect on diastereoselectivity. The apparently similar influence exerted by two groups of very different Lewis basicities may indicate that the reduced diastereoselection originates in sterically induced conformational changes rather than a disruption of the H-bond transition state.

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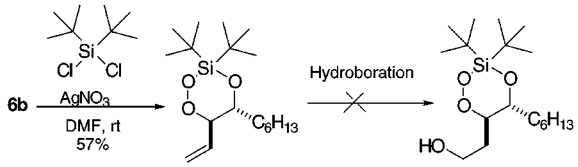
Table 2. ^{1}H NMR Shifts and Coupling Constants for CHOO

	minor diastereomer		major diastereomer	
product	δ (ppm)	J (Hz)	δ (ppm)	J (Hz)
6a	4.39	multiplet	4.34	6.9
6b	4.32	7.9, 2.6	4.18	7.9
6c	4.36	7.9, 2.3	4.24	7.6
6d	4.37	7.2, 3.3	4.28	7.6
6e	4.35	7.3, 3.2	4.26	7.3
6f	4.18	7.7, 4.0	4.21	7.3
6g	4.36	8.1, 3.2	4.3	8.1
6h	4.40	8.1, 4.0	4.35	7.7
6i	4.42	8.1, 4.1	4.40	7.7

Scheme 4



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Stereochemical Assignments. Assigment of relative configuration for the major and minor hydroperoxy alcohols was achieved through inspection of the ^{1}H NMR of the hydroperoxy alcohol products (Table 2). The proton adjacent to the hydroperoxide protons was nearly always downfield in the minor diastereomer relative to that of the major diastereomer. Furthermore, in the minor isomer, this proton was consistently observed as a doublet of doublets with a 7−8 Hz coupling to the alkene hydrogen and a much smaller coupling to the vicinal CHOH unit. In the major diastereomer, this peak group was consistently observed as an apparent triplet with large and similar couplings to both neighboring hydrogens. Both observations are consistent with previous reports in related systems.[15]

Application. Previous experience with the high kinetic stability of protected peroxides toward a variety of hydride and carbanion nucleophiles[19] led us to assume that the hydroboration of a protected hydroperoxide would be relatively straightforward. Simultaneous protection of the hydroperoxide and hydroxyl groups of **6b** was achieved through reaction with di-*tert*-butyldichlorosilane and $AgNO_3$ to form silatrioxane **7** (Scheme 4).[20] However, all attempts at hydroboration of the alkene (BH_3, 9-BBN,[21] catechol borane/Wilkinson's catalyst[22] or catechol borane/*N*,*N*-dimethylacetamide[23]) led only to decomposition of the peroxide.

Conclusions

The addition of $^1O_2$ to chiral 2-alkenols is a potentially powerful transformation that has seen little use in functionalized systems. Our investigations reveal that a neighboring carbonyl significantly decreases the diastereoselectivity of hydroxyl-directed photooxygenation, presumably due to competitive hydrogen bonding with the directing hydroxyl. Ethers or an alcohol in the 3-position relative to the directing hydroxyl have surprisingly little impact on reaction diastereoselectivity, given that intramolecular hydrogen-bonding, while weaker than for the carbonyl, is still present to some degree. Ethers and alcohols in the 2-position have a significant negative impact on reaction diastereoselectivity which may reflect a combination of hydrogen bonding and steric effects.

Experimental Section

Caution: As in any work involving peroxides, standard precautions (use of safety shields, avoidance of heat, light, or metal salts, performance of reactions on minimal scale) should be faithfully observed.[24−26]

General Methods. General experimental details are provided as Supporting Information.

General Procedure for Oxygenation of Alkenes. To a 0 °C jacketed Pyrex cell containing 10 mL of CCl_4 were added alkene (1.0 mmol) and 5,10,15,20-tetraphenyl-21*H*,23*H*-porphine (2×10^{-4} M). The solution was aspirated with oxygen and photolyzed with a 200 Wvisible illuminator (Dolan-Jenner Industries) from a distance of 3 cm until starting material was no longer observed by TLC. The solvent was removed in vacuo, and the residue was purified by flash chromatography.

(3*R,4*R**)-4-Hydroperoxy-3-hydroxyhex-5-enoic acid, methyl ester (6a):** R_f = 0.2 (40% EtOAc/hexanes); ^{1}H NMR (500 MHz) δ 9.36 (br s, 1H), 5.85 (ddd, 0.6H, J = 13.7, 10.9, 8.1 Hz), 5.44−5.38 (m, 2H), 4.41−4.37 (m, 0.6H), 4.34 (apt t, 0.6H, J = 6.9 Hz), 4.25 (ddd, 0.6H, J = 6.9, 8.5, 3.6 Hz), 3.70 (s, 3H), 2.57 (dd, 0.6H, J = 16.1, 3.6 Hz), 2.50 (dd, 0.6H, J = 16.5, 8.9 Hz); ^{13}C NMR (125 MHz) (major) δ 172.9, 132.4, 121.45, 88.6, 68.8, 52.0, 37.5, (minor) δ 172.6, 131.6, 121.54, 88.4, 68.2, 36.7; IR (neat) 3400, 1740 cm^{-1}.

3-Hydroperoxy-1-decen-4-ol (6b): R_f = 0.5 (40% EtOAc/hexanes); ^{1}H NMR (300 MHz) 9.52 (br s, 1H), 5.92−5.74 (m, 1H), 5.24−5.35 (m, 2H), 4.32 (dd, 0.45H, J = 7.9, 2.6 Hz), 4.18 (apparent t, 0.95H, J = 7.9 Hz), 4.01−3.96 (m, 0.05H), 3.67 (t, 0.95H, J = 7.6 Hz), 3.12 (br s, 1H), 1.56−1.15 (m, 10H), 0.85 (t, 3H, J = 6.9 Hz); ^{13}C NMR (75 MHz) 133.5, 131.4, 121.7, 121.0, 90.5, 89.5, 72.0, 71.1, 32.6, 32.2, 31.7, 29.2, 25.7, 25.1, 22.6, 14.0; IR (neat) 3401, 1086 cm^{-1}. Anal. Calcd for $C_{10}H_{20}O_3$: C, 63.80; H, 10.71. Found: C, 63.80; H,10.59.

(3*R,4*R**)-3-Hydroperoxyhepta-1,6-dien-4-ol (6c):** R_f = 0.4 (40% EtOAc/hexanes); ^{1}H NMR (300 MHz) δ 9.28 (br s, 1H), 5.90−5.76 (m, 2H), 5.42 (d, 1H, J = 17.4 Hz), 5.39 (d, 1H, J = 11.0 Hz), 5.11 (d, 2H, J = 13.6 Hz), 4.36 (dd, 0.1H, J = 7.9, 2.3 Hz), 4.24 (apparent t, 0.9H, J = 7.6 Hz), 4.1−4.02 (m, 0.1H), 3.77 (dt, 0.9H, J = 7.9, 3.8 Hz), 2.96 (br s, 1H), 2.38−2.33 (m, 1H), 2.24−2.1 (m, 1H); ^{13}C NMR (75 MHz) (major) δ 133.7, 133.0, 121.3, 118.3, 89.6, 71.3, 37.2, (minor) δ 134.1, 131.4, 121.9, 118.2, 88.9, 70.4, 36.8; IR (neat) 3491, 3281, 1644 cm^{-1}; HRMS(FAB) calcd for $C_7H_{12}O_3$ (M + Li)$^+$ 151.0946, found 151.0940.

(3*R,4*R**)-1-(Dimethyl-1,1-dimethylethylsilyloxy)-4-hydroperoxyhex-5-en-3-ol (6d):** R_f = 0.5 (40% EtOAc/hexanes); ^{1}H NMR (300 MHz) δ 9.58 (br s, 1H), 5.80 (ddd, 1H, J = 18.1, 10.5, 7.8 Hz), 5.40 (d, 1H, J = 16.0 Hz), 5.35 (d, 1H, J = 10.3 Hz), 4.37 (dd, 0.12H, J = 7.2, 3.3 Hz), 4.28 (apparent t, 0.88H, J = 7.6 Hz), 4.14 (dt, 0.12H, J = 9.3, 3.3 Hz), 3.98 (td, 0.88H, J = 7.6, 4.8 Hz), 3.91−3.76 (m, 2H), 1.71−1.65 (m, 2H), 0.87 (s, 9H) 0.06 (s, 6H); ^{13}C NMR (75 MHz) (major) δ 133.1, 120.9, 89.6, 72.4, 61.7, 34.3, 25.8, 18.1, −5.6, (minor) δ 132.3, 120.8, 89.05, 71.6, 62.05, 33.6; IR (neat) 3500, 3303 cm^{-1}; HRMS(FAB) calcd for $C_{12}H_{26}O_4Si$ (M + H)$^+$ 263.1678, found 263.1689.

(3*R,4*R**)-1-(Benzyloxy)-4-hydroperoxyhex-5-en-3-ol (6e):** R_f = 0.25 (40% EtOAc/hexanes); ^{1}H NMR (500 MHz) δ 9.55 (br s, 1H), 7.45−7.30 (m, 5H), 5.81 (ddd, 1H, J = 17.3, 10.5, 8.1 Hz), 5.38 (d, 1H, J = 18.5 Hz), 5.35 (d, 1H, J = 10.9 Hz), 4.51 (s, 2H), 4.35 (dd, 0.11H, J = 7.3 Hz), 4.26 (apt t, 0.89H, J

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= 7.3 Hz), 4.15 (apt dt, 0.11H, J = 7.7, 3.6 Hz), 3.96 (ddd, 0.89H, J = 9.3, 7.3, 2.8 Hz), 3.70 (ddd, 1H, J = 9.3, 6.9, 4.9 Hz), 3.64 (ddd, 1H, J = 9.7, 7.3, 5.2 Hz), 3.55 (br s, 1H), 1.82 (dddd, 1H, J = 14.5, 7.7, 4.8, 2.8 Hz), 1.73 (dddd, 1H, J = 14.5, 9.3, 6.9, 4.8 Hz); ^{13}C NMR (125 MHz) (major) δ 137.8, 133.1, 28.4, 127.7, 120.9, 89.7, 73.2, 71.3, 67.9, 32.4, (minor) δ 132.1, 121.0, 89.2, 70.5, 68.2, 31.7; IR (neat) 3515, 3207 cm^{-1}.

(3*R,4*R**)-4-Hydroperoxyhex-5-en-1,3-diol (6f):** R_f = 0.2 (EtOAc); ^{1}H NMR (500 MHz, $(CD_3)_2O$) δ 10.7 (br s, 1H), 5.85 (ddd, 1H, J = 17.3, 10.9, 7.7 Hz), 5.30 (d, 1H, J = 17.7 Hz), 5.23 (d, 1H, J = 10.9 Hz), 4.21 (apparent t, 0.88H, J = 7.25 Hz), 4.18 (dd, 0.12H, J = 7.7, 4.0), 3.97 (br s, 1H), 3.92−3.89 (m, 1H), 3.70 (t, 2H, J = 6.4), 3.12 (br s, 1H) 1.74−1.51 (m, 2H); ^{13}C NMR (125 MHz, $(CD_3)_2O$) δ 135.0, 128.5, 89.8, 69.7, 59.5, 35.3.

(2*R*,3*R*,4*E*)-3-Hydroperoxynon-4-en-1,2-diol (6g): R_f = 0.2 (5% MeOH/CH_2Cl_2); ^{1}H NMR (500 MHz) δ 10.18 (br s, 1H), 5.85 (dt, 1H, J = 15.3, 6.9 Hz), 5.45 (dd, 1H, J = 15.3, 8.1 Hz), 4.36 (dd, 0.19H, J = 8.1, 3.2 Hz), 4.3 (apparent t, 0.81H, J = 8.1 Hz), 4.08−4.05 (m, 0.19H), 3.81 (td, 0.81H, J = 7.3, 2.8 Hz), 3.7 (dd, 2H, J = 11.7, 2.8 Hz), 3.55 (dd, 2H, J = 11.7, 6.1 Hz), 2.07 (apparent q, 2H, J = 7.3), 1.38−1.28 (m, 4H), 0.89 (t, 3H, J = 7.3); ^{13}C NMR (125 MHz) (major) δ 138.7, 124.2, 87.3, 72.6, 63.4, 32.2, 31.0, 22.2, 13.8, (minor) δ 139.3, 122.9, 87.1, 72.0, 63.1, 31.5, 22.5; IR (Neat): 3347, 2964 cm^{-1}; HRMS calcd for $C_9H_{18}O_4$ (M + Li)$^+$ 197.1365, found 197.1358.

(2*R*,3*R*,4*E*)-1-(Dimethyl-1,1-dimethylethylsilyoxy)-3-hydroperoxynon-4-en-2-ol (6h): R_f = 0.6 (40% EtOAc/hexanes); ^{1}H NMR (500 MHz) δ 9.41 (br s, 0.7H), 8.99 (br s, 0.3H), 5.84 (dt, 1H, J = 15.3, 6.9 Hz), 5.51 (dd, 0.3H, J = 15.7, 8.1 Hz), 5.44 (dd, 0.7H, J = 15.7, 8.5 Hz), 4.40 (dd, 0.3H, J = 8.1, 4.0 Hz), 4.35 (apt dt, 0.7H, J = 7.65 Hz), 3.96−3.93 (m, 0.3H), 3.77−3.74 (m, 0.3H), 3.70 (dd, 0.7H J = 10.5, 3.6 Hz), 3.65−3.63 (m, 0.7H), 3.58 (dd, 0.7H, J = 10.5, 4.8 Hz), 2.88 (br s, 0.7H), 2.70 (br s, 0.3H), 2.10−2.02 (m, 2H), 1.39 (m, 4H), 0.88 (s, 9H) 0.87 (t, 3H, J = 6.9 Hz), 0.06 (s, 3H) 0.05 (s, 3H); ^{13}C NMR (125 MHz) (major) δ 138.5, 124.2, 87.1, 73.3, 63.8, 32.15, 30.98, 25.8, 22.2, 18.3, 13.8, −5.47, −5.53, (minor) δ 138.9, 123.4, 86.8, 71.9, 63.5, 32.20, 31.02; IR (neat) 3557, 3050 cm^{-1}; HRMS(FAB) calcd for $C_{15}H_{32}O_4Si$ (M + Li)$^+$ 311.2230, found 311.2238.

(2*R*,3*R*,4*E*)-1-(Benzyloxy)-3-hydroperoxynon-4-en-2-ol (6i): R_f = 0.4 (40% EtOAc/hexanes); ^{1}H NMR (500 MHz) δ 9.06 (br s, 0.68H), 8.75 (br s, 0.32H), 7.36−7.28 (m, 5H), 5.83 (dt, 0.68H, J = 15.7, 6.9 Hz), 5.49 (ddt, 0.68H, J = 15.3, 8.1, 1.2 Hz), 5.42 (ddt, J = 15.3, 8.1, 1.2 Hz), 4.57 (d, 0.68H, J = 12.1 Hz), 4.51 (d, 0.68H, J = 11.7 Hz), 4.42 (dd, 0.32H, J = 8.1, 4.1 Hz), 4.40 (apparent t, 0.68H, J = 7.7 Hz), 4.12 (dt, 0.32H, J = 6.0, 4.4 Hz), 3.91 (ddd, 0.68H, J = 6.9, 5.6, 3.2 Hz), 3.58 (dd, 0.68H, J = 10.1, 3.2 Hz), 3.47 (dd, 0.68H, J = 10.1, 5.6 Hz), 2.85 (br s, 1H), 2.08−2.02 (m, 2H), 1.36−1.25 (m, 6H), 0.88 (t, 3H, J = 6.9 Hz); ^{13}C NMR (125 MHz) (major) δ 138.8, 137.6, 128.5, 127.9, 127.8, 123.9, 123.0, 87.2, 73.63, 72.1, 70.9, 32.1, 30.9, 22.2, 13.8, (minor) δ 139.2, 123.0, 87.0, 73.57, 70.7, 70.6, 32.2, 31.0; IR (neat) 3329, 2937 cm^{-1}; HRMS(FAB) calcd for $C_{10}H_{24}O_4$ (M + Li)$^+$ 287.1835, found 287.1825.

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Supporting Information Available: Experimental details for the preparation of **1**−**5** and **7** as well as ^{1}H and ^{13}C spectra for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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