Total Synthesis of the Alkoxydioxines (+)- and (−)-Chondrillin and (+)- and (−)-Plakorin via Singlet Oxygenation/Radical Rearrangement

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The sequential application of singlet oxygenation and peroxyl radical rearrangement provides an asymmetric entry to 4-peroxy-2-enols and 4-peroxy-2-enones. Enantiomerically enriched 2-hydroperoxy-3-alkenols, obtained via hydroxyl-directed addition of $^1O_2$ to *Z*-allylic alcohols, undergo stereospecific radical rearrangement to form 4-hydroperoxy-2-alkenols. The yields of the rearrangement are improved in the presence of excess *tert*-butyl hydroperoxide, which limits dimerization of the substrate peroxyl radicals. However, the rearrangement equilibrium is unaffected by the presence of polar co-solvents or by the incorporation of a group able to selectively hydrogen bond to the product hydroperoxide. Photoisomerization of the (*E*)-4-hydroperoxy-2-enone rearrangement products results in irreversible ring closure to furnish diastereomeric mixtures of enantiomerically enriched dioxinols. The strategy is applied to the total synthesis of the alkoxydioxine natural products chondrillin and plakorin. Comparison of the optical rotation of the synthetic material against literature reports indicates that the natural products are either enantiomerically pure or highly enriched in one enantiomer. In addition, our results conclusively demonstrate that the reported configuration of chondrillin is in error.

The identification of chondrillin (**1**) in extracts from a Great Barrier Reef sponge of the genus *Chondrilla* marked the first reported isolation of a cyclic peroxide from marine sources.[1] Since that time, a number of other alkoxydioxines, exemplified by plakorin (**2**), xestin A, and xestin B, have been isolated from several different marine sponges (Figure 1).[2] Individual alkoxydioxines differ in the nature of the C_6 side chain and in the relative stereochemistry of the dioxin substituents. In most cases, both the cis and trans diastereomers have been isolated. Members of the family have demonstrated interesting biological properties. For example, plakorin is a potent activator of sarcoplasmic reticulum calcium-ATPase, and both plakorin and the xestins have demonstrated activity against cancer cell lines in the μg/mL confine.[3−6] Despite the structural novelty and potential biological importance of this family, no asymmetric synthesis of an alkoxydioxin natural product had been reported prior to our enantioselective synthesis of plakorin.[7] We now describe a general approach to the asymmetric synthesis of 1,4-dioxygenated peroxide subunits which is illustrated with the first asymmetric syntheses of chondrillin (**1**) and plakorin (**2**).

Our initial retrosynthetic approach (Scheme 1) took advantage of the purported (vida infra) epimeric relationship of chondrillin and plakorin in proposing simultaneous formation of the two alkoxydioxines through acid-catalyzed etherification of a mixture of epimeric C_6-dioxinols. The dioxinols would in turn arise through photomediated cyclization of an enantiomerically pure 4-hydroperoxyenone which would in turn be obtained through free radical rearrangement of a 2-hydroperoxyenone. The corresponding 2-hydroperoxyalkenol would be obtained from the hydroxyl-directed addition of singlet oxygen to an enantiomerically pure *Z*-allylic alcohol.

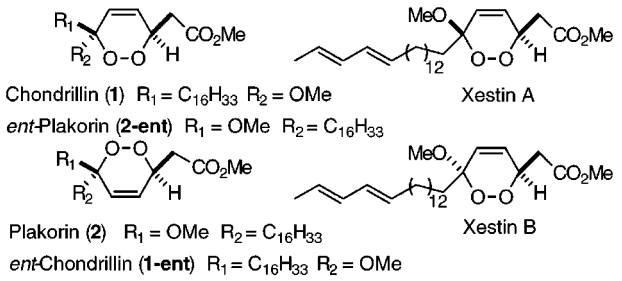
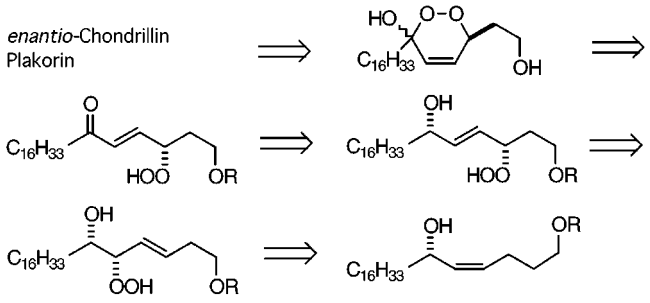


Figure 1. Representative alkoxydioxines.

Scheme 1. Retrosynthesis of Plakorin and Chondrillin



The planned hydroperoxyenone cyclization was based upon mechanistic observations reported during a racemic approach to the alkoxydioxines. In the course of attempts to prepare the alkoxydioxines through direct addition of singlet oxygen to dienol ethers, Snider and co-workers

(1) Wells, R. J. *Tetrahedron Lett.* **1976**, 2637−2638.
(2) Casteel, D. A. *Nat. Prod. Rep.* **1992**, 289−311.
(3) Sakemi, S.; Higa, T.; Anthoni, U.; Christophersen, C. *Tetrahedron* **1987**, *43*, 263−268.
(4) De Guzman, F. S.; Schmitz, F. J. *J. Nat. Prod.* **1990**, *53*, 926−931.
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(6) Murayama, T.; Ohizumi, Y.; Nakamura, H.; Sasaki, T.; Kobayashi, J. *Experentia* **1989**, *45*, 898−899.
(7) Dussault, P. H.; Woller, K. R. *J. Am. Chem. Soc.* **1997**, *119*, 3824. It should be noted that the C_3 configuration of compound **11** was misrepresented and should be *S*.

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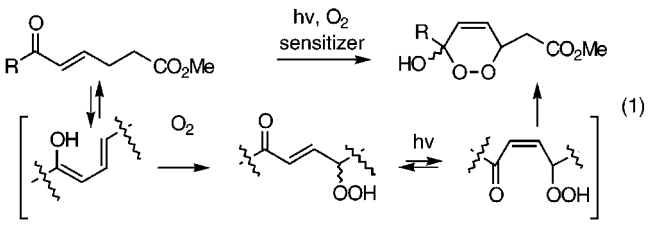
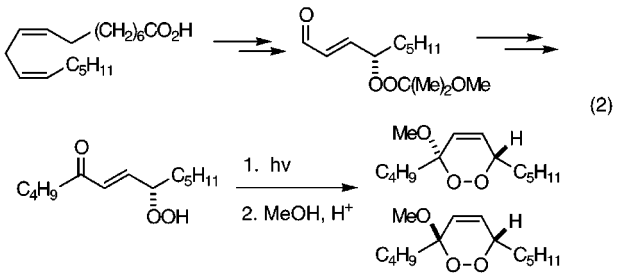
discovered a one-step synthesis of dioxinols based upon aerobic photolysis of enones or enals (eq 1).[8] Initial



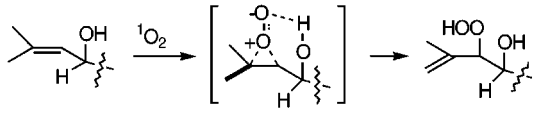
(1)

photoenolization to a dienol is postulated to set the stage for a still poorly understood oxygenation to form an intermediate (*E*)-4-hydroperoxyenone. Photochemically induced *E*-to-*Z* isomerization is followed by spontaneous ring closure. Because the stereochemistry is determined by the addition of oxygen to a prochiral dienol, this otherwise efficient approach is limited to racemic syntheses.[9] We have since demonstrated that model dioxinols can be obtained in optically active form through photolysis of hydroperoxyenones derived from enantiomerically enriched fatty acid hydroperoxides (eq 2).[10] However, the inability of lipoxygenase enzymes to perform dioxygenation of appropriate substrates frustrated application of this chemoenzymatic strategy to the synthesis of alkoxydioxine natural products.[11]



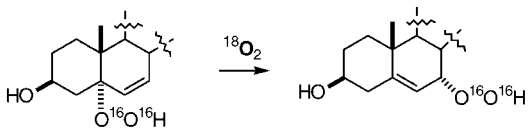
(2)

The sequential application of stereoselective oxygenation and peroxyl radical rearrangement would directly address the lack of a general asymmetric approach to 1,4-dioxygenated peroxide synthons. The two reactions are individually well-precedented in simple model systems. The addition of singlet oxygen ($^1O_2$) to chiral (*Z*) allylic alcohols is highly selective for synthesis of *syn*-2-hydroperoxy-3-alkenols.[12] In the case of allylic alcohols not bearing additional electron-withdrawing groups, the reaction is believed to proceed through a transition state involving hydrogen bonding to either $^1O_2$ or the developing perepoxide (eq 3).[13] However, prior to the present studies, application of this reaction outside of simple systems had been quite limited.



(3)

The rearrangement of allyl hydroperoxides, first observed more than 40 years ago as the stereospecific conversion of 5α- to 7α-cholestene hydroperoxide (eq 4), has recently been described with a coherent mechanistic picture (eq 5).[14−16] Abstraction of the peroxyl hydrogen,



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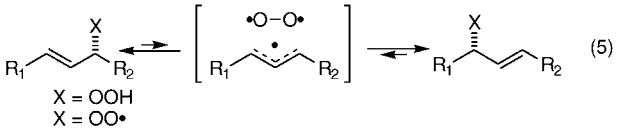
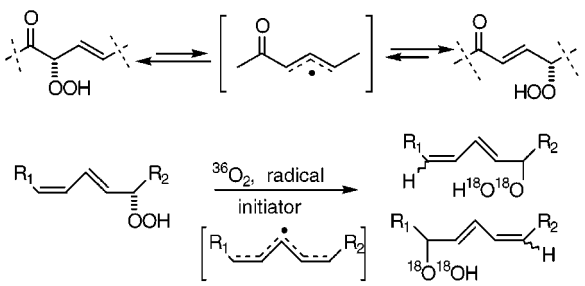


(5)

a rapid reaction despite the strength of the OO−H bond,[17,18] furnishes a peroxyl radical which undergoes reversible allylic rearrangement to an isomerized peroxyl radical. The nearly stereospecific nature of this rearrangement is due to the intermediacy of a tightly caged allyl radical/oxygen pair.[19] Abstraction of another hydroperoxide hydrogen propagates the reaction and leads to the rearranged hydroperoxide.

However, little was known about the scope and limitations of the peroxyl radical rearrangement. The proposed rearrangment of a 2-hydroperoxy-3-en-1-one moiety, intended to drive the rearrangement equilibrium through formation of a conjugated enone, required an intermediate oxo allyl radical (eq 6a). Rearrangement of diene



(6a)
(6b)

hydroperoxides through a topologically similar pentadienyl radical intermediate (eq 6b) proceeds with extensive incorporation of external label and a complete lack of stereospecificity.[20,21]

Model Studies. The proposed synthetic strategy was tested on a simple model which would permit comparison of products with materials derived from our earlier chemoenzymatic route. Reduction of 5-tridecyn-6-one (**4**) with (*S*)-Alpine−borane furnished the propargyl alcohol **5** in 91% ee, as judged by NMR analysis of the corre-

(8) Snider, B. B.; Shi, Z. *J. Org. Chem.* **1990**, *55*, 5669−5671.
(9) Snider, B. B.; Shi, Z. *J. Am. Chem. Soc.* **1992**, *114*, 1790−1800.
(10) Dussault, P.; Sahli, A.; Westermeyer, T. *J. Org. Chem.* **1993**, *58*, 5469−5474.
(11) Westermeyer, T. A. M.S. Thesis, University of Nebraska-Lincoln, 1994.
(12) Prein, M.; Adam, W. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 477−494.
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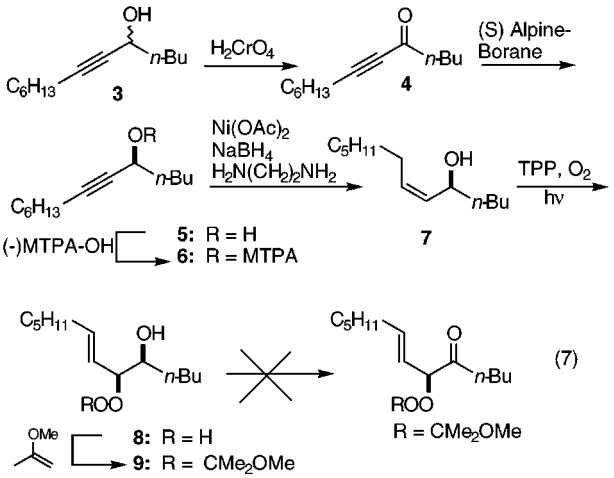
(16) Porter, N. A.; Mills, K. A.; Caldwell, S. E.; Dubay, G. R. *J. Am. Chem. Soc.* **1994**, *116*, 6697−6705.
(17) Funk, M. O.; Isaac, R.; Porter, N. A. *J. Am. Chem. Soc.* **1975**, *97*, 1281−2.
(18) Dussault, P. H. In *Active Oxygen in Chemistry*; Foote, C. S., Valentine, J. S., Greenberg, A., Liebman, J. F., Eds.; Blackie A & P: London, 1995; pp 141−203.
(19) Mills, K. A.; Caldwell, S. E.; Dubay, G. R.; Porter, N. A. *J. Am. Chem. Soc.* **1992**, *114*, 9689−9691.
(20) Porter, N. A. *Acc. Chem. Res.* **1986**, *19*, 262−268.
(21) Chan, H. W.-S.; Levett, G.; Matthew, J. A. *Chem. Phys. Lipids* **1979**, *24*, 245−256.

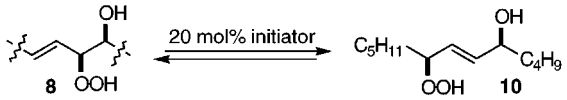
sponding Mosher ester (**6**).[22,23] Semihydrogenation of the propargyl alcohol with poisoned P2 nickel selectively afforded *Z*-alkenol (**7**).[24] Photooxygenation proceeded slowly to produce a separable 90:10 mixture of *syn*- and *anti*-6-hydroperoxy-7-tridecen-5-ol (**8**) in which the expected intramolecular hydrogen bond was evident in the sharp singlet at δ 9.5 ppm in the ^{1}H NMR spectrum.[25,26] Selective conversion of the hydroperoxide to form the methoxypropyl ketal was easily accomplished via acid-catalyzed addition of 2-methoxypropene.[10,27] However, all attempts to oxidize the secondary alcohol resulted in decomposition (eq 7). Given the typical stability of



peroxides toward oxidants,[18] the decomposition presumably reflects E_1CB fragmentation of the corresponding enol/enolate, a process previously observed for 2-peroxyaldehydes.[27]

The inability to prepare the desired hydroperoxyenone substrate led us to investigate equilibration of hydroperoxyalkenol **8**, where the presence of a hydrogen bond in the starting material, combined with the absence of any equivalent stabilizing factor in the product, seemed to preordain an unfavorable equilibrium. In a pleasant surprise, addition of substoichiometric di-*tert*-butyl hyponitrite (DTBN) to a 60−70 °C benzene solution of the hydroperoxide resulted in a nearly equal mixture of the starting 2-hydroperoxyenol and the desired 4-hydroperoxyenol **10** (Table 1).[28−30] The easily separated regioisomers each consisted of a single diastereomer, demonstrating that rearrangement proceeded without loss of stereochemistry. Resubmission of isolated product to the reaction conditions verified that the product distributions reflected equilibrium or near-equilibrium conditions. Attempts to perform room temperature rearrangement using Et_3B or through photolysis of DTBN were unsuccessful. The favorable outcome presumably reflects bonding advantages in the 1,4-dioxygenated-2-ene of sufficient

Table 1[a]

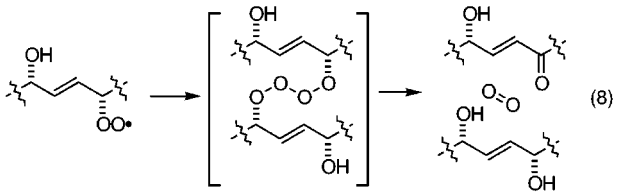


Conditions	Initiator	T (°C)	Time (h)	Yield (%)	Recovered Yield **8** (%)	Isolated Yield **10** (%)
A	DTBN	60	6.5	40	23	17
B	DTBN	55	7	41	20	21
B	DTBN	68	5	45	23	22
A	Et_3B	RT	6	NR	-	-
A	DTBN/hν	RT	1	decomp.	-	-
C	DTBN	50	7	77	34	30
C	DTBN	46	16	81	29	41

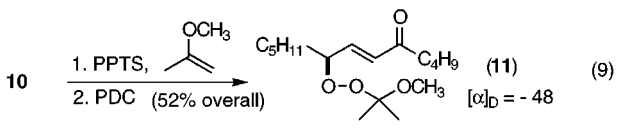
[a] A: 0.01 M in C_6H_6. B: 0.01 M in C_6H_6/H_2O (9:1). C: 0.01 M in C_6H_6 in the presence of 10 equiv of *t*-BuOOH.

magnitude to compensate for the loss of a hydrogen bond. Attempts to disrupt the hydrogen bond by performing the reaction in a benzene/water emulsion or in the presence of added HMPA had little effect.

While the rearrangements were stereospecific, the total amount of recovered hydroperoxides (both starting material and product) was low. The formation of significant amounts of hydroxyalkenones and alkenediones was diagnostic for Russell termination, a process involving dimerization of peroxyl radicals to form unstable tetroxides (eq 8).[28,31]



Similar problems have been encountered during preparative autoxidations, which also proceed via intermediate peroxyl radicals. Addition of *tert*-butyl hydroperoxide (TBHP), a radical reservoir which replaces substrate as the chain carrier, was found to greatly increase yields of peroxide products.[32] More recently, the TBHP reservoir effect has been successfully applied to peroxyl radical cyclizations and isomerizations.[15,33] As seen in Table 1, the addition of 10 equiv of TBHP to the rearrangement doubled the recovery of hydroperoxide. Protection and oxidation of the separated rearrangement product **10** afforded peroxyenone **11** (eq 9), which was judged to be 87% ee, based upon comparison with material derived from a chemoenzymatic process.[10]



The strategy was now applied to the total synthesis of chondrillin and plakorin (Scheme 2). The appropriate propargyl ketone was prepared through addition of a lithiated alkynol ether to the Weinreb amide of hepta-

(22) Midland, M. M.; Tramontano, A.; Kazubski, A.; Graham, R. S.; Tsai, D. J. S.; Cardin, D. B. *Tetrahedron* **1984**, *40*, 1371−1380.
(23) Dale, J. A.; Mosher, H. S. *J. Am. Chem. Soc.* **1973**, *95*, 512.
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(27) Dussault, P.; Sahli, A. *Tetrahedron Lett.* **1990**, *31*, 5117−5120.
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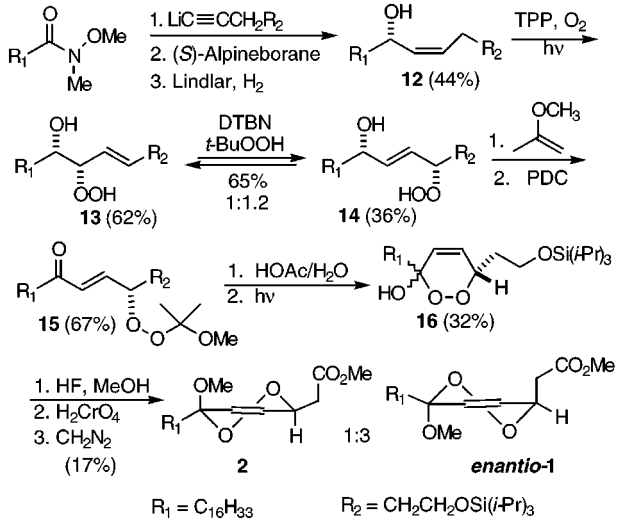
(30) Kiefer, H.; Traylor, T. G. *Tetrahedron Lett.* **1966**, 6163−6168.
(31) Russell, G. A. *J. Am. Chem. Soc.* **1957**, *79*, 3871−3879.
(32) Courtneidge, J. L.; Bush, M. *J. Chem. Soc., Perkin Trans. 1* **1992**, 1531−1538.
(33) Boukouvalas, J.; Pouliot, R.; Fréchette, Y. *Tetrahedron Lett.* **1995**, *36*, 4167−4170.

Scheme 2. Total Synthesis of Plakorin and *ent*-Chondrillin

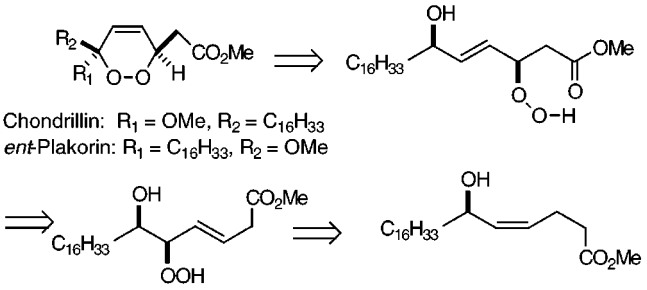


decanoic acid.[34] Reduction with (*S*)-alpine−borane provided a propargyl alcohol in 91% ee, based upon analysis of the Mosher ester. Semihydrogenation to *Z*-alkenol **12** was most efficiently accomplished with a Lindlar catalyst. Dye-sensitized photooxygenation proceeded with remarkable stereoselectivity to furnish a 98:2 syn/anti mixture of 2-peroxyenols **13**. Equilibration in the presence of DTBN and TBHP resulted in a 44:56 mixture of recovered **13** and 1,4-hydroperoxy alcohol **14**, each isolated as single diastereomers. Protection of **14** as the corresponding peroxy ketal was followed by oxidation of the allylic alcohol to form peroxy enone **15**. Deprotection of the hydroperoxide was followed by photocyclization, as per the procedure of Snider, to afford the dioxinol **16**.[8] Treatment with methanolic HF resulted in simultaneous deprotection of the silyl ether and ketalization to form the methoxydioxine. Oxidation and esterification resulted in a mixture of alkoxydioxines **1** and **2** which were separated, albeit with difficulty, by normal-phase HPLC.

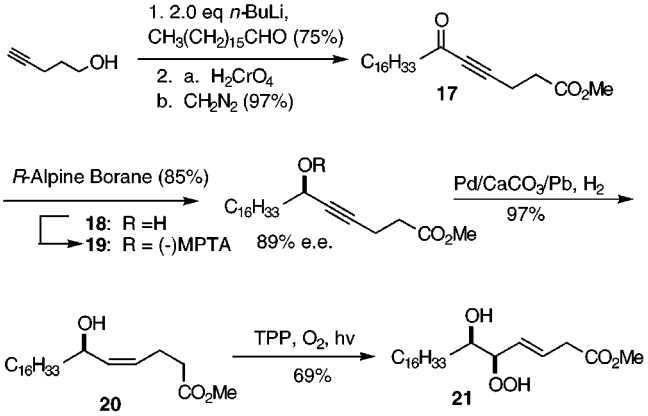
The ^{1}H NMR spectra of the first and second eluting isomers exactly matched data previously reported for plakorin and chondrillin, respectively.[3,4,6,9] Although the inconsistency in the reported rotations for plakorin make it difficult to ascertain the enantioselectivity of our synthesis, the optical rotation obtained for synthetic plakorin (**2**), $[\alpha]_D = +26-29$, indicated the material to be 85−95% ee.[35] However, the rotation observed for the first eluting isomer, $[\alpha]_D = -19$ ($c = 0.5$, MeOH), is *opposite* in sign to values previously reported for chondrillin and was therefore assigned as *ent*-**1**.[1,3] These results suggest the actual configuration of chondrillin to be 3(*R*),6(*S*), the enantiomer of the previously reported structure.

Synthesis of Chondrillin and Enantio Plakorin. Following the discovery that the published stereochemical assignment for chondrillin might be incorrect and that our initial synthesis had in fact yielded the enantiomer of chondrillin, we now planned a revised, more efficient, synthetic route to chondrillin itself (Scheme 3).

Scheme 3. Synthesis of Chondrillin and *ent*-Plakorin



Scheme 4. Synthesis of Chondrillin and *ent*-Plakorin



A key feature of the new route was the introduction of a hydrogen-bonding functional group intended to selectively stabilize the 4-hydroperoxyalkenol product of the rearrangement.

The revised chondrillin synthesis began with addition of a dilithiated alkynol to heptadecanal. Oxidation of the resulting alcohol afforded oxoalkynoate **17** (Scheme 4). Asymmetric reduction with (*R*)-Alpine−borane furnished the (*R*)-propargyl alcohol **18**, which was demonstrated to be 89% ee through conversion to the corresponding Mosher ester (**19**). Semihydrogenation with a Lindlar catalyst produced *Z*-alkenol **20**, which underwent photooxygenation as before to furnish the 1,2-hydroperoxyalkenol **21** as an inseparable 90:10 mixture of diastereomers.

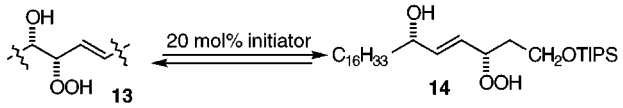
Reinvestigation of the rearrangement of hydroperoxyenol **13** demonstrated the ability to replace DTBN with commercially available AIBN (Table 2). Rearrangement of hydroperoxyalkenol **21** to the 1,4-hydroperoxyalkenol **22** proceeded using either DTBN or AIBN as the reaction initiator, and in either benzene or acetonitrile as reaction solvent (Table 2). Despite evidence for a hydrogen-bonded hydroperoxide by ^{1}H NMR (δ 9.3), the reaction equilibrium was unaffected by the presence of the carbomethoxy group.

Protection of the hydroperoxide furnished the peroxy ketal **23**. Oxidation produced an unstable enone which was directly subjected to a one-pot deprotection, photocyclization and transetherification to afford a mixture of chondrillin (**1**) and *ent*-plakorin (**2**) in good overall yield (Scheme 5). Considering the limitation on stereochemical purity imposed by the Alpine−borane reduction and the inability to separate the minor (10%) photooxygenation diastereomer, the observed rotation of synthetic chon-

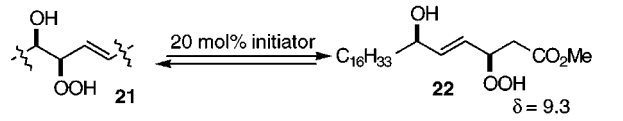
(34) Nahm, S.; Weinreb, S. M. *Tetrahedron Lett.* **1981**, *22*, 3815−3818.

(35) The two reported (refs 4 and 6) specific rotations for plakorin have the same sign yet differ in magnitude. The value of $[\alpha]_D = 30.5$ is utilized in this work due to the higher concentration ($c = 1.09$ in ref 4 versus $c = 0.2$ in ref 6) of plakorin used in the measurement.

Table 2[a]



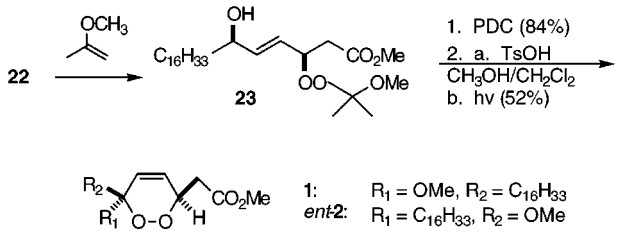
Conditions	Initiator	T (°C)	Time (h)	Yield (13+14) (%)	Ratio 13:14
A	DTBN	60	20	65	55:45
A	AIBN	60	18	84	42:58



Conditions	Initiator	T (°C)	Time (h)	Yield (21+22) (%)	Ratio 21:22
A	AIBN	60	20	50	54:46
B	AIBN	70	16	54	44:56
C	AIBN	70	22	68	49:51

[a] Conditions: A = 0.01 M in C_6H_6 containing 10 equiv of TBHP; B = 0.01 M in CH_3CN containing 10 equiv of TBHP; C = 0.005 M in CH_3CN containing 20 equiv of TBHP.

Scheme 5. Synthesis of Chondrillin and *ent*-Plakorin

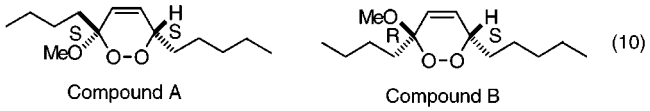


drillin, $[\alpha]_D = +30 - 33$, agrees well with the literature value of +40.[3,36]

Stereochemistry and Relevance to Biosynthesis. The first alkoxydioxine to be isolated, chondrillin, was assigned as having 3(*S*),6(*S*) stereochemistry on the basis of NMR and CD studies.[1] Plakorin was subsequently isolated and identified as the 6(*S*) epimer of chondrillin.[4] However, comparison of the optical rotation of synthetic chondrillin with literature reports implies the previously assigned configuration to be incorrect, the molecule in fact having 3(*R*),6(*S*) stereochemistry. This finding suggests that the configurations of other alkoxydioxin natural products, which have often been assigned in analogy with chondrillin/plakorin, may need to be reviewed.[2] However, it should be noted that xestin A and xestin B were demonstrated to have identical stereochemistry at the C_3 center.[5] Curiously, xestin A and xestin B have the same sign for optical rotation, whereas each pair of diastereomers produced from our synthetic routes displayed rotations which were opposite in sign (Table 3). Although we are unable to account for this discrepancy, it is interesting to note that our stereochemical assignments are supported by our earlier observations for simple alkoxydioxines A and B, which are epimeric at the peroxy ketal center and also rotate polarized light in opposite directions (eq 10).[10]

Table 3

	lit. config.	lit. $[\alpha]_D$	this work	obsd $[\alpha]_D$	ref
chondrillin	3*S*,6*R*	+40.0	3*R*,6*S*	+31.5	3
ent-chondrillin			3*S*,6*R*	−19	
plakorin	3*S*,6*S*	+30.5	3*S*,6*S*	+27.5	4
ent-plakorin			3*R*,6*R*	−29	
xestin A	3*R*,6*R*	+26.5			5
xestin B	3*R*,6*S*	+19.6			5
compound A	*S*,*S*			+45.8	10
compound B	*S*,*R*			−20.3	10



(10)

Our results also provide some of the first evidence into the mechanism of dioxygen introduction during the biosynthesis of cyclic peroxides from marine sources. It is apparent that the natural products are either enantiomerically pure or at least highly enriched in one enantiomer. Synthetic plakorin, assumed to 90% ee, based upon the assay of the propargyl alcohol intermediate, displayed a specific rotation between 85 and 90% of the values reported from isolation studies. Although the range of values reported for the optical rotation of chondrillin renders direct comparison less straightforward, it is nonetheless clear that chondrillin is at least highly enriched in one enantiomer.[1,3] These results strongly support introduction of the dioxygen bridge through a controlled enzymatic reaction rather than via nonenzymatic oxygenation. Furthermore, the observation that chondrillin and plakorin share the same absolute stereochemistry at the epimerizable C_6 peroxy ketal and differ at C_3 is also of interest. Given the precedent for 6-exo cyclization of peroxyanions or hydroperoxides onto enoates,[37] our observations could support a biosynthetic route involving oxidation to an enantiomerically enriched hydroperoxy ketal, followed by conjugate addition onto an enoate.

Experimental Section

All reagents and solvents were used as supplied commercially, except THF and CH_2Cl_2, which were distilled from Na/Ph_2CO and CaH_2, respectively. ^1H, ^{13}C, and ^{19}F NMR spectra were recorded on 300- or 500-MHz spectrometers; individual peaks are reported as (multiplicity, number of hydrogens, coupling constant in hertz). Infrared spectra were recorded on an FT-IR spectrophotometer as neat films unless otherwise stated. Selected absorbances are reported in wavenumber (cm^{-1}). Elemental analyses were obtained from M-H-W Laboratories, Phoenix, AZ, Desert Analytics, Tucson, AZ, or Quantitative Technologies, Inc., NJ. Progress of reactions involving peroxides were monitored by TLC, using a phenylenediamine indicator;[38] hydroperoxides and peracids yield an immediate reddish-pink spot while perketals or peresters exhibit a pink or green-red color after mild charring. Much of the chromatography was performed with recycled ethyl acetate/hexane (EA/hex), which was purified and quantitated by a reported procedure.[39] All hydroperoxides were stabilized with a few drops of 0.1% solution of BHT in CH_2Cl_2 prior to concentration.

6-Tridecyn-5-ol (3). To a 0 °C solution of 1-octyne (7.5 g, 67.8 mmol) in THF (100 mL) was added *n*-butyllithium (35 mL, 2.0 M in hexane) until the presence of free alkyllithium

(36) The two reported (refs 1 and 3) specific rotations for chondrillin have the same sign yet differ in magnitude. The value of $[\alpha]_D = +40$ (ref 3) is utilized in this work since the concentration of chondrillin was indicated (*c* = 4.5).

(37) Bartlett, P. A.; Chapuis, C. *J. Org. Chem.* **1986**, *51*, 2799−2806.
(38) Smith, L. L.; Hill, F. L. *J. Chromatogr.* **1972**, *66*, 101−109.

was indicated (1,10-phenanthroline). The solution was stirred for 5 min, and valeraldehyde (5.8 g, 67.3 mmol) was added. The solution was stirred for 2 h, quenched with saturated NH_4Cl (20 mL), and washed with saturated $NaHCO_3$ (20 mL) and brine (20 mL). The aqueous layer was extracted with ether (2 × 25 mL), and the combined organics were dried over anhydrous Na_2SO_4. Removal of solvent at reduced pressure followed by flash chromatography on silica gel (10% EA/hex) afforded 9.8 g (74%) of alcohol **3**: $R_f = 0.44$, (20% EA/hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.27 (dt, 1H, J = 6.5, 5.6), 2.42 (s, 1H), 2.12 (dt, 2H, J = 7.3, 1.2), 1.60 (m, 2H), 1.43 (m, 2H), 1.17−1.45 (10H), 0.84 (t, 3H, J = 7.3), 0.82 (t, 3H, J = 7.3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 85.8, 82.2, 63.2, 38.5, 32.0, 29.3, 29.1, 28.0, 23.1, 23.0, 19.3, 14.5; IR 3340, 2955, 2935, 2835, 2872, 2860, 1468, 1433, 1380, 1038, 1008 cm^{-1}. Anal. Calcd for $C_{13}H_{24}O$: C, 79.53; H, 12.32. Found: C, 79.34; H, 12.54.

6-Tridecyn-5-one (4). To a solution of **3** (5.60 g, 28.5 mmol) in acetone (250 mL) at 0 °C was added Jones reagent (8 N) until the orange color persisted. Excess oxidant was quenched with 2-propanol, and the mixture was stirred for 15 min. Water was added, and the mixture was extracted with ether. The combined organic layers were dried with $MgSO_4$ and concentrated. The crude mixture was purified by distillation (bp 169−171 °C) under reduced pressure (aspirator) to yield 3.91 g (71%) of **4**: $R_f = 0.7$ (20% EA/hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.48 (t, 2H, J = 7.3), 2.32 (t, 2H, 7.3), 1.61 (m, 2H), 1.65 (m, 2H), 1.20−1.40 (m. 8H), 0.88 (t, 3H, J = 7.3), 0.86 (t, 3H, J = 7.3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 189.0, 94.8, 81.6, 45.8, 31.8, 29.1, 28.3, 26.9, 23.1, 22.7, 19.5, 14.6, 14.3; IR 2958, 2932, 2872, 2861, 2214, 1676, 1468 cm^{-1}.

(*S*)-6-Tridecyn-5-ol (5). To a solution of **4** (3.69 g, 19.0 mmol) in THF (100 mL) was added (*S*)-Alpine−borane (76 mL of a 0.5 M solution in THF). The mixture was stirred for 3 days, and then acetaldehyde (2 mL) was added. After 15 min NaOH (75 mL of a 1 M solution) was added, and the aqueous phase was extracted with ether. The combined organic layers were dried with Na_2SO_4, filtered, and concentrated. The crude concentrate was directly subjected to flash chromatography (10% EA/hex) to yield 2.54 g (68%) of **5**: $[\alpha]_D = -3.0$ (c = 0.7, CH_2Cl_2). Spectra were identical to those of compound **3**.

(*S*)-6-Tridecyn-5-ol-[(2*S*)-(−)-2-methoxy-2-(trifluoromethyl)phenylacetate Ester (6). To a solution of **5** (83 mg, 0.42 mmol) in CH_2Cl_2 was added (*S*)-(−)-α-methoxy-α-(trifluoromethyl)phenylacetic acid (108 mg, 0.46 mmol) followed by DMAP (13 mg, 0.10 mmol). The solution was stirred at rt for 15 min, and 1,3-dicyclohexylcarbodiimide (DCC) (108 mg, 0.52 mmol) was added. The reaction mixture was stirred at rt overnight (convenience) and directly subjected to column chromatography on silica gel (5% EA/hex) to give 134 mg (77%) of the desired Mosher ester **6** in 91% ee by ^{19}F NMR: ^{19}F NMR (470 MHz, $CDCl_3$) δ −72.05 (major), −72.29 (minor); $R_f = 0.64$ (20% EA/hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58−7.55 (m, 2H), 7.41−7.37 (m, 3H), 5.48 (tt, 1H, J = 6.5, 2.0), 3.60 (s, 3H), 2.21 (td, 2H, J = 1.6, 6.9), 1.80−1.70 (m, 2H), 1.51−1.73 (m, 2H), 1.39−1.23 (m, 12H), 0.90−0.84 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.0, 129.4, 128.3, 128.2, 127.4, 87.4, 76.6, 66.7, 55.4, 34.5, 31.2, 28.4, 26.9, 22.5, 22.0, 18.6, 13.9, 13.8.

(*S*)-6(*Z*)-Tridecen-5-ol (7). To a solution of nickel acetate tetrahydrate (1.8 g, 7.4 mmol) in EtOH (50 mL) was added a solution of sodium borohydride (278 mg, 7.4 mmol) in EtOH (5 mL). The mixture was stirred until the hydrogen evolution ceased (approximately 30 min). The catalyst was poisoned with 1 equiv of ethylenediamine (1.2 mL, 18.4 mmol) followed by addition of **5** (3.6 g, 18.4 mmol) dissolved in EtOH (5 mL). The reaction flask was placed under 1 atm of hydrogen, and the progress of the reaction was monitored by GC. After 3 h the reaction was quenched with water (50 mL), and the crude mixture was filtered through Celite. The mixture was extracted with 50% EA/hex (3 × 50 mL), and the combined organics were dried over anhydrous $MgSO_4$ to give 3.11 g (85%) of allylic alcohol **7**: $R_f = 0.52$ (20% EA/hex); $[\alpha]_D = -15$ (c = 2.2, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.46 (dt, 1H, J = 11.0, 7.4), 5.34 (dd, 1H, J = 11.0, 8.8), 4.40 (dt, 1H, J = 8.6, 6.7), 2.1 (m, 2H), 1.26 (16H), 0.87 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 133.3, 132.9, 68.3, 37.9, 32.4, 30.3, 29.6, 28.4, 28.2, 23.3, 23.2, 14.7; IR 3339, 3006, 2956, 2925, 2858, 1715, 1462, 1381, 1323, 1010 cm^{-1}. Anal. Calcd for $C_{13}H_{26}O$: C, 78.72; H, 13.21. Found: C, 78.48; H, 13.17.

(6*S*,5*S*)-6-Hydroperoxy-7(*E*)-tridecen-5-ol (8). Allylic alcohol **7** (3.1 g, 15.5 mmol) was dissolved in CCl_4 (50 mL) containing 1.0 mM 5,10,15,20-tetraphenyl-21*H*,23*H*-porphine (TPP) in a water-cooled Pyrex cell (10−15 °C) into which oxygen was bubbled. The solution was photolyzed (200 W incandescent) at a distance of 10 cm for 6 h. The solvent was removed in vacuo. Flash chromatography on silica gel (20% EA/hex) gave 2.4 g (67%) of the hydroperoxide **8**: $R_f = 0.29$ (20% EA/hex); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.5 (bs, 1H), 5.8 (dt, 1H, J = 15.5, 6.7), 5.4 (dd, 1H, J = 15.5, 8.6), 4.1 (t, 1H, J = 8.4), 3.7 (bt, 1H, J = 7.6), 2.0 (q, 2H, J = 7.2), 1.2−1.5 (12H), 0.9 (t, 6H, J = 6.9); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.4, 125.6, 91.2, 72.8, 33.1, 32.0, 29.2, 28.0, 23.3, 23.1, 14.7, 14.6; IR 3349, 2957, 2929, 2872, 2859, 1468, 1457, 1437, 1379, 974 cm^{-1}. Anal. Calcd for $C_{13}H_{26}O_3$: C, 67.79; H, 11.38. Found: C, 67.66; H, 11.16.

(6*S*,5*S*)-6-(1-Methoxy-1-methylethyldioxy)-7(*E*)-tridecen-5-ol (9). To a solution of **8** (394 mg, 1.61 mmol) in CH_2Cl_2 (15 mL) was added 2-methoxypropene (116 mg, 1.61 mmol) and pyridinium *p*-toluenesulfonate (PPTS) (30 mg, 0.1 mmol). The reaction was quenched after 30 min with water. The aqueous layer was extracted with CH_2Cl_2, and the combined organic layers were dried with $MgSO_4$ filtered and concentrated. The concentrate was purified by flash chromatography (15% EA/hex) to yield 353 mg (70%) of compound **9**: $R_f = 0.52$ (20% EA/hex); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.73 (dt, 1H, J = 15.5, 6.7), 5.37 (dd, 1H, J = 15.5, 8.6), 4.12 (t, 1H, J = 8.1), 4.1 (t, 1H, J = 6.7), 3.24 (s, 3H), 2.85 (bs, 1H), 2.03 (app q, 2H, J = 7.2, 6.9), 1.47−1.24 (m, 20H), 0.88−0.82 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.3, 125.6, 105.0, 89.3, 72.0, 49.4, 32.4, 31.3, 28.5, 27.4, 23.0, 22.6, 22.5, 14.0.

(8*S*,5*S*)-8-Hydroperoxy-6(*E*)-tridecen-5-ol (10). To a solution of **8** (230 mg, 0.89 mmol) in benzene (80 mL) was added a solution of *t*-BuOOH (3.3 mL of a 2.7 M solution in benzene) and DTBN (31 mg, 0.18 mmol). The mixture was stirred at 46 °C for 16 h. The reaction mixture was cooled to room temperature and concentrated. The concentrate was purified by flash chromatography (20% EA/hex) to yield 59 mg (29%) of recovered starting material **8** and 84 mg (41%) of **10**: $R_f = 0.53$ (50% EA/hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.55 (bs, 1H), 5.67 (dd, 1H, J = 15.3, 7.3), 5.51 (dd, 1H, J = 15.3, 8.5), 4.24 (dt, 1H, J = 6.5, 6.9), 4.06 (dt, 1H, J = 6.4, 6.9), 1.61−1.54 (m, 2H), 1.47−1.25 (m, 14H), 0.88−0.83 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.0, 131.0, 86.4, 72.9, 36.4, 32.1, 31.6, 27.5, 24.9, 22.5, 22.4, 14.0, 13.9; IR 3780, 3674 cm^{-1}.

(8*S*,5*S*)-8-(1-Methoxy-1-methylethyldioxy)-6(*E*)-tridecen-5-one (11). To a solution of **10** (42 mg, 0.18 mmol) in CH_2Cl_2 (4 mL) was added 2-methoxypropene (13 mg, 0.18 mmol) and PPTS (2.3 mg, 0.01 mmol). The mixture was stirred for 30 min at room temperature. The reaction was quenched with 1 mL of a saturated $NaHCO_3$ solution and extracted with CH_2Cl_2. The combined organic layers were dried and concentrated. The concentrate was directly subjected to column chromatography (20% EA/hex) to yield 34 mg of the peroxyketal: R_f = 0.35 (20% EA/hex); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.70−5.54 (m, 2H), 4.32 (dt, 1H, J = 6.7, 6.2), 4.09 (dt, 1H, J = 6.2, 6.2), 3.27 (s, 3H), 1.90 (br s, 1H), 1.70−1.20 (m, 22H), 0.89−0.83 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.2, 130.6, 104.6, 84.3, 72.4, 49.2, 36.7, 32.9, 31.7, 27.5, 24.9, 23.0, 22.7, 22.5, 22.4, 14.0, 13.9.

To a solution of 8-(1-methoxy-1-methylethyldioxy)-6-tridecen-5-ol (34 mg, 0.11 mmol) in CH_2Cl_2 (2 mL) was added pyridinium dichromate (116 mg, 0.33 mmol). After 23 h of stirring, the reaction contents were filtered through silica gel and concentrated to yield 29 mg (87%) of **11**: $R_f = 0.80$ (20% EA/hex); $[\alpha]_D = -48.5$ (c = 0.014, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.67 (dd, 1 H, J = 16.2,6.7), 6.25 (dd, 1H, J = 16.2, 1.0), 4.53 (q, 1H, J = 7.2), 3.27 (s, 3 H), 2.57 (dt, 2H, J = 7.6, 3.2), 1.25−1.50 (m, 12H), 0.91 (6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 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.

1-((Triisopropylsilyl)oxy)-4-pentyne. To a solution of 4-pentyn-1-ol (3.6 g, 43 mmol) in DMF (150 mL) was added imidazole (4.4 g, 65 mmol) and triisopropylsilyl chloride (9.1 g, 47 mmol). After 24 h the reaction was quenched with $NaHCO_3$ (75 mL) and washed with H_2O (75 mL). The solution was extracted with hexane (3 × 50 mL), and the solvent was removed at reduced pressure. The crude oil was subjected to column chromatography on silica gel (10% EA/hex) to give 9.38 g (91%) of the protected alcohol: $R_f = 0.81$ (20% EA/hex); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.76 (t, 2H, $J = 6.0$) 2.29 (dt, 2H, $J = 7.2, 2.6$) 1.91 (t, 1H, $J = 2.9$) 1.74 (m, 2H), 1.05 (18H), 1.04 (bs, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 85.0, 68.8, 62.3, 32.4, 18.6, 15.5, 12.6; IR 3316 cm^{-1}. Anal. Calcd for $C_{14}H_{28}OSi$: C, 69.93; H, 11.74. Found: C, 70.0; H, 11.68.

***N*-Methoxy-*N*-methylheptadecanoylamide.** Heptadecanoic acid (10 g, 37 mmol) suspended in CH_2Cl_2 (200 mL) was cooled to 0 °C. To the suspension were added triethylamine (10.4 mL, 75 mmol), isobutyl chloroformate (5 mL, 38 mmol), and *N*,*O*-dimethylhydroxylamine (3.6 g, 37 mmol). The solution was warmed to rt and stirred overnight (ca. 20 h). The reaction was quenched with saturated $NaHCO_3$ (25 mL) and washed with brine (25 mL). The aqueous layer was extracted with ether (3 × 25 mL), and the organic layers were combined. The solvent was removed at reduced pressure, and the crude oil was subjected to flash chromatography on silica gel (20% EA/hex) to furnish 10.97 g (95%) of the amide as a clear oil that solidified upon standing (mp = 27−30 °C): $R_f = 0.36$ (20% EA/hex); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.63 (s, 3H), 3.12 (s, 3H), 2.36 (t, 2H, $J = 7.6$), 1.57 (m, 2H), 1.20 (26H), 0.83 (t, 3H, $J = 6.2$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 61.8, 32.6, 30.3, 30.1, 30.0, 29.9, 25.3, 23.3, 14.7; IR 1674 cm^{-1}. Anal. Calcd for $C_{19}H_{39}NO_2$: C, 72.79; H, 12.54; N, 4.47. Found: C, 72.71; H, 12.57; N, 4.48.

1-((Triisopropylsilyl)oxy)-4-docosyn-6-one. To a 0 °C solution of 1-((triisopropylsilyl)oxy)-4-pentyne (3.43 g, 14.3 mmol) in THF (100 mL) was added dropwise *n*-BuLi (7.5 mL, 2.0 M in hexane). The solution was stirred at 0 °C for 15 min, and a solution of the *N*-methoxy-*N*-methylheptadecanoyl amide (4.2 g, 14.3 mmol) in THF (25 mL) was added via cannula. The reaction was allowed to warm to rt and stirred for 6 h whereupon it was quenched with saturated NH_4Cl (25 mL), and washed with brine (25 mL). The aqueous layers were extracted with ether (3 × 20 mL) and the combined organics were dried over Na_2SO_4. The solvent was removed at reduced pressure and the crude oil was subjected to column chromatography on silica gel (20% EA/hex) to give 6.45 g (92%) of the ketone: $R_f = 0.67$ (20% EA/hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.76 (t, 2H, $J = 6.0$) 2.48 (dt, 2H, $J = 7.3, 4.1$), 1.78 (t, 2H, $J = 6.0$), 1.64 (m, 2H), 1.24 (26H), 1.05 (18H), 1.04 (s, 3H), 0.87 (t, 3H, $J = 6.9$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 94.5, 81.6, 62.1, 46.2, 32.6, 31.7, 30.3, 30.1, 30.0, 29.6, 24.8, 23.3, 16.6, 16.1, 12.6; IR 1678 cm^{-1}. Anal. Calcd for $C_{31}H_{60}O_2Si$: C, 75.54; H, 12.27. Found: C, 75.80; H, 12.50.

(*S*)-1-((Triisopropylsilyl)oxy)-4-docosyn-6-ol. To neat propargyl ketone (10.4 g, 21 mmol) in a flame-dried 250-mL round bottom flask was added a solution of (*S*)-alpine−borane (84 mL, 0.5 M in THF). The reaction was stirred at rt for 24 h and then quenched with acetaldehyde (5 mL) and washed with 1 M NaOH (75 mL). The aqueous layer was extracted with ether (3 × 25 mL), and the combined organics were dried over Na_2SO_4. The solvent was removed at reduced pressure, and the resulting yellow oil was subjected to column chromatography on silica gel (10% EA/hex) to give 4.95 g (48%) of the *S*-alcohol: $R_f = 0.69$ (20% EA/hex); $[\alpha]_D = -3.0$ ($c = 0.85$, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.30 (q, 1H, $J = 6.5$), 3.75 (t, 2H, $J = 6.0$), 2.31 (dt, 2H, $J = 7.3, 2.0$), 1.71 (t, 2H, $J = 6.5$), 1.64 (m, 2H), 1.41, (m, 2H), 1.24 (26H), 1.05 (18H), 1.04 (s, 3H), 0.87 (t, 3H, $J = 6.9$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 85.7, 82.2, 63.4, 62.5, 38.9, 32.6, 30.3, 30.24, 30.21, 30.0, 25.9, 23.3, 18.6, 15.8, 14.7, 12.7; IR 3392 cm^{-1}. Anal. Calcd for $C_{31}H_{62}O_2Si$: C, 75.23; H, 12.63. Found: C, 75.31; H, 12.97.

(*S*)-1-((Triisopropylsilyl)oxy)-4-docosyne-6-ol, 5-[(2*S*)-(−)-2-Methoxy-2-(trifluoromethyl)phenylacetyl]. To a solution of (*S*)-1-((triisopropylsilyl)oxy)-4-docosyn-6-ol (165 mg, 0.33 mmol) in CH_2Cl_2 was added (*S*)-(−)-α-methoxy-α-(trifluoromethyl)phenylacetic acid (86 mg, 0.37 mmol) followed by DMAP (10 mg, 0.08 mmol). The solution was stirred at rt for 15 min, and DCC (85 mg, 0.41 mmol) was added. The reaction mixture was stirred at rt overnight (convenience) and directly subjected to column chromatography on silica gel (5% EA/hex) to give 234 mg (quantitative) of the desired Mosher ester with 92% ee by ^{19}F NMR: $R_f = 0.67$ (10% EA/hex); ^{19}F NMR (470 MHz, $CDCl_3$) δ −71.85 (major), −72.07 (minor); $[\alpha]_D = -3.9$ ($c = 0.98$, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35−7.55 (m, 5H), 5.56 (tt, 1H, $J = 6.5, 2.0$), 3.73 (t, 2H, $J = 6.1$), 3.57 (s, 3H), 2.35 (dt, 2H, $J = 6.9, 2.0$), 1.70−1.78 (m, 4H), 1.27 (24H), 1.06 (18H), 1.05 (s, 3H), 0.87 (t, 3H, $J = 6.9$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.4, 133.2, 130.1, 128.9, 128.0, 88.8, 67.3, 62.4, 56.1, 35.5, 32.6, 32.5, 30.3, 30.1, 30.0, 29.6, 25.4, 23.3, 18.6, 15.8, 14.7, 12.6; IR 1757 cm^{-1}.

(*S*)-1-((Triisopropylsilyl)oxy)-4-(*Z*)-docosen-6-ol (12). To a solution of (*S*)-1-((triisopropylsilyl)oxy)-4-docosyn-6-ol (3.83 g, 7.7 mmol) in pentane (75 mL) were added $Pd/CaCO_3$/Pb (154 mg) and a few drops of quinoline. The reaction flask was placed under a balloon (1 atm) of hydrogen, and the reaction was followed by ^{1}H NMR. Following the disappearance of alkyne by NMR, the solution was filtered through Celite and concentrated under vacuum to furnish 3.83 g (quantitative) of the *Z*-allylic alcohol **12**: $R_f = 0.67$ (20% EA/hex); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.42 (m, 2H), 4.42 (dt, 1H, $J = 6.9, 6.2$), 3.69 (t, 2H, $J = 6.4$), 2.09−2.31 (m, 2H), 1.74 (bs, 1H), 1.56 (m, 2H), 1.24 (24H), 1.05 (18H), 1.04 (s, 3H), 0.86 (t, 3H, $J = 6.9$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 134.2, 132.1, 68.1, 63.0, 38.0, 33.4, 32.6, 30.4, 30.3, 30.0, 26.1, 24.6, 23.4, 18.7, 12.7; IR 3337 cm^{-1}.

(5*S*,6*S*)-1-[[Tris(1-methylethyl)silyl]oxy]-5-hydroperoxy-3(*E*)-docosen-6-ol (13). The allylic alcohol **12** (1.77 g, 3.56 mmol) was dissolved in CCl_4 (50 mL) containing 1.0 mM TPP in a water-cooled (10−15 °C) Pyrex cell into which oxygen was bubbled. The solution was photolyzed (200 W) at a distance of 10 cm for 3.5 h. The solvent was removed in vacuo. Flash chromatography on silica gel (20% EA/hex) gave 1.17 g (62%) of the hydroperoxide **13**: $R_f = 0.42$ (20% EA/hex); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.87 (dt, 1H, $J = 15.7, 6.7$), 5.47 (dd, 1H, $J = 15.5, 8.4$), 4.14 (t, 1H, $J = 8.1$), 3.74 (t, 2H, $J = 6.4$), 3.65 (bt, 1H, $J = 8.1$), 2.33 (q, 2H, $J = 6.7$), 1.23 (26H), 1.04 (18H), 1.02 (s, 3H), 0.86 (t, 3H, $J = 6.4$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.1, 127.4, 91.0, 72.8, 63.3, 36.9, 33.5, 32.6, 30.4, 30.3, 30.0, 26.0, 23.3, 18.6, 14.7, 12.6; IR 3339 cm^{-1}; HRMS calcd for $C_{31}H_{64}O_4Si$ (M + Na) 551.4472; found 551.4464.

(3*S*,6*S*)-1-[[Tris(1-methylethyl)silyl]oxy]-3-hydroperoxy-4(*E*)-docosen-6-ol (14). To a solution of **13** (1.8 g, 3.4 mmol) in benzene (300 mL, 0.01 M) was added a solution of *tert*-butyl hydroperoxide (8.7 mL, 3.9 M in benzene). To this mixture was added DTBN (118 mg, 0.68 mmol), and the flask was placed in an oil bath at 60 °C for 20 h. The reaction was quenched with a few drops of a BHT solution (0.1% solution of BHT in CH_2Cl_2), and the solvent was removed at reduced pressure. The crude oil was subjected to column chromatography on silica gel (10% EA/hex) to give 517 mg (29%) of the starting material **13** and 642 mg (36%) of rearranged hydroperoxide **14**: $R_f = 0.18$ (20% EA/hex); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.72 (dd, 1H, $J = 15.5, 6.7$), 5.59 (dd, 1H, $J = 15.5, 7.6$), 4.49 (dt, 1H, $J = 6.9, 6.7$), 4.06 (dt, 1H, $J = 7.4, 6.7$), 3.75 (m, 2H), 1.35−2.27 (m, 5H), 1.23 (s, 28H), 1.04 (s, 18H), 1.02 (s, 3H), 0.85 (t, 3H, $J = 6.4$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.4, 130.7, 83.9, 73.3, 60.5, 37.5, 36.4, 32.6, 30.4, 30.3, 30.2, 30.0, 26.1, 23.3, 18.6, 14.8, 12.5; HRMS calcd for $C_{19}H_{39}NO_2$ (M + Na) 551.4472, found 551.4482.

Synthesis of 15: (3*S*,6*S*)-1-[[Tris(1-methylethyl)silyl]-oxy]-3-[(1-methoxy-1-methylethyl)dioxy]-4(*E*)-docosen-6-ol. To a solution of **14** (611 mg, 1.2 mmol) in CH_2Cl_2 (10 mL) was added PPTS (20 mg, 0.008 mmol) followed by 2-methoxypropene (90.4 mg, 1.3 mmol). The reaction was stirred overnight (convenience) and quenched with saturated $NaHCO_3$ (1 mL). The crude mixture was directly subjected to flash

chromatography on silica gel (10% EA/hex) to give 482 mg (70%) of the peroxy ketal: $R_f = 0.43$ (20% EA/hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.72 (dd, 1H, $J = 15.7, 6.5$), 5.64 (dd, 1H, $J = 15.7, 7.3$), 4.61 (dt, 1H, $J = 7.3, 6.4$), 4.10 (dt, 1H, $J = 6.5, 6.4$), 3.74 (m, 2H), 3.28 (s, 3H), 1.40−2.00 (5H), 1.36 (s, 6H), 1.24 (28H), 1.044 (18H), 1.035 (s, 3H), 0.86 (t, 3H, $J = 6.9$); 13C NMR (125 MHz, $CDCl_3$) δ 137.0, 130.9, 105.2, 81.8, 73.1, 60.2, 49.9, 37.8, 37.1, 32.6, 30.3, 30.0, 26.0, 23.7, 23.4, 23.3, 18.6, 14.7, 12.6; IR 3454 cm^{-1}.

(*S*)-1-[[Tris(1-methylethyl)silyl]oxy]-3-[(1-methoxy-1-methylethyl)dioxy]-4(E)-docosen-6-one (15). To a solution of the ketalized peroxy alcohol (482 mg, 0.8 mmol) was added pyridinium dichromate (838 mg, 2.4 mmol). The reaction was allowed to stir at rt for 20 h whereupon the mixture was filtered through a Celite plug and the solvent was removed at reduced pressure. Flash chromatography on silica gel (10% EA/hex) afforded 453 mg (95%) of the desired protected peroxy enone **15**: $R_f = 0.74$ (20% EA/hex); $[\alpha]_D = -19.8$ ($c = 1.13$, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.77 (dd, 1H, $J = 16.7, 6.7$), 6.25 (d, 1H, $J = 16.2$), 4.79 (dt, 1H, $J = 6.7, 6.4$), 3.67−3.86 (m, 2H), 3.26 (s, 3H), 2.54 (t, 2H, $J = 7.6$), 1.57−1.94 (m, 2H), 1.35 (s, 6H), 1.23 (28H), 1.03 (18H), 1.02 (s, 3H), 0.85 (t, 3H, $J = 6.9$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.3, 145.6, 131.0, 105.5, 80.7, 59.8, 49.9, 41.0, 36.7, 32.6, 30.3, 30.2, 30.1, 30.0, 29.9, 24.8, 23.5, 23.4, 23.3, 18.6, 14.8, 12.6, 12.5; IR 1679 cm^{-1}.

(3*S*,6*S*)- and (3*S*,6*R*)-6-Hexadecyl-3-[2-[tris(1-methylethyl)silyloxy]ethyl]-3,6-dihydro-1,2-dioxin-6-ol (16). Compound **15** (120 mg, 0.20 mmol) was dissolved in 3 mL of freshly prepared 9:1 HOAc/H_2O, containing a few drops of a 0.1 M BHT solution (in CH_2Cl_2). Upon disappearance of starting material by TLC, the solvent was removed in vacuo and the crude product was subjected to flash chromatography (20% EA/hex) to give 57 mg (54%) of hydroperoxy enone: $R_f = 0.33$ (10% EA/hex); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.64 (s, 1H) 6.77 (dd, 1H, $J = 16.2, 6.0$), 6.29 (dd, 1H, $J = 16.2, 1.4$), 4.72 (dt, 1H, $J = 6.7, 6.4$), 3.82 (m, 2H), 2.54 (t, 2H, $J = 7.6$), 1.81−1.98 (m, 2H), 1.58 (t, 2H, $J = 6.9$), 1.22 (26H), 1.05 (18H), 1.03 (s, 3H), 0.85 (t, 3H, $J = 6.9$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 201.5, 144.3, 131.0, 82.8, 60.5, 41.4, 36.0, 32.6, 30.3, 30.2, 30.1, 30.0, 24.7, 23.3, 18.6, 14.8, 12.5; IR 2927, 1697, 1682 cm^{-1}. Anal. Calcd for $C_{31}H_{62}O_4Si$: C, 70.66; H, 11.86. Found: C, 69.88; H, 11.59.

The hydroperoxy enone (244 mg, 0.5 mmol) was dissolved in a 19:1 mixture of CH_2Cl_2/MeOH (20 mL) and placed in a jacketed Pyrex cell. A stream of N_2 was passed through the solution, and the flask was illuminated with a sun lamp at a distance of 20 cm for 4 h.[40] The solvent was removed at reduced pressure, and the crude oil was subjected to column chromatography on silica gel (10% EA/hex) to furnish 144 mg (60%) of dioxinol **16**: $R_f = 0.55$ (20% EA/hex); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.06 (dd, 0.5H, $J = 10.3, 4.3$), 5.99 (dd, 0.5H, $J = 10.3, 0.7$), 5.88−5.83 (m, 1H), 4.83 (m, 0.5H), 4.51 (m, 0.5H), 3.8 (m, 2H), 3.35 (s, 0.5H), 3.29 (s, 0.5H), 2.06−1.57 (4H), 1.22 (28H), 1.04 (18H), 1.03 (s, 3H), 0.86 (t, 3H, $J = 6.9$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 131.6, 130.8, 128.6, 127.9, 98.6, 98.3, 75.4, 75.2, 37.3, 37.2, 35.9, 35.7, 32.6, 30.41, 30.40, 30.3, 30.2, 30.1, 30.0, 23.8, 23.6, 23.3, 18.6, 14.8, 12.6.

Synthesis of 2 and *ent*-1: (3*S*,6*S*)- and (3*S*,6*R*)-6-Hexadecyl-2-(hydroxyethyl)-6-methoxy-3,6-dihydro-1,2-dioxine. To a solution of dioxinol **16** (144 mg, 0.3 mmol) in MeOH (25 mL) was added a 70% solution of HF−pyridine (4 mL). The solution was stirred at rt for 2 h and directly subjected to column chromatography on silica gel (10 → 20% EA/hex) to afford 40 mg (39%) of a white solid: mp = 39−41 °C; $R_f = 0.10$ (20% EA/hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.14 (dd, 0.5H, $J = 10.5, 4.4$), 6.05 (d, 0.5H, $J = 10.5, 1.2$), 5.83 (dd, 0.5H, $J = 4.8, 2.0$), 5.81 (dd, 0.5H, $J = 4.8, 2.4$), 4.79 (m, 0.5H), 4.50 (m, 0.5H), 3.87−3.72 (m, 2H), 3.39 (s, 1.5H), 3.38 (s, 1.5H), 2.05 (m, 2H), 1.90−1.76 (m, 2H), 1.62 (s, 2H), 1.24 (s, 26H), 0.86 (t, 3H, $J = 6.9$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 131.8, 131.2, 126.9, 126.2, 76.1, 60.4, 59.9, 51.8, 51.6, 35.6, 35.3, 35.1, 32.6, 30.4, 30.3, 30.2, 30.1, 29.9, 24.1, 23.9, 23.3, 14.7; HRMS calcd for $C_{23}H_{44}O_3$ (M − $HOCH_3$) 352.2977, found 352.2975.

Plakorin (2) and *ent*-Chondrillin (*ent*-1). To a solution of the alkoxydioxinol (31 mg, 0.08 mmol) in acetone (5 mL) was added Jones reagent (8 N) dropwise until the orange color persisted. The reaction was washed with H_2O (1 mL), and the solution was extracted with ether (2 × 3 mL). The combined organics were dried over $MgSO_4$, and the solvent was removed at reduced pressure. The crude acid was dissolved in ether (5 mL), and a solution of diazomethane (at 0.25 M in ether) was added dropwise until the yellow color persisted (ca. 4 mL). Excess diazomethane was purged with N_2, and the solvent was removed at reduced pressure. The crude product was subjected to analytical HPLC. Elution with 10% EA/hex afforded, after 7.5 min, 3.7 mg of plakorin (**1**), followed by 10.4 mg of (−)-*ent*-chondrillin (**2**) at 8.3 min. The total isolated yield of endoperoxides **1** and **2** was 14.1 mg (43%): *ent*-chondrillin $[\alpha]_D = -19$ ($c = 0.5$, CH_3OH); plakorin $[\alpha]_D = +26-29$ ($c = 0.2$, $CHCl_3$).

Synthesis of 17: 4-Docosyne-1,6-diol. To a solution of 4-pentyn-1-ol (3.36 g, 4.0 mmol) in THF (100 mL) at −78 °C was added *n*-BuLi (35.6 mL of a 2.25 M solution in hexane). After 30 min the solution was transferred via double-ended needle into a −78 °C solution of heptadecanal (8.77 g, 34.5 mmol) in THF (200 mL) and allowed to slowly warm to room temperature. After 12 h, the reaction was quenched with 5% aqueous HCl and extracted with ether (2 × 100 mL). The combined organic phases were dried with $MgSO_4$ and filtered through Celite. Evaporation of solvent produced a white solid (mp = 56−58 °C) which was subjected to flash chromatography (40% EA/hex) to give 8.81 g (75%) of diol: $R_f = 0.36$ (40% EA/hex); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.32 (tt, 1H, $J = 6.7, J = 1.7$), 3.74 (t, 2H, $J = 6.2$), 2.31 (td, 2H, $J = 6.9, J = 1.7$), 1.96 (b s, 2H), 1.79−1.70 (m, 2H), 1.68−1.6 (m, 2H), 1.43−1.38 (m, 2H), 1.24 (b s, 28H), 0.86 (t, $J = 6.2$); ^{13}C NMR (75 MHz) δ 84.5, 82.1, 62.7, 61.7, 38.2, 31.9, 31.2, 29.7−29.3, 25.2, 22.7, 15.9, 14.1; IR (KBr) 3386 cm^{-1}. Anal. Calcd for $C_{22}H_{42}O_2$: C, 78.05; H, 12.50. Found: C, 78.01; H, 12.54.

Methyl 6-Oxo-4-docosynoate (17). To a 0 °C solution of 4-docosyne-1,6-diol (5.21 g, 15.4 mmol) in acetone (200 mL) was dropwise added Jones reagent (8 *N*) until the orange color persisted. 2-Propanol was added to quench the remaining oxidant. Water was added, and the mixture was extracted three times with ether/hexane (4:1). After drying with $MgSO_4$, the combined organic layers were dried with $MgSO_4$ and filtered. After removal of solvent in vacuo, the product was redissolved in ether and treated with a solution of diazomethane (at 0.25 M in ether) until the yellow color persisted. Excess diazomethane was removed with a stream of nitrogen. Concentration afforded 5.12 g (97%) of **17** as an analytically pure white solid: mp = 45−47 °C; $R_f = 0.59$ (20% EA/hex); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.68 (s, 3H), 2.64−2.44 (m, 4H), 2.47 (t, 2H, $J = 7.6$), 1.65−1.55 (m, 2H), 1.21 (s, 26H), 0.84 (t, 3H, $J = 6.0$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 188.1, 171.5, 91.2, 81.0, 51.9, 45.4, 32.2, 31.9, 29.6−28.9, 24.0, 22.6, 14.7, 14.0; IR (KBr) 1729, 1679 cm^{-1}. Anal. Calcd for $C_{22}H_{42}O_2$: C, 75.78; H, 11.06. Found: C, 75.64; H, 11.08.

(*R*)-Methyl 6-Hydroxy-4-docosynoate (18). A solution of (*R*)-Alpine−borane (57.2 mL, 0.5 M in THF) was slowly added to **17** (5.21 g, 14.3 mmol). The resulting solution was stirred for 36 h. After removal of solvent in vacuo, the residue was diluted in ether (200 mL). Ethanolamine (1.72 mL, 28.6 mmol) was slowly added, producing a yellow precipitate which was removed by filtration through Celite. The filtrate was concentrated and directly subjected to flash chromatography to yield 4.44 g (85%) of **18** as a white solid: (mp = 53−56 °C); $R_f = 0.61$ (30% EA/hex); $[\alpha]_D = +1.8$ ($c = 1.15$, MeOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.30 (t, 1H, $J = 6.4$), 3.67 (s, 3H), 2.51 (s, 4H), 1.67−1.58 (m, 2H), 1.21 (s, 26H), 1.45−1.20 (m, 28H), 0.85 (t, 3H, $J = 6.2$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.3, 83.1, 82.2, 62.5, 51.7, 38.0, 33.3, 31.9, 29.6−29.3, 25.1, 22.6, 14.6, 14.0;

(39) Dussault, P.; Woller, K. *The Chemical Educator* **1996**, *1*, 1−6.

(40) Snider, B. B.; Shi, Z.; O'Neil, S. V.; Kreutter, K. D.; Arakaki, T. L. *J. Org. Chem.* **1994**, *59*, 1726−1729. This reference describes a method for performing the photochemical isomerization using a 350 nm light source in place of a sun lamp, which is no longer commercially available.

IR (KBr) 3325, 1737 cm^{-1}; HRMS (M − H) calcd 365.3045, found 365.3063.

(*R*)-Methyl 6-[(2*S*)-(−)-2-Methoxy-2-(trifluoromethyl)-phenylacetyl]docosynoate (19). To a solution of **18** (50 mg, 0.14 mmol) in CH_2Cl_2 was added (*S*)-(−)-α-methoxy-α-(trifluoromethyl)phenylacetic acid (32 mg, 0.14 mmol) followed by 4-(dimethylamino)pyridine (DMAP) (5 mg, 0.04 mmol). The solution was stirred at rt for 15 min and DCC (31 mg, 0.15 mmol) was added. The reaction mixture was stirred at RT for 18 h and directly subjected to column chromatography on silica gel (15% EA/hex) to give 53 mg (66%) of the desired Mosher ester with 89% ee by ^{19}F NMR: $R_f = 0.52$ (10% EA/hex); ^{19}F NMR (190 MHz, $CDCl_3$) δ −71.18 (minor), −72.38 (major); ^1H NMR (300 MHz, $CDCl_3$) δ 7.53−7.39 (m, 5H), 5.47 (t, 1H, J = 6.7), 3.67 (t, 2H, J = 6.1), 3.54 (s, 3H), 2.50 (s, 4H), 1.83−1.74 (m, 2H), 1.40−1.24 (28H), 0.87 (t, 3H, J = 6.9); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.0, 165.6, 132.0, 129.5, 128.3, 127.5, 85.1, 77.1, 66.8, 55.5, 51.7, 34.6, 33.0, 31.9, 29.6−29.3, 28.9, 25.0, 22.7, 14.6, 14.0; IR 1753 cm^{-1}.

(*R*)-Methyl 6-Hydroxy-4(*Z*)-docosenoate (20). A solution of **18** (7.11 g, 19.4 mmol), Pd/$CaCO_3$/Pb (290 mg), and quinoline (∼0.01 mL) in EA/hex (32%, 200 mL) was placed under a balloon of hydrogen, and the contents of the reaction flask were subjected to two vacuum purge cycles. After 24 h the reaction was vented and filtered through a silica gel/Celite plug. The filtrate was concentrated to give 6.90 g (97%) of **20** as a white solid (mp = 29−32 °C): $R_f = 0.61$ (30% EA/hex); $[\alpha]_D = +9.4$ (c = 1.15, MeOH); ^1H NMR (300 MHz, $CDCl_3$) δ 5.48−5.35 (m, 2H), 4.44 (dd, 1H, J = 6.9, 7.2), 3.65 (s, 3H), 2.64−2.21 (m, 4H), 1.85−1.75 (m, 2H), 1.64−1.20 (28H), 0.86 (t, 3H, J = 6.4); ^{13}C NMR (75 MHz) δ 173.7, 67.2, 51.7, 37.1, 33.6, 31.9, 29.7−29.7, 25.4, 22.9, 22.7, 14.1; IR (KBr) 3600, 3550, 1740 cm^{-1}.

***syn*-(5*R*,6*R*)-Methyl-5-hydroperoxy-6-hydroxy-3(*E*)-docosenoate (21).** A solution of **20** (2.20 g, 5.97 mmol) and TPP (37 mg, 0.06 mmol) in CCl_4 (60 mL) was cooled (−3 °C) in a jacketed Pyrex cell into which oxygen was bubbled. The solution was photolyzed (200 W) at a distance of 10 cm for 20 h. The reaction was stabilized with three drops of a BHT (0.10 M in CH_2Cl_2) solution and concentrated under vacuum. The concentrate was rapidly subjected to flash chromatography (30% EA/hex) to yield 1.64 g (69%) of **21**: $R_f = 0.33$ (30% EA/hex); ^1H NMR (300 MHz, $CDCl_3$) δ 5.88 (dt, 1H, J = 15.5, 7.2), 5.57 (dd, 1H, J = 15.7, 8.1), 4.14 (app t, 1H, J = 7.6), 3.65−3.63 (m, 4H), 3.10 (d, 2H, J = 6.9), 1.50−1.15 (m, 30H), 0.86 (t, 3H, J = 6.4); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.0, 129.8, 128.3, 89.3, 71.8, 51.9, 37.5, 32.7, 31.8, 29.6−29.3, 25.2, 14.0; IR (neat) 3397, 3324, 1751 cm^{-1} .

(3*R*,6*R*)-Methyl 3-Hydroperoxy-6-hydroxy-4(*E*)-docosenoate (22). A solution of **21** (1.30 g, 3.25 mmol), AIBN (0.10 g, 0.65 mmol), and *tert*-butyl hydroperoxide (13 mL of a 5 M solution in decane) in acetonitrile (650 mL) was heated to 70 °C for 22 h. The reaction was cooled and stabilized with several drops of BHT solution (0.10 M in CH_2Cl_2). The reaction was concentrated and directly subjected to flash chromatography (20% EA/hex) to afford 0.44 g of recovered **21** (34%) followed by 0.45 g (35%) of **22**: $R_f = 0.22$ (20% EA/hex); ^1H NMR (300 MHz, $CDCl_3$) δ 9.3 (br s, 1H), 5.82 (dd, 1H, J = 15.5, 6.4), 5.65 (dd, 1H, J = 15.7, 7.6), 4.77 (dd, 1H, J = 7.2, 6.0), 4.08 (app q, 1H, J = 6.4), 3.74 (s, 3H), 2.76 (dd, 1H, J = 15.3, 7.6), 2.54 (dd, 1H, J = 15.3, 6.0), 1.55−1.45 (m, 2H), 1.25−1.15 (m, 28H), 0.86 (t, 3H, J = 7.2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.2, 138.7.8, 127.3, 81.8, 72.2, 52.0, 38.0, 36.9, 31.9, 29.7−29.4, 25.3, 14.0; IR (neat) 3397, 3367, 1748 cm^{-1}.

(3*R*,6*R*)-Methyl 3-(1-Methyl-1-methoxyethyldioxy)-6-hydroxy-4(*E*)-docosenoate (23). To a solution of **22** (510 mg, 1.27 mmol) and 2-methoxypropene (0.12 mL, 1.27 mmol) in CH_2Cl_2 (25 mL) was added PPTS (32 mg, 0.13 mmol). After 4 h, the reaction was extracted with water. The separated organic layer was dried ($MgSO_4$) and stabilized with three drops of a solution of BHT (0.10 M in CH_2Cl_2). Concentration afforded 504 mg (84%) of **23**: $R_f = 0.46$ (20% EA/hex); ^1H NMR (300 MHz, $CDCl_3$) δ 5.80 (dd, 1H, J = 15.7, 6.2), 5.66 (dd, 1H, J = 15.7, 7.2), 4.87 (dd, 1H, J = 6.9, 6.7), 4.10 (m, 1H), 3.74 (s, 3H), 3.28 (s, 3H), 2.81 (dd, 1H, J = 15.0, 6.9), 2.50 (dd, 1H, J = 15.0, 6.2), 1.38 (s, 6H) 1.36−1.10 (m, 30H), 0.86 (t, 3H, J = 7.2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.8, 137.5, 127.3, 104.8, 80.2, 72.1, 51.7, 49.3, 38.6, 37.0, 31.9, 29.6−29.3, 25.2, 22.6, 14.0; IR (neat) 3494, 3465, 3324, 1743 cm^{-1}; HRMS (M + Na) calcd 495.3653, found 495.3662.

Synthesis of 1 and *ent*-2: (3*R*)-Methyl 3-(1-Methyl-1-methoxyethyldioxy)-6-oxo-4(*E*)-docosenoate. To a solution of **23** (200 mg, 0.42 mmol) in CH_2Cl_2 (8 mL) was added PDC (0.64 g, 1.69 mmol). After 8 h the solution was filtered through Celite/silica gel. The filtrate was concentrated under reduced pressure to yield 0.16 g (82%) of peroxyenone as an unstable oil which was directly subjected to deprotection and cyclization: $R_f = 0.47$ (20% EA/hex); ^1H NMR (300 MHz, $CDCl_3$) δ 6.70 (dd, 1H, J = 16.0, 6.0), 6.27 (d, 1H, J = 16.2), 5.0 (app q, 1H, J = 7.2, 6.2), 3.65 (s, 1H), 3.23 (s, 3H), 2.73 (dd, 1H, J = 16.0, 7.4), 2.50 (m, 3H), 1.60−1.55 (m, 2H), 1.35 (s, 6H), 1.36−1.10 (m, 30H), 0.86 (t, 3H, J = 6.7); ^{13}C NMR (75 MHz, $CDCl_3$) δ 200.0, 170.0, 141.7, 130.8, 105.1, 79.0, 51.8, 49.2, 40.6, 37.7, 31.8, 59.6−29.1, 23.9, 22.6, 13.9.

Chondrillin (1) and *ent*-Plakorin (*ent*-2). A solution of (3*R*,4*E*)-methyl 3-(1-methyl-1-methoxyethyldioxy)-6-oxo-4-docosenoate (260 mg, 0.55 mmol) in 4:3 CH_2Cl_2/MeOH (14 mL) was stirred with *p*-toluenesulfonic acid monohydrate (TsOH·H_2O) (48 mg, 0.25 mmol) for 5 min, whereafter the solution was irradiated (sunlamp) for 2 h at a distance of 20 cm.[40] After irradiation was terminated, a second portion of TsOH·H_2O (30 mg, 0.16 mmol) was added and the solution was stirred for an additional 10 h. The organic layer was washed with water, and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were dried and concentrated. Flash chromatography furnished 118 mg (52%) of a 1:1 mixture of chondrillin and *ent*-plakorin. Chondrillin was purified by analytical HPLC (7.5% EA/hex). The rotation for chondrillin was determined to be $[\alpha]_D = +30-33$ (c = 1.6, MeOH). Chondrillin (**1**): $R_f = 0.60$ (20% EA/hex); ^1H NMR (300 MHz, $CDCl_3$) δ 6.17 (dd, 1H, J = 10.3, 4.3), 5.86 (dd, 1H, J = 10.0, 1.7), 4.82−4.75 (m, 1H), 3.73 (s, 1H), 3.40 (s, 3H), 2.93 (dd, 1H, J = 16.0, 7.9), 2.60 (dd, 1H, J = 16.2, 5.5), 1.68−1.60 (m, 2H), 1.36−1.20 (s, 30H), 0.86 (t, 3H, J = 6.9); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.9, 130.3, 126.4, 100.5, 73.7, 52.0, 51.0, 37.2, 34.2, 31.9, 29.8−29.4, 23.5, 22.7, 14.1.

The rotation for *ent*-plakorin (*ent*-2) was determined to be $[\alpha]_D = -28-30$ (c = 0.35, CH_2Cl_2): $R_f = 0.62$ (20% EA/hex); ^1H NMR (500 MHz, $CDCl_3$) δ 6.10 (dd, 1H, J = 10.1, 1.2), 5.83 (dd, 1H, J = 10.0, 2.0), 5.0−4.98 (m, 1H), 3.71 (s, 1H), 3.40 (s, 3H), 2.60 (dd, 1H, J = 16.0, 7.4), 2.49 (dd, 1H, J = 16.0, 6.4), 1.69−1.60 (m, 2H) 1.36−1.20 (s, 30H), 0.86 (t, 3H, J = 6.7); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.0, 130.3, 126.9, 101.1, 73.5, 52.1, 51.3, 36.3, 34.7, 31.9, 29.8−29.4, 23.3, 22.7, 14.1.

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Supporting Information Available: ^1H and ^{13}C NMR spectra for compunds **1**−**23**. This material is available free of charge via the Internet at http://pubs.acs.org.

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