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An Organometallic Approach to Peroxyketals

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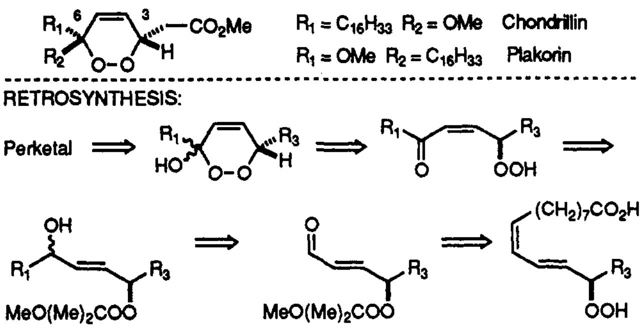
A new method for peroxyketal synthesis is presented based upon formation of carbon–carbon bonds in the presence of a protected hydroperoxide. The 2-methoxypropyl perketal of 4(*S*)-hydroperoxy-2(*E*)-nonenal (2) undergoes reaction with a variety of metal hydrides and organometallic reagents to produce 4-peroxy 2-enols in good to excellent yields via chemoselective addition to the carbonyl carbon. Oxidation of the allylic alcohol to the 4-peroxy 2-enone is followed by deprotection to furnish a single enantiomer of a 4-hydroxyperoxy 2(*E*)-enone. Photochemical isomerization by the method of Snider induces spontaneous cyclization to epimeric 3-hydroxy-1,2-dioxins (hydroxy endoperoxides). Acidic methanolysis furnishes readily separable diastereomeric perketals as single enantiomers.

The last several decades have brought an increased recognition of the importance of peroxide-containing natural products.[1] However, the sensitivity of the peroxide linkage and the limited number of methods available for introduction of the peroxide group have combined to greatly restrict synthetic progress in this area. For example, chondrillin (Scheme I), a sponge-derived peroxyketal displaying *in vitro* antitumor activity, and the epimeric plakorin, a potent ATPase activator, have only recently yielded to a racemic synthesis centered about photooxygenation of a prochiral enone.[2] In general, most peroxide syntheses rely on penultimate photooxygenation or displacement with hydrogen peroxide for introduction of the peroxide group.[2–6] Recent research in our labs has targeted new methods for construction of hydroperoxide and peroxide natural products based upon the construction of carbon–carbon bonds in the presence of a protected peroxide group.[7–10] We wish to report the chemoselective addition of hydrides and organometallic nucleophiles to aldehydes in the presence of a masked peroxide and the application of this chemistry toward the enantioselective synthesis of cyclic peroxyketals.

Our retrosynthetic approach toward peroxyketals is illustrated in Scheme I. The cyclic peroxide arises through spontaneous cyclization of a 4-hydroxyperoxy-2(*Z*)-alkenone. The two C_6 (peracetal) epimers undergo acid-catalyzed equilibration, and absolute control of C_6 stereochemistry therefore depends upon control of hydroperoxide stereochemistry in the acyclic precursor. The peroxy enone will be obtained via oxidation of a peroxy alcohol derived through chemoselective addition of an organometallic nucleophile to a protected peroxy enal in which the stereogenic peroxide-bearing carbon represents C_3 of the future cyclic peroxyketal. Synthesis of enantiomerically pure peroxy enals through regioselective ozonolysis of enzymatically derived hydroperoxy dienes has been previously reported.[9]

Scheme I



A number of workers have reported the spontaneous cyclization of hydroperoxy ketones or aldehydes to the corresponding hemiketals, and cyclization of 4-hydroperoxy ketones or aldehydes was postulated as a key step in a recent photooxygenation-based synthesis of racemic perketals.[2,11–13] However, the application of organometallic reagents for synthesis of the requisite peroxy enone was expected to be more problematic; attack of organometallic reagents on peroxides is, in fact, a known procedure for the synthesis of alkyl and aryl ethers.[14] A few isolated examples point to the possible use of organometallic reagents in the presence of peroxides. Reaction of organometallic nucleophiles with α-chloro peroxides has been employed for the synthesis of dialkyl peroxides, and addition of an acetylide to a carbonyl group has been reported to occur in the presence of a tertiary hydroperoxide.[15,16] Reduction of β-*tert*-butylperoxyorganomercurials with sodium borohydride is known to proceed via selective attack on mercury,[17,18] and borohydride reduction has also been employed for the chemoselective reduction of a lactone in the presence of a bicyclic peroxide.[19] Finally, the well-known autoxidation of or-

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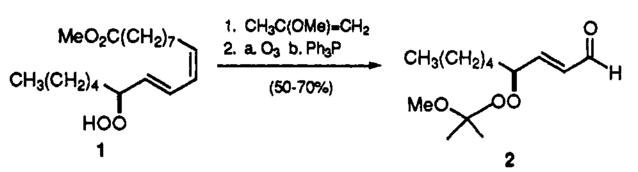
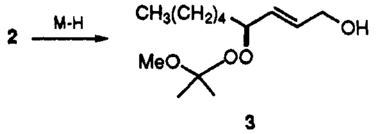
Scheme II

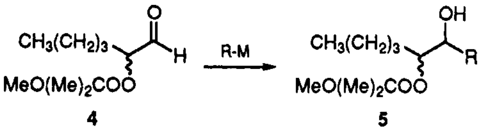


Scheme III

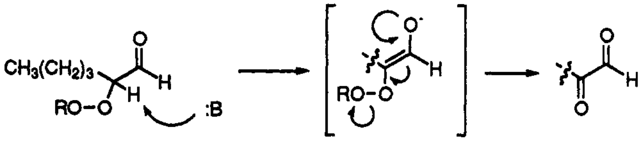


M-H	Yield
NaBH$_4$/iPrOH	31%
DIBAL-H/THF	88%
LAH/THF	97%

Scheme IV



R-M	Yield of 5	R
PhMgBr	NR	Ph
PhLi	NR	Ph
nBuMgBr	NR	nBu
LAH	37%	H



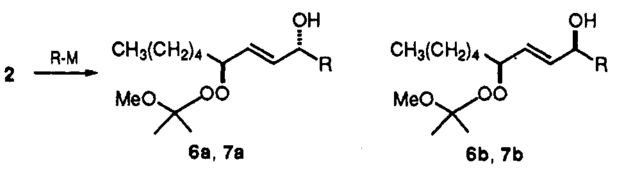
ganometallics to hydroperoxides implies at least the transient coexistence of peroxides and organometallic reagents.[20]

Our initial attempts involved the addition of various metal hydrides to aldehyde **2**, available in three steps from linoleic acid[9] (Scheme II). The metal hydride was added to a solution of the peroxy aldehyde until no starting material remained by thin-layer assay (Scheme III). We were pleasantly surprised to find that reaction of **2** with either lithium aluminum hydride (LAH) or diisobutylaluminum hydride (DIBAL) afforded excellent yields of the corresponding 4(*S*)-peroxy-2-alken-1-ol (**3**). Surprisingly, reduction of the peroxy aldehyde with the less reactive sodium borohydride furnished a greatly reduced yield of peroxy alcohol. In each case, the desired unsaturated peroxy alcohol was the only major product observed and was isolated in analytically pure form following flash chromatography.

Addition of LAH to a saturated peroxy aldehyde (**4**) resulted in a much lower yield of the 2-peroxy-1-alkanol **5**, and additions of other organometallic nucleophiles failed completely (Scheme IV). This was not entirely unexpected; our previous experiences with Wittig olefinations of 2-peroxyalkanals had demonstrated the reduced ability of a saturated peroxy aldehyde toward base-mediated elimination relative to the corresponding peroxy enal.[10]

We next turned to the addition of alkyl organometallics. We were pleasantly surprised to find that addition of

Scheme V



R-M	Product	Yield	anti/syn
nBuLi	6 (R = nBu)	60%	40 : 60
nBuLi/CeCl$_3$		NR	-
nBuLi/Ti(OiPr)$_4$		NR	-
nBuMgBr	6 (R = nBu)	85%	40 : 60
PhLi	7 (R = Ph)	95%	42 : 58
PhMgBr	7 (R = Ph)	>95%	44 : 56

n-butyllithium to the peroxy aldehyde **2** resulted in a 60% isolated yield of the homologated alkyl alcohol as a 40:60 mixture of diastereomers **6a** and **6b** (Scheme V). Literature precedent led us to believe that use of less basic organotitanium or organocerium reagents might result in an improved yield relative to the organolithium reagent.[21,22] The cerium and titanium reagents, *n*-BuCeCl$_2$ and *n*-BuTi(O-*i*-Pr)$_3$, were preformed through reaction of *n*-BuLi with either cerium(III) chloride or chlorotitanium triisopropoxide. Surprisingly, no reaction was observed upon addition of the peroxyaldehyde to a slight excess of either the preformed organocerium or organotitanium reagents, and substantial amounts of starting material were recovered. Fortunately, addition of a THF solution of *n*-butylmagnesium bromide to the peroxy aldehyde afforded an 80% isolated yield of the peroxy alcohols as a 40:60 mixture of diastereomers **6a** and **6b**. The two diastereomers were readily separated by preparative HPLC, and each diastereomer was shown to be a single enantiomer upon Mosher ester analysis. Absolute stereochemistries were assigned by comparison of degree of aromatic shielding induced upon formation of Mosher esters.[23] The butyl ether, a minor byproduct under the reported conditions, became the major product upon addition of excess Grignard reagent.[14] Addition of either phenyllithium or phenylmagnesium bromide also proceeded in excellent yield to produce approximately 40:60 mixtures of readily separable diastereomeric benzyl alcohols **7a** and **7b**.

We next explored the application of our discovery toward the enantioselective synthesis of peroxy ketals, as illustrated in Scheme I. Organometallic addition to a (*Z*)-peroxy enal was anticipated to allow selective introduction of one alkyl substituent. Oxidation of the allylic alcohol to the (*Z*)-enone and deprotection of the peroxide was expected to furnish spontaneous closure to the hemiketal. However, synthesis of the requisite (*Z*)-peroxy enal was unprecedented and appeared to require olefination of a saturated peroxy aldehyde with a (*Z*)-selective Horner–Emmons reagent.[10] Fortunately, a mechanistic intermediate invoked in Snider's recent total synthesis of racemic chondrillin offered a more efficient alternative (Scheme VI, Snider (1992)). Photooxidation of enones to racemic peroxyhemiketals was shown to proceed via dioxygenation of a dienol to an intermediate 4-hydroxyperoxy-2(*E*)-

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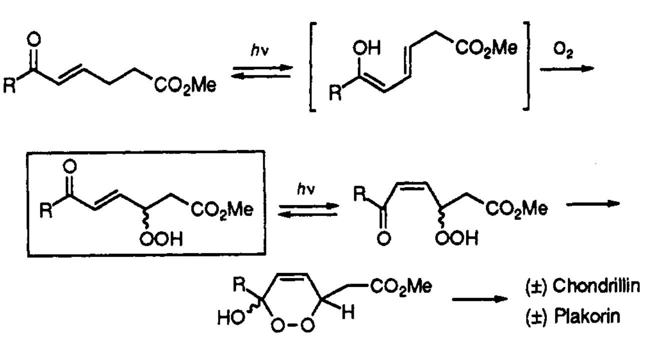
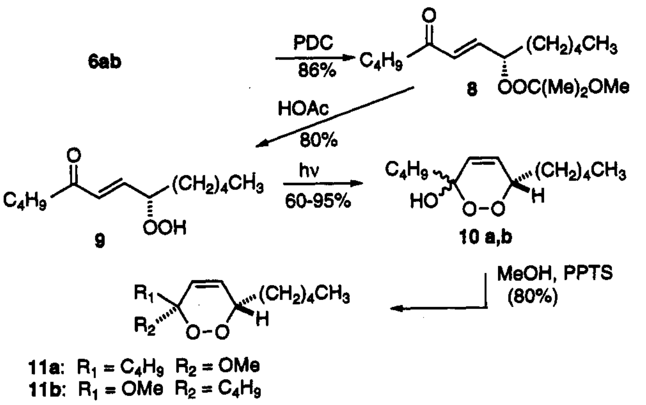
Scheme VI



Scheme VII

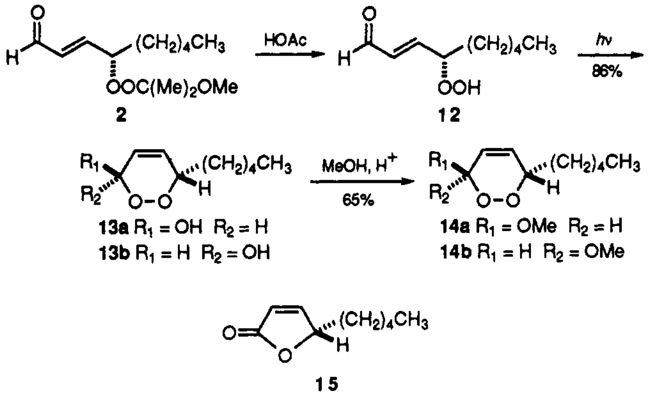


enone; E/Z photoisomerization of this hydroperoxyenone set the stage for ring closure to the product hemiketals.[2] Our ability to independently synthesize (E)-4-hydroperoxy 2-enones as a single enantiomer offers an enantioselective entry to peroxyketals, and we would now like to report the asymmetric synthesis of several model peroxyketals.

As described above, allyl alcohols **6a**/**6b** were obtained upon addition of n-BuMgBr to aldehyde **2** (Scheme VII). Oxidation of the mixed diastereomers with pyridinium dichromate cleanly produced peroxy enone **8**, which was deprotected with acetic acid to the free hydroperoxide **9**. Ultraviolet irradiation resulted in rapid cyclization to a 3:2 mixture of readily separable hemiketal epimers **10a** and **10b**. Snider's procedure, involving photolysis with a tanning lamp, proved most convenient; photolysis with 300-nm Hg lamps (Rayonet) performed the same transformation but at a greatly reduced rate. Treatment of either hemiketal epimer with methanol and pyridinium p-toluenesulfonate cleanly afforded a 58:42 mixture of readily separable cis/trans peroxyketals **11a** and **11b**. Stereochemical assignments for hemiketals and peroxyketals were based upon comparison of the ^1H chemical shifts for the ring hydrogens with data reported by Snider.[2]

Peroxy aldehyde **2** underwent the same sequence of reactions to afford a good yield of a cyclic peroxy acetal (Scheme VIII). Not surprisingly, the intermediate hydroperoxy enal **12** was relatively unstable, and a one-pot sequential deprotection/photolysis in acetic acid was required for optimal yields of the hemiacetals (hydroxydioxins), **13a** and **13b**, isolated as a 1:1 mixture. Acid-catalyzed ketalization of the hemiketals to the methyl peracetals **14ab** required careful control of reaction conditions due to rapid decomposition in the presence of strong acids to form lactone **15**. The use of 0.3–0.4 equiv of $TsOH{\cdot}H_2O$ in methanol was optimal for formation of the desired methyl peracetals as a 1:1 mixture of diastereomers.

Scheme VIII



In summary, we have demonstrated that the chemoselective addition of organometallic nucleophiles to peroxy aldehydes affords a new method for the enantioselective construction of functionalized peroxyketals. Application of this strategy to modified peroxy aldehydes should offer a versatile and efficient route for the enantioselective synthesis of peroxyketal natural products. Efforts in this area will be reported in due course.

Caution. Peroxides are unstable materials capable of rapid and exothermic decomposition. Although we have encountered no specific problems in the course of this research, the application of standard precautions (safety shields, stabilization of peroxides with radical inhibitors, avoidance of heat, light, or metal salts) is strongly recommended.

Experimental Section

All reagents and solvents were used as supplied commercially, except THF, which was distilled from Na/Ph_2CO. ^1H and ^{13}C NMR spectra were recorded on 300-, 360-, or 500-MHz spectrometers in $CDCl_3$; individual peaks are reported as (multiplicity, number of hydrogens, coupling constant (Hz), assignment). Infrared (IR) spectra were recorded on neat films. Optical rotations were obtained in a 1-dm cell in $CHCl_3$ unless otherwise noted. Elemental analyses were obtained from M-H-W Laboratories, Phoenix, AZ. Semipreparative HPLC was performed with a 2.1- × 25-cm Rainin Dynamax Si column with refractive index detection. All peroxides and hydroperoxides were handled and stored in the presence of approximately 0.1% butylated hydroxytoluene (BHT), added from a 1 M stock solution in CH_2Cl_2. Progress of reactions involving peroxides was monitored by TLC, using an N,N'-dimethyl-p-phenylenediamine indicator; hydroperoxides yield an immediate reddish-pink spot, while perketals or peroxides exhibit a pink or green-red color after standing or after mild charring.[24]

13(*S*)-Hydroperoxy-9(*Z*),11(*E*)-octadecadienoic Acid Methyl Ester (1). To a 0 °C solution of pH 9 borate buffer (1000 mL, 0.2 M) aerated with a stream of O_2 was added soybean type I lipoxygenase (85 mg, Sigma). Linoleic acid (2.00 g, 7.1 mmol) was dissolved in cold EtOH (60 mL) and pipetted below the surface of the solution over a 30-min period during which the flow of oxygen was adjusted to prevent excess foaming. After 5 h, the reaction was acidified to pH 3 with 10% HCl and extracted with CH_2Cl_2 (3 × 300 mL, initial emulsion). The organic extracts were dried over Na_2SO_4 and concentrated in the presence of a small amount of butylated hydroxytoluene (BHT). The crude hydroperoxy acid was redissolved in 20 mL of ether at 0 °C, and a solution of 0.3 M CH_2N_2/ether was added until the yellow color persisted. Excess CH_2N_2 was purged with a stream of dry N_2, and the solvent was removed on a rotary evaporator. A small sample of the hydroperoxy methyl ester was purified by flash chromatography (20% EA/hex); the majority of the material was

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carried on without purification: R_f = 0.20 (10% EA/hex); $[\alpha]_D$ = 5.35 (*c* = 0.5, MeOH); ^{1}H NMR (360 MHz) δ 7.97 (s, 1 H, OO*H*), 6.57 (dd, 1 H, *J* = 15.2, 11.1, $CH{=}CHCHOO$), 6.01 (t, 1 H, *J* = 10.9, $CH_2CH{=}CH$), 5.57 (dd, 1 H, *J* = 15.0, 8.3, $={CH}CHCOOH$), 5.45 (dt, 1 H, *J* = 10.9, 7.8, $CH_2CH{=}$), 4.38 (qt, 1 H, *J* = 7.0, $CH_2CH(OOH)CH{=}$), 3.65 (s, 3 H, OCH_3), 2.28 (t, 2 H, *J* = 7.4, CH_2CH_2COO), 2.19 (qt, 2 H, *J* = 7.0, allylic CH_2), 1.66–1.29 (m, 18 H), 0.88 (t, 3 H, *J* = 6.5 CH_3); ^{13}C NMR (50 MHz) 174.4, 133.9, 131.3, 130.0, 127.6, 86.8, 51.5, 34.1, 32.5, 31.7, 29.4, 29.0, 29.0, 28.9, 27.7, 25.0, 24.9, 22.5, 14.0; IR (neat) 2929, 2931, 2856, 1741, 1436, 1367, 1207, 1182, 1162, 1072 cm^{-1}; HRMS *m/z* calcd for $C_{19}H_{34}O_4Li$ $[M + Li]^+$ 333.2617, found 333.2614.

Methyl 13(*S*)-[(1-Methoxy-1-methylethyl)dioxy]-9(*Z*),11-(*E*)-octadecadienoate. To a solution of the crude hydroperoxy ester in 15 mL of CH_2Cl_2 at 0 °C were added 2-methoxypropene (1.0 mL, 0.768 mmol, 1.5 equiv) and PPTS (90 mg, 0.038 mmol). After 15 min, the solution was washed with 10% $NaHCO_3$ (15 mL) and the organic layer was concentrated *in vacuo*. The crude oil was directly subjected to flash chromatography (2.5–10% EA/hex) to yield 2.18 g (77%, three steps) of the perketal methyl ester as a colorless oil: R_f = 0.26 (10% EA/hex); $[\alpha]_D$ = −3.1 (*c* = 0.85, MeOH), −7.88 (*c* = 2.2, $CHCl_3$); ^{1}H NMR (360 MHz) δ 6.46 (dd, 1 H, *J* = 15.2, 11.1, $OOCHCH{=}CHCH{=}CH$), 5.98 (t, 1 H, *J* = 10.9, $CH{=}CHCH{=}CH–$), 5.59 (dd, 1 H, *J* = 15.1, 8.0, $OOCHCH{=}CHCH$), 5.42 (dt, 1 H, *J* = 10.8, 7.6, $CHCH{=}CHCH_2$), 4.37 (qt, 1 H, *J* = 7.61, $OOCHCH{=}CH$), 3.65 (s, 3 H, OCH_3), 3.28 (s, 3 H, OCH_3), 2.29 (t, 2 H, *J* = 7.4, CH_2CH_2COOMe), 2.16 (qt, 2 H, *J* = 6.7, allylic CH_2) 1.57–1.29 (m, 24 H), 0.87 (t, 3 H, *J* = 6.3, CH_3), ^{13}C NMR (50 MHz) δ 174.3, 132.9, 132.7, 128.0, 127.9, 104.6, 84.7, 51.4, 49.3, 34.1, 33.1, 31.8, 29.5, 29.1, 29.1, 29.0, 27.7, 24.9, 20.1, 22.9, 22.5, 14.0; IR (neat) 2931, 2857, 1741, 1376, 1367, 1259, 1207, 1162, 1072, 983 cm^{-1}; HRMS *m/z* calcd for $C_{23}H_{42}O_5Li$ $[M + Li]^+$ 405.3192, found 405.3184.

4(*S*)-4-[(1-Methoxy-1-methylethyl)dioxy]-2(*E*)-nonenal (2). Into a −78 °C solution of the perketal methyl ester (1.0 g, 2.5 mmol) in 10 mL of 15% $MeOH/CHCl_2$ was bubbled a gentle stream of O_3/O_2 for 5 min (approximately 0.5–1 mmol O_3/min); excess O_3 was subsequently purged with a stream of dry N_2. A slight excess of Ph_3P was added, and the reaction was allowed to warm to 0 °C. After 30 min, the reaction was brought to room temperature and the solvent was removed *in vacuo*. Flash chromatography on silica gel (2.5–10% EA/hex) afforded 380 mg (63%) of the peroxy aldehyde 2 as a colorless oil: R_f = 0.5 (10% EA/hex); $[\alpha]_D$ = −82.6 (*c* = 0.5); ^{1}H NMR (360 MHz) δ 9.56 (d, 1 H, *J* = 7.8, COH), 6.77 (dd, 1 H, *J* = 15.9, 6.3, $CH{=}CHCOH$), 6.26 (dd, 1 H, *J* = 15.9, 7.8, $CH{=}CHCOH$), 4.64 (qt, 1 H, *J* = 5.8, $OOCHCH{=}CH$), 3.25 (s, 2 H, OCH_3), 1.54–1.25 (m, 14 H), 0.85 (t, 3 H, *J* = 6.7, CH_3); ^{13}C NMR (50 MHz) δ 193.4, 156.3, 132.4, 105.1, 82.7, 49.3, 32.5, 31.6, 24.9, 22.9, 22.7, 22.4, 13.9; IR (neat) 2933, 1695, 1378, 1369, 1209, 1182, 1128, 1070, 1018, 973 cm^{-1}; UV λ_{max} 246 nm (ε = 905, $CHCl_3$).

4(*S*)-[(1-Methoxy-1-methylethyl)dioxy]-2(*E*)-1-nonenol (3). DIBAL Reduction. To a −78 °C solution of aldehyde 2 (25 mg, 0.102 mmol) in THF (1 mL) under an atmosphere of nitrogen was added DIBAL (0.070 mL, nominally 1.5 M in hexane). After 15 min an additional aliquot of DIBAL (0.034 mL) was added. The reaction was judged to be complete within 30 min, whereupon $Na_2SO_4{\cdot}10H_2O$ (1 equiv) and excess Celite were added. After 1 h of stirring, the suspension was filtered, and the concentrated filtrate was directly subjected to flash chromatography (20% EA/hex) to afford 3 mg (>10%) of recovered starting material and 22 mg (88%) of alcohol 3: $[\alpha]_D$ = −42.7 (*c* = 1.8); ^{1}H NMR (300 MHz) δ 5.85 (dt, 1 H, *J* = 15.6, 5.4, $CH{=}CHCH_2OH$), 5.68 (dd, 1 H, *J* = 15.6, 7.5, $CH{=}CHCH_2OH$), 4.36 (q, 1 H, *J* = 6.8, 6.7, $CH_2CH(OOR)CH{=}$), 4.17 (d, 2 H, *J* = 4.9, CH_2OH), 3.28 (s, 3 H, OCH_3), 1.37 (m, 15 H), 0.87 (t, 3 H, *J* = 6.5, CH_3); ^{13}C NMR (300 MHz) 132.0, 131.2, 104.6, 84.1, 62.9, 49.2, 32.9, 31.7, 24.9, 23.0, 22.7, 22.4, 13.9; IR (neat) 3428, 2933, 1465, 1379, 1259, 1186, 1163, 1072, 993, 842 cm^{-1}. Anal. Calcd for $C_{13}H_{26}O_4$: C, 63.38; H, 10.64. Found: C, 63.45; H, 10.57.

LAH Reduction. To a −78 °C solution of aldehyde 2 (25 mg, 0.102 mmol) in THF (1 mL) under an atmosphere of N_2 was added LAH (0.1 mL, nominally 1 M solution in THF). The reaction was quenched after 5 min by the sequential addition of 50 μL of H_2O/50 μL of 6 N NaOH/150 μL of H_2O. After the mixture was dried over Na_2SO_4, purification by flash chromatography afforded 24.4 mg (97%) of alcohol 3.

$NaBH_4$ Reduction. To a 0 °C stirring solution of aldehyde 2 (99.7 mg, 0.41 mmol) in 2-propanol (2.05 mL under an atmosphere of N_2) was added $NaBH_4$ (1.2 equiv). The reaction was quenched after 20 min with the addition of H_2O (6 mL). The ether extract was dried and subjected to flash chromatography to afford 31.5 mg (31.3%) of alcohol 3.

2-[(1-Methoxy-1-methylethyl)dioxy]-1-hexanol (5). LAH Reduction of Saturated Aldehyde. To a 0 °C solution of 2-[(1-methoxy-1-methylethyl)dioxyl]-1-hexanal (4) (86 mg, 0.42 mmol) in THF (4.2 mL) was added a solution of LAH/THF (0.4 mL, nominally 0.63 M). The reaction was immediately quenched with 20 μL of H_2O/20 μL of 6 N NaOH/60 μL of H_2O. The suspension was diluted with ether and filtered through Celite. Flash chromatography (20% EA/hex) afforded 32.1 mg (37%) of alcohol 5 as a colorless oil: R_f = 0.24 (20% EA/hex); ^{1}H NMR (300 MHz) δ 4.05 (m, 1 H, $CHOOR$), 3.76 (ddd, 1 H, *J* = 9.2, 6.2, 2.9, CHO), 3.63 (m, 1 H, CHO), 3.32 (s, 3 H, OCH_3), 2.51 (t, 1 H, *J* = 6.2, OH), 1.423 (s, 3 H, CH_3), 1.41 (s, 3 H, CH_3), 1.4–1.3 (6 H), 0.90 (t, 3 H, *J* = 7.0, CH_3); ^{13}C NMR (75 MHz) δ 105.0, 84.6, 63.8, 49.6, 28.9, 27.9, 22.8, 22.7, 22.6, 13.8 ppm; IR (neat) 3452, 2994, 2960, 2942, 2873, 1379, 1369, 1211, 1186, 1159, 1072 cm^{-1}. Anal. Calcd for $C_{10}H_{22}O_4$: C, 58.22; H, 10.75. Found: C, 54.87; H, 10.43.

(8*S*,5*R*)- and (8*S*,5*S*)-8-[(1-Methoxy-1-methylethyl)dioxy]-6(*E*)-tridecan-5-ol (6). Addition of BuMgBr. To a 0 °C solution of peroxy aldehyde 2 (310 mg, 1.2 mmol) in THF (10 mL) was added, dropwise, a solution of *n*-BuMgBr (1.2 mL, nominally 1.2 M in THF), and the reaction was stirred for 4–6 h at 0 °C. The reaction was quenched with saturated $NaHCO_3$ and extracted with ether (2 × 10 mL). Flash chromatography (15% EA/hex) provided a mixture of diastereomeric allylic alcohols (305 mg, 85%). Semipreparative HPLC (15% EA/hex) was used to separate the *SR* diastereomer (**6a**) eluting at 17.3 min (125 mg, 40%) from the *SS* isomer (**6b**) (180 mg, 60%) eluting at 22.3 min.

Addition of *n*-BuLi. By a similar procedure, addition of a hexane solution of *n*-BuLi to a THF solution of aldehyde 2 afforded a 60% yield of a 40:60 mixture of the 5*R*,8*S* (**7a**) and 5*S*,8*S* (**7b**) isomers:

(8*S*,5*R*)-8-[(1-Methoxy-1-methylethyl)dioxy]-6(*E*)-tridecan-5-ol (6a): R_f = 0.50 (20% EA/Hex); $[\alpha]_D$ = −26.0 (*c* = 1.4); ^{1}H NMR (300 MHz) δ 5.69 (dd, 1 H, *J* = 15.6, 5.7, $={CH}\ CH_2O$) 5.62 (dd, 1 H, *J* = 15.6, 7.3, $={CH}CH_2OO$), 4.35 (q, 1 H, *J* = 6.9, $–CHOOR$), 4.13 (m, 1 H, $–CHROH$), 3.28 (s, 3 H, OCH_3), 1.60–1.25 (18 H), 0.88 (6 H, $CH_3–$); ^{13}C NMR (125 MHz) 136.1, 130.6, 104.6, 72.5, 84.2, 49.3, 36.9, 32.9, 31.71, 27.5, 25.0, 23.1, 22.7, 22.6, 22.5, 14.0, 13.96; IR (neat) 3438, 2993, 2860, 1466, 1379, 1209, 1157, 1072, 970 cm^{-1}. Anal. Calcd for $C_{17}H_{34}O_4$: C, 67.51; H, 11.33. Found: C, 67.67; H, 11.33.

(8*S*,5*S*)-[(1-Methoxy-1-methylethyl)dioxy]-6(*E*)-tridecan-5-ol (6b): R_f = 0.45 (20% EA/Hex); $[\alpha]_D$ = −34.4 (*c* = 1.4); ^{1}H NMR (500 MHz) δ 5.67 (dd, 1 H, *J* = 15.6, 6.0, $={CH}\ CH_2O$) 5.58 (dd, 1 H, *J* = 15.5, 6.9, $={CH}CH_2OO$), 4.35 (q, 1 H, *J* = 6.9, $–CHOOR$), 4.08 (q, 1 H, *J* = 6.5, $–CHROH$), 3.27 (s, 3 H, OCH_3), 1.60–1.25 (18 H), 0.89 (6 H, $CH_3–$); ^{13}C NMR (125 MHz) 136.1, 130.6, 104.6, 72.4, 84.2, 49.3, 36.8, 32.9, 31.7, 27.5, 25.0, 23, 22.7, 22.6, 22.5, 13.9, 13.9; IR 3438, 2993, 2860, 1466, 1379, 1209, 1157, 1072, 970 cm^{-1}.

Mosher Esters of 6a and 6b. To a solution of DCC (22 mg), DMAP (1 mg), and (*R*)-(+)-methoxy(trifluoromethyl)phenylacetic acid (Mosher acid) in CH_2Cl_2 (2 mL) was added 20 mg of the individual peroxy alcohol. After 3 h, the reaction was quenched with aqueous $NaHCO_3$ and extracted with ether (2 × 10 mL). The dried organic layer was concentrated and subjected to filtration through silica (5% EA/hex) to afford colorless oils which were analyzed without further purification. Differences in the chemical shifts of the olefinic hydrogens of the esters were used to determine absolute stereochemistry according to the procedure of Ohtani.[23]

Ester from 6a: R_f = 0.75 (20% EA/Hex); ^{1}H NMR (500 MHz) δ 7.5–7.3 (m, 5 H, Ph), 5.81 (dd, 1 H, *J* = 15.3, 7.3, $–HC{=}CH–$), 5.70 (dd, 1 H, *J* = 15.3, 7.7, $–HC{=}CH–$), 5.49 (q, 1 H, *J* = 7.3, $–CHCOOR$), 4.34 (q, 1 H, *J* = 6.9, $–CHOOR$), 3.54 (s, 3 H, $–CF_3$-OCH_3), 3.27 (s, 3 H, OCH_3), 1.7–1.25 (18 H), 0.84 (m, 6 H).

Ester from 6b: $R_f = 0.70$ (20% EA/Hex); ^{1}H NMR (500 MHz) δ 7.5–7.3 (m, 5 H, Ph), 5.70 (dd, 1 H, $J = 15.3, 8.1$, $-\mathrm{HC{=}C}H-$), 5.55 (dd, 1 H, $J = 15.3, 6.9$, $-H\mathrm{C{=}CH}-$), 5.44 (q, 1 H, $J = 6.9$, $-\mathrm{C}H\mathrm{COOR}$), 4.30 (q, 1 H, $J = 6.9$, $-\mathrm{C}H\mathrm{OOR}$), 3.54 (s, 3 H, $-\mathrm{CF_3\text{-}OC}H_3$), 3.25 (s, 3 H, $\mathrm{OC}H_3$), 1.7–1.25 (m, 18 H), 0.85 (m, 6 H, $\mathrm{C}H_3-$).

4-[(1-Methoxy-1-methylethyl)dioxy]-1-phenyl-2(*E*)-nonen-1-ol (7ab). Addition of PhMgBr. By a similar procedure as employed for the synthesis of **6**, PhMgBr (0.46 mmol) was added to peroxy enal **2** (0.46 mmol) to afford, after chromatography (15% EA/hex), 147 mg (100%) of alcohol **7**. Semipreparative HPLC (15% EA/hex) afforded 52.6 mg of 1*S*,4*S* diasteromer (**7a**) eluting at 26 min followed by 66.4 mg of the 1*R*,4*S*-diastereomer (**7b**) eluting at 31.2 min.

Addition of PhLi. By a similar procedure as outlined above, addition of a cyclohexane/ether solution of PhLi (nominally 1.8 M) to aldehyde **2** afforded a 95% yield of **7a** and **7b** as a 42:58 mixture.

7a (1*S*,4*S*): $R_f = 0.43$ (20% EA/hex); $[\alpha]_D = -32.5$ ($c = 0.37$); ^{1}H NMR (300 MHz) δ 7.35 (5 H), 5.91 (dd, 1 H, $J = 15.1, 5.6$, $=\mathrm{C}H\mathrm{CHOH}$), 5.76 (dd, 1 H, $J = 15.5, 7.4$, $H\mathrm{C{=}C}$), 5.24 (d, 1 H, $J = 5.7$, $\mathrm{C}H\mathrm{OH}$), 4.37 (q, 1 H, $J = 6.7$, $\mathrm{C}H\mathrm{OOR}$), 3.23 (s, 3 H, $\mathrm{C}H_3$), 1.3–1.07 (15 H), 0.87 (t, 3 H, $J = 6.4$, $\mathrm{C}H_3$); ^{13}C NMR δ 142.8, 135.0, 131.1, 128.4, 127.6, 126.3, 104.5, 84.0, 74.4, 49.2, 32.9, 31.7, 25.0, 23.0, 22.7, 22.5, 13.9; IR (neat) 3436, 2933, 1379, 1367, 1207, 1186, 1157, 1070, 845, 700 cm^{-1}. Anal. Calcd for $C_{19}H_{30}O_4$: C, 70.77; H, 9.38. Found: C, 70.73; H, 9.14.

7b (1*R*,4*S*): $R_f = 0.40$ (20% EA/hex); $[\alpha]_D = -36.2$ ($c = 0.38$); ^{1}H NMR (300 MHz) δ 7.35 (5 H), 5.90 (dd, 1 H, $J = 15.6, 6.1$, $=\mathrm{C}H\mathrm{CHOH}$), 5.74 (dd, 1 H, $J = 15.5, 7.4$, $H\mathrm{C{=}C}$), 5.22 (d, 1 H, $J = 5.8$, $\mathrm{C}H\mathrm{OH}$), 4.37 (q, 1 H, $J = 6.7$, $\mathrm{C}H\mathrm{OOR}$), 3.26 (s, 3 H, $\mathrm{OC}H_3$), 1.7–1.25 (15 H), 0.85 (t, 3 H, $J = 6.4$, $\mathrm{C}H_3$); ^{13}C NMR δ 142.8, 135.1, 131.0, 128.4, 127.6, 126.3, 104.6, 84.0, 74.3, 49.2, 32.9, 31.6, 24.9, 23.0, 22.6, 22.4, 13.9; IR (neat) 3436, 2931, 2857, 1377, 1367, 1207, 1184, 1155, 1070, 970, 700 cm^{-1}. Anal. Calcd for $C_{19}H_{30}O_4$: C, 70.77; H, 9.38. Found: C, 70.95; H, 9.17.

8(*S*)-[(1-Methoxy-1-methylethyl)dioxy]-5-oxo-6(*E*)-tridecene (8). To a solution of alcohols **6ab** (200 mg, 0.8 mmol) in CH_2Cl_2 (6 mL) was added pyridinium dichromate (1.23 g, 2.4 mmol), and the reaction was allowed to stir for 12 h. The brown solution was directly subjected to flash chromatography (5% EA/Hex) to afford 176 mg of ketone 8 (88%): $R_f = 0.75$ (20% EA/Hex); $[\alpha]_D = -55$ ($c = 0.7$); ^{1}H NMR (300 MHz) δ 6.67 (dd, 1 H, $J = 16.2, 6.7$, $-\mathrm{HC{=}C}H\mathrm{CO}$), 6.25 (dd, 1 H, $J = 16.2, 1.0$, $-H\mathrm{C{=}CHCO}$), 4.53 (q, 1 H, $J = 7.2$, $-\mathrm{C}H\mathrm{OOH}$), 3.27 (s, 3 H, $\mathrm{OC}H_3$), 2.57 (dt, 2 H, $J = 7.6, 3.2$, $-\mathrm{C}H\mathrm{CO}$), 1.25–1.50 (m, 12 H), 0.91 (6 H, $\mathrm{C}H_3$); ^{13}C NMR (125 MHz) 200.5, 145.1, 130.3, 104.8, 83.1, 49.2, 39.9, 32.6, 31.6, 26.0, 24.9, 22.9, 22.6, 22.3, 22.3, 13.9, 13.8; IR (neat) 2954, 2929, 2860, 1699, 1681, 1367, 1209, 1182, 1155, 1070 cm^{-1}. Anal. Calcd for $C_{17}H_{32}O_4$: C, 67.96; H, 10.96. Found: C, 68.08; H, 10.88.

8(*S*)-Hydroperoxy-5-oxo-6(*E*)-tridecene (9). Peroxy ketone 8 (0.176 g, 0.7 mmol) and BHT (two drops of a 0.1 M solution in CH_2Cl_2) were dissolved in a freshly prepared solution of 90:10 $HOAc/H_2O$ (3 mL) and stirred for 2 h. The reaction was concentrated *in vacuo* and directly subjected to flash chromatography (5% EA/Hex) to afford 142 mg of hydroperoxide 9 (85%): $R_f = 0.45$ (20% EA/Hex); $[\alpha]_D = -14$ ($c = 1$); ^{1}H NMR (500 MHz) δ 8.87 (s, 1 H, $\mathrm{OO}H$), 6.67 (dd, 1 H, $J = 16.2, 6.9$, $-\mathrm{HC{=}C}H\mathrm{CO}$), 6.28 (d, 1 H, $J = 16.2$, $-H\mathrm{C{=}CHCO}$), 4.49 (q, 1 H, $J = 7.1$, $-\mathrm{C}H\mathrm{OOH}$), 2.57 (t, 2 H, $J = 7.3$, $-\mathrm{C}H\mathrm{CO}$), 1.25–1.50 (12 H), 0.91 (6 H); ^{13}C NMR (125 MHz) 201.1, 144.5, 130.9, 84.9, 40.3, 32.2, 31.6, 26.2, 24.8, 22.4, 22.3, 13.9, 13.8; IR (neat) 3363(b), 2929, 2860, 1682, 1633, 1465, 1405, 1376, 1267, 978 cm^{-1}.

(3*RS*,6*S*)-3-Butyl-3,6-dihydro-6-pentyl-1,2-dioxin-3-ol (10ab). A solution of the enone (140 mg, 6 mmol) in 19:1 CH_2Cl_2–MeOH (30 mL) in a water-cooled Pyrex photolysis cell was irradiated with a 275-W sunlamp from a distance of 7 cm for 2.5 h; N_2 was bubbled into the solution throughout the irradiation. The solution was concentrated and directly subjected to semipreparative HPLC. Elution with 20% EA/Hex afforded, after 12.3 min, 74 mg of the 3*S*,6*S* isomer **10a**, followed after 19.1 min by 46 mg of the 3*R*,6*S* isomer **10b**. The total isolated yield of endoperoxides (**10a** and **10b**) was 120 mg (86%).

10a (3*S*,6*S*): $R_f = 0.64$ (20% EA/Hex); $[\alpha]_D = +19.0$ ($c = 1.2$); ^{1}H NMR (500 MHz) δ 5.93 (dd, 2 H, $J = 10.2, 1.2$, $-\mathrm{C}H\mathrm{{=}C}H-$), 5.78 (dd, 1 H, $J = 10.3, 1.6$) 4.65 (t, 1 H, $J = 6.9$, $-\mathrm{C}H\mathrm{OOR}$), 1.7–1.25 (m, 14 H), 0.89 (t, 6 H, $J = 7.1$, $\mathrm{C}H_3-$); ^{13}C NMR (75 MHz) 130.7, 128.1, 97.9, 77.2, 36.2, 31.9, 31.7, 25.1, 24.5, 22.8, 22.4, 13.9, 13.8; IR (neat) 3462, 2956, 2931, 2862, 1468, 1379, 1118, 1055, 906, 739 cm^{-1}. Anal. Calcd for $C_{13}H_{24}O_3$: C, 68.38; H, 10.59. Found: C, 68.38; H, 11.13.

10b (3*R*,6*R*): $R_f = 0.60$ (20% EA/Hex); $[\alpha]_D = +17.68$ ($c = 0.8$); ^{1}H NMR (500 MHz) δ 6.10 (dd, 1 H, $J = 10.6, 4.2$, $-\mathrm{CH{=}C}H\mathrm{CRROH}-$), 5.6 (dd, 1 H, $J = 10.1, 1.6$, $-\mathrm{C}H\mathrm{{=}CHCRROH}$), 4.20 (m, 1 H, $-\mathrm{C}H\mathrm{OOR}$), 1.7–1.25 (m, 14 H), 0.89 (t, 6 H, $J = 6.9$, $\mathrm{C}H_3-$); ^{13}C NMR (125 MHz) 129.9, 127.2, 98.0, 78.0, 36.3, 32.1, 31.6, 25.5, 25.2, 22.8, 22.5, 13.9, 13.8; IR (neat) 3462, 2956, 2931, 2862, 1468, 1379, 1118, 1055, 906, 739 cm^{-1}. Anal. Calcd for $C_{13}H_{24}O_3$: C, 68.38; H, 10.59. Found: C, 68.45; H, 10.53.

3-Butyl-3,6-dihydro-3-methoxy-6-pentyl-1,2-dioxine (11ab). To a mixture of the epimeric dioxines **10ab** (45 mg, 0.19 mmol) in MeOH (4 mL) was added $TsOH{\cdot}H_2O$ (5 mg, 0.02 mmol). After being stirred for 3 h, the reaction was quenched with aqueous $NaHCO_3$ (10 mL) and extracted with ether (3 × 10 mL). The organic layer was dried over Na_2SO_4 and concentrated. Semipreparative normal-phase HPLC (10% EA/hex) afforded, in 6.2 min, the 3*S*,6*R* methoxydioxine (22 mg) followed, at 8.0 min, by the 3*S*,6*S* dioxine (16 mg) (total, 38 mg, 80%).

11a (3*S*,6*S*): $R_f = 0.60$ (20% EA/Hex); $[\alpha]_D = -20.3$ ($c = 0.7$); ^{1}H NMR (300 MHz) δ 6.1 (dd, 1 H, $J = 10.3, 1.2$, $-\mathrm{CH{=}C}H\mathrm{CRROMe}-$), 5.8 (dd, 1 H, $J = 10.3, 2.1$, $-\mathrm{C}H\mathrm{{=}CHCRROMe}-$), 4.60 (bt, 1 H, $J = 6.2$, $-\mathrm{C}H\mathrm{OOR}$), 3.4 (bs, 1 H, $\mathrm{O}H$), 1.6–1.25 (m, 14 H), 0.88 (t, 6 H, $J = 6.8$, $\mathrm{C}H_3-$); ^{13}C NMR (75 MHz) 132.1, 125.7, 100.7, 77.4, 51.3, 34.3, 31.8, 31.6, 25.5, 24.6, 22.8, 22.4, 13.9, 13.9; IR (neat) 2958, 2935, 2871, 2862, 1468, 1136, 1117, 1084, 974, 740 cm^{-1}. Anal. Calcd for $C_{14}H_{26}O_3$: C, 69.38; H, 10.81. Found: C, 69.20; H, 10.58.

11b (3*R*,6*S*): $R_f = 0.64$ (20% EA/Hex); $[\alpha]_D = +45.8$ ($c = 1.2$); ^{1}H NMR (300 MHz) δ 6.1 (dd, 1 H, $J = 10.3, 4.1$, $-\mathrm{CH{=}C}H\mathrm{CRROMe}-$), 5.8 (dd, 1 H, $J = 10.5, 2.0$, $-\mathrm{C}H\mathrm{{=}CHCRROMe}-$), 4.20 (m, 1 H, $J = 10.3$, $-\mathrm{C}H\mathrm{OOR}$), 3.4 (bs, 1 H, OH), 1.6–1.25 (m, 14 H), 0.88 (t, 6 H, $J = 6.8$, $\mathrm{C}H_3-$); ^{13}C NMR (75 MHz) 131.0, 125.0, 100.5, 77.7, 50.7, 34.1, 32.1, 31.6, 25.6, 25.6, 22.8, 22.5, 14.0, 13.9; IR (neat) 2958, 2935, 2871, 2862, 1468, 1136, 1117, 1084, 974, 740 cm^{-1}. Anal. Calcd for $C_{14}H_{26}O_3$: C, 69.38; H, 10.81. Found: C, 69.15; H, 10.75.

4(*S*)-Hydroxyperoxy-2(*E*)-nonenal (12). A solution of peroxy aldehyde **2** (757 mg, 3.1 mmol) in 9:1 acetic acid/water (6 mL) was stirred for 90 min and then extracted with ether. The organic layer was dried and rapidly concentrated *in vacuo* to afford unstable hydroperoxide 12 which was used without further purification: $R_f = 0.3$ in 20% EA/hex; ^{1}H NMR (300 MHz) δ 9.55 (d, 1 H, $J = 7.6$, $\mathrm{C}H\mathrm{O}$), 6.80 (dd, 1 H, $J = 15.9, 6.3$, $\mathrm{C}H\mathrm{{=}CHCHO}$), 6.28 (dd, 1 H, $J = 11.9, 7.9$, $\mathrm{CH{=}C}H\mathrm{CHO}$), 4.61 (q, 1 H, $J = 6.2$, $\mathrm{C}H\mathrm{(OOH)}$), 1.67–1.26 (m, 8 H), 0.87 (t, 3 H, $J = 6.7$, $\mathrm{C}H_3$); ^{13}C NMR (75 MHz) δ 193.9, 155.7, 132.9, 84.4, 32.0, 31.5, 24.7, 22.3, 13.9; IR (neat) 3363, 2954, 2929, 2860, 1695, 1468, 1379, 1134, 976 cm^{-1}.

3,6-Dihydro-6-pentyl-1,2-dioxin-3-ol (13ab). A solution of the crude hydroperoxide 12 (approximately 3 mmol) in 19:1 CH_2Cl_2/MeOH (60 mL) in a water-cooled Pyrex cell was sparged with N_2 and irradiated for 4 h with a 275-W sun lamp. The solvent was removed, and the residue was subjected to flash chromatography (30% EA/hex) to afford dioxinols **13ab** (459 mg, two steps 86%) as a 1:1 mixture. The epimers were separated by semipreparative HPLC; the 3*S*/6*S* isomer eluted at 14.3 min, while the 3*S*,6*R* isomer eluted at 16.5 min.

13a (3*S*,6*S*): $R_f = 0.28$ in 20% EA/hex; $[\alpha]_D = -11.4$ ($c = 0.7$, hexane); ^{1}H NMR (300 MHz) δ 6.06 (dt, 1 H, $J = 10.0, 1,1$, $\mathrm{CH{=}C}H\mathrm{CHOH}$), 5.95 (ddd, 1 H, $J = 10.0, 5.7, 3.3$, $\mathrm{C}H\mathrm{{=}CHCHOH}$), 5.35 (app d, 1 H, $J = 3$, $\mathrm{C}H\mathrm{O}$), 4.68 (m, 1 H, $\mathrm{C}H\mathrm{OO}$), 3.12 (s, 1 H, $\mathrm{O}H$), 1.55–1.27 (m, 8 H), 0.87 (t, 3 H, $J = 6.7$, $\mathrm{C}H_3$); ^{13}C NMR (75 MHz) δ 132.6, 124.2, 91.9, 77.4, 31.7, 31.7, 24.5, 22.4, 13.9; IR (neat) 3392, 2954, 2931, 2858, 1691, 1466, 1379, 1065, 1043, 1003 cm^{-1}. Anal. Calcd for $C_9H_{16}O_3$: C, 62.77, H, 9.36. Found: C, 63.03; H, 9.12.

13b (3*R*,6*S*): $R_f = 0.28$ in 20% EA/hex; $[\alpha]_D = +39.4$ ($c = 1.5$, hexane); ^{1}H NMR (300 MHz) δ 6.14 (dd, 1 H, $J = 10.0, 4.2, 1.1$, $\mathrm{CH{=}C}H\mathrm{CHOH}$), 5.93 (ddd, 1 H, $J = 10.3, 3.7, 1.7$, $\mathrm{C}H\mathrm{{=}CHCHOH}$), 5.28 (d, 1 H, $J = 3.3$, $\mathrm{C}H\mathrm{OH}$), 4.22 (m, 1 H, $\mathrm{CH_2C}H\mathrm{OO}$), 3.12 (bs, 1 H, O*H*), 1.84 (m, 2 H), 1.61–1.29 (6 H), 0.87 (t, 3 H, *J* = 6.7, C*H*$_3$); ^{13}C NMR (75 MHz) δ 131.6, 123.4, 91.7, 78.3, 31.8, 31.5, 25.6, 22.6, 14.0.

3-Methoxy-3,6-dihydro-6-pentyl-1,2-dioxine (14ab). To a solution of the dioxinols **13ab** (300 mg, 1.74 mmol) in MeOH (17 mL) was added TsOH·H_2O (132 mg, 0.4 equiv), and the reaction was stirred for 14 h. The reaction was quenched with water and extracted with hexane. The organic layer was dried and concentrated. Flash chromatography (10% EA/hex) afforded a 1:1 mixture of diastereomeric methoxydioxines **14ab** (254 mg, 78%) which were separable by semipreparative HPLC (15% EA/hex); the 3*S*,6*S* diastereomer **14a** eluted at 14.6 min followed by the 3*S*,6*R* diastereomer **14b** at 16.8 min.

14a (3*S*,6*S*): R_f = 0.64 in 20% EA/hex; $[\alpha]_D$ = +126 (*c* = 0.7, hexane); ^{1}H NMR (300 MHz) δ 6.06 (dt, 1 H, *J* = 10.3, 1.2, CH=C*H*CHOMe), 5.88 (ddd, 1 H, *J* = 10.0, 5.7, 3.3, C*H*=CHCHOMe), 4.94 (dt, 1 H, *J* = 3.3, 2.6, CH=CHC*H*OMe), 4.66 (m, 1 H, CH_2C*H*OO), 3.52 (s, 3H, OC*H*$_3$), 1.55–1.27 (8 H), 0.87 (t, 3H, *J* = 6.7, C*H*$_3$); ^{13}C NMR (75 MHz) δ 132.7, 122.4, 98.1, 77.2, 55.8, 31.6, 31.6, 24.6, 22.3, 13.9; IR (neat) 2954, 2931, 2858, 1468, 1394, 1194, 1103, 1047, 1018, 985 cm^{-1}. Anal. Calcd for $C_{10}H_{18}O_3$: C, 64.49; H, 10.43. Found: C, 64.74; H, 10.18.

14b (3*R*,6*S*): R_f = 0.62 in 20% EA/hex; $[\alpha]_D$ = −72 (*c* = 1.7, hexane); ^{1}H NMR (300 MHz) δ 6.14 (ddd, 1 H, *J* = 10.3, 4.3, 1.2, CH=C*H*CHOMe), 5.84 (ddd, 1 H, *J* = 10.3, 3.6, 1.7, C*H*=CHCHOMe), 4.86 (d, 1 H, *J* = 3.6, C*H*OMe), 4.21 (m, 1 H, CH_2C*H*OO), 3.52 (s, 3 H, OC*H*$_3$), 1.81–1.27 (m, 8 H), 0.87 (t, 3 H, *J* = 6.7, C*H*$_3$); ^{13}C NMR (75 MHz) δ 131.9, 121.7, 97.7, 78.2, 55.7, 31.9, 31.5, 25.6, 22.5, 13.9; Anal. Calcd for $C_{10}H_{18}O_3$: C, 64.49; H, 10.43. Found: C, 64.67; H, 10.20.

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Supplementary Material Available: ^{1}H NMR spectra of **5**, **9**, and **12** (3 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.