Table I. Rate Constants (k_H)[a] for Hydrogen Atom Transfer Reactions

H atom donor	$^3Pt_2$*	t-BuO•	t-Bu•
Et_3SiH	2.0×10^4	5.7×10^6 [b]	
Ph_3SiH	1.6×10^5	1.1×10^7 [b]	
Ph_3GeH	2.9×10^7	8.9×10^7 [b]	
Ph_3SnH	1.0×10^8	4.0×10^8 [b]	3.1×10^6 [d]
Bu_3SnH	1.2×10^7	2.2×10^8 [c]	7.4×10^5 [d]
Bu_3SnD	6.9×10^6	1.8×10^8 [c]	2.7×10^5 [d]

[a] Rate constants in M^{-1} s^{-1}. Values for $^3Pt_2$* measured in acetonitrile at 298 K, t-BuO• reactions studied in 1:2 (v/v) benzene/t-Bu_2O_2. [b] Chatgilialoglu, C.; Ingold, K. U.; Lusztyk, I.; Nazran, A. S.; Scaiano, J. C. *Organometallics* **1983**, *2*, 1332-1335. T = 300 K. [c] Scaiano, J. C. *J. Am. Chem. Soc.* **1980**, *102*, 5399-5400. T = 295 K. [d] Carlsson, D. J.; Ingold, K. U. *J. Am. Chem. Soc.* **1968**, *90*, 7047-7055. T = 298 K in benzene.

Table II. Hydrogen Atom Transfer from Bu_3SnH to Electronically Excited Acceptors

acceptor	excited state	E_T[a]	k_H[c]
acetone	$n\pi^*$	78	2×10^8 [d,g]
benzophenone	$n\pi^*$	69	4.7×10^7 [e,g]
2-acetylnaphthalene	$\pi\pi^*$	58	2.0×10^6 [e,g]
Pt_2	$d\sigma^*p\sigma$	57.7[b]	1.2×10^7 [f]
1-naphthaldehyde	$\pi\pi^*$	56.4	1.1×10^6 [e,g]
biacetyl	$n\pi^*$	55	1.5×10^7 [e,g]

[a] Triplet energies in kcal mol^{-1}; data from ref 13, p 290, and from: Murov, S. L. *Handbook of Photochemistry*; Marcel Dekker: New York, 1973; pp 3-21. [b] Heuer, W. B.; Totten, M. D.; Rodman, G. S.; Hebert, E. J.; Tracy, H. J.; Nagle, J. K. *J. Am. Chem. Soc.* **1984**, *106*, 1163-1164. [c] Rate constants in M^{-1} s^{-1} measured at room temperature. [d] In *n*-hexane. [e] In benzene. [f] In acetonitrile. [g] Reference 14, p 93.

$^3Pt_2$* faster than the trialkyls, which is analogous to rates found with both *tert*-butoxy and *tert*-butyl radicals (Table I).

The kinetic isotope effect measured for the reaction of $^3Pt_2$* with Bu_3SnH, $k_2(H)/k_2(D) = 1.7$, is in accord[10] with H atom transfer involving a linear Pt-H-Sn transition state with negligible charge transfer.[12-14] This value lies between those found for the reaction of Bu_3SnH with alkyl[15] (2.3 for Me• and *n*-Bu•, 1.9 for Et•) and t-BuO• radicals (1.2, Table I). Relative to the zero-point energy value,[10] the isotope effect is only slightly lower for the H atom transfer to $^3Pt_2$* from Bu_3SnH than from the α-(C-H) bond in $PhCH(OH)CH_3$ (4.7).[16]

Interestingly, the rate constants for H atom transfer are at least 2 orders of magnitude lower than those for electron transfer[3,17] at comparable driving forces.[18] A severe orientation requirement related to the formation of a linear Pt-H-E transition state is the likely explanation of this difference.

Rate constants for H atom transfer from Bu_3SnH to different excited triplet acceptors are set out in Table II. It is interesting that the reactivity of $^3Pt_2$* toward Bu_3SnH is comparable to that of the $n\pi^*$ excited states of ketones with similar triplet energies, being greater than that of $\pi\pi^*$ excited states of organic carbonyls. All d^8-d^8 complexes possess two open axial coordination sites. Excitation of Pt_2 strongly activates these sites, producing a highly energetic (E_T = 57.7 kcal mol^{-1}) species with an unpaired electron in an axially localized $d\sigma$-antibonding orbital. It would appear that this localized $d\sigma^*$ electron plays the same role in the reactivity of $^3Pt_2$* as a nonbonding, oxo-localized electron does in the chemistry[13,14] of excited organic carbonyls.

Acknowledgment. We thank N. J. Turro and D. C. Smith for helpful comments. This research was supported by National Science Foundation Grant CHE84-19828.

(9) Armitage, D. A.; Riviere, P.; Riviere-Baudet, M.; Satge, J.; Davies, A. G.; Smith, P. J. In *Comprehensive Organometallic Chemistry*; Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds.; Pergamon Press: Oxford, 1982; Vol. 2, pp 1-203, 399-627.

(10) Taking into account the low Sn-H force constant in R_3SnH species ($\bar{\nu}$(Sn-H) = 1837 cm^{-1} in $(CH_3)_3SnH$[11], $k_f \approx 2 \times 10^2$ N m^{-1}), the value of the zero-point energy isotope effect for Sn-H bond breaking may be estimated[12] as 3.6; this is much smaller than the analogous value for a typical C-H bond (6.9). The observed isotope effect is quite large, as it accounts for about 47% of the zero-point energy value.

(11) Nakamoto, K. *Infrared and Raman Spectra of Inorganic and Coordination Compounds*, 3rd ed.; Wiley: New York, 1978; pp 380-381.

(12) Melander, L.; Saunders, W. H., Jr. *Reaction Rates of Isotopic Molecules*: Wiley: New York, 1980; pp 4-45, 129-170.

(13) Turro, N. J. *Modern Molecular Photochemistry*; Benjamin/Cummings: Menlo Park, CA, 1978; pp 363-385.

(14) Scaiano, J. C. *J. Photochem.* **1973/1974**, *2*, 81-118.

(15) Chatgilialoglu, C.; Ingold, K. U.; Scaiano, J. C. *J. Am. Chem. Soc.* **1981**, *103*, 7739-7742.

(16) Harvey, E. L.; Gray, H. B., unpublished results.

(17) Peterson, J. R.; Kalyanasundaram, K. *J. Phys. Chem.* **1985**, *89*, 2486-2492.

(18) Assuming a Pt_2-H dissociation energy of 60 kcal mol^{-1} (Pearson, R. G. *Chem. Rev.* **1985**, *85*, 41-49), the driving force for H atom transfer is roughly estimated to be ($60 - D_{EH} + E_T$) $\geq$30 kcal mol^{-1}.

Total Synthesis and Absolute Configuration of 7,20-Diisocyanoadociane

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7,20-Diisocyanoadociane (**1** or mirror image), a marine natural product from *Adocia* sp.,[1] is noteworthy in terms of structure, unprecedented biosynthesis,[1,2] and key position in a growing class of diterpenoid isocyanides.[3] The synthesis of **1** has been a conspicuous problem which has been taken as a challenge by a number of research groups. Reported herein is the first synthesis of this interesting perhydropyrene by an enantioselective route which permits assignment of the absolute configuration indicated in **1**.[4]

The acid chloride **2**, readily available in two steps from (1*R*, 2*S*, 5*R*)-(-)-menthol and glutaric anhydride (heating at 90 °C for 10 h followed by reaction with oxalyl chloride in benzene at 23 °C, 75% overall), was converted into vinyl ketone **3** (1.1 equiv of vinyltri-*n*-butylstannane in tetrahydrofuran (THF) with 0.34 mol % of $Pd(PPh_3)_4$ at 70 °C for 2 h, 90% yield).[5,6] Enone **3** was transformed into the corresponding ethylene ketal (90% overall yield) by a new method consisting of two steps: (1) treatment of a 1 M solution of **3** in $CHCl_2$ with (phenylseleno)trimethylsilane[7] (1.3 equiv), ethylene glycol (5 equiv), and I_2 (0.025 equiv) at 65 °C for 4 h to form the β-(phenylseleno) ethylene ketal (99%); (2) oxidation of selenide to selenoxide (1.5 equiv of *m*-chloroperbenzoic acid in CH_2Cl_2 at -20 °C for 15 min) followed by addition of dimethyl sulfide (0.8 equiv) and diisopropylamine (3 equiv) and warming to 60 °C to effect elimination (6.5 h at 60 °C), and finally gradient elution chromatography on silica gel (sg)(hexane–ether). Attempts to prepare this ketal by conventional acid-catalyzed direct ketalization were not successful.

The conversion of the ethylene ketal of **3** to diester **4** depended on new methodology for enantioselective and diastereoselective Michael addition which has recently been reported.[8] The ester enolate of the ketal **3** was generated at -78 °C in THF using 1.1 equiv of lithium diisopropylamide (LDA) for 45 min, methyl crotonate (1.1 equiv, *E* isomer) was added, the reaction mixture was quenched (HOAc) after 1 h at -78 °C, and the product was isolated by extractive workup and sg flash chromatography. The major Michael adduct (80% yield) was, as expected, the desired threo isomer **4** (threo/erythro ratio 8:1, ca. 60% ee).[8,9] Removal

(1) Baker, J. T.; Wells, R. J.; Oberhänsli, W. E.; Hawes, G. B. *J. Am. Chem. Soc.* **1976**, *98*, 4010.

(2) Garson, M. J. *J. Chem. Soc., Chem. Commun.* **1986**, 35.

(3) (a) Kazlauskas, R.; Murphy, P. T.; Wells, R. J.; Blount, J. F. *Tetrahedron Lett.* **1980**, *21*, 315. (b) Faulkner, D. J. *Tetrahedron* **1977**, *33*, 1421. (c) Faulkner, D. J. *Nat. Prod. Rep.* **1984**, *1*, 551.

(4) The original X-ray crystallographic determination of structure[1] did not allow assignment of absolute configuration.

(5) (a) Kosugi, M.; Shimizu, Y.; Migita, T. *Chem. Lett.* **1977**, 1423. (b) The reaction byproduct, Bu_3SnCl, was removed by washing an ether extract with 50% aqueous KF solution.

(6) All reactions involving air-sensitive materials were conducted under an inert (N_2 or Ar) atmosphere.

(7) Detty, M. R.; Seidler, M. D. *J. Org. Chem.* **1981**, *46*, 1283.

(8) Corey, E. J.; Peterson, R. T. *Tetrahedron Lett.* **1985**, *26*, 5025.

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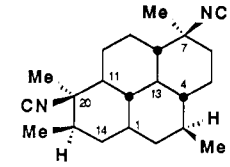

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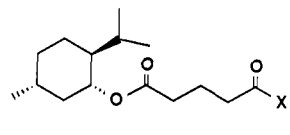
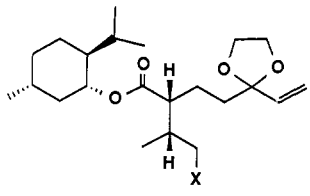
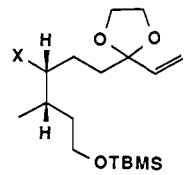


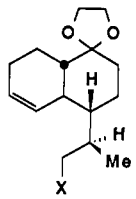
2 X = Cl
3 X = CH=CH$_2$

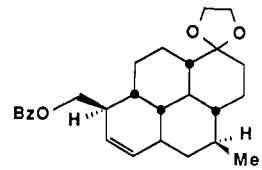


4 X = CO$_2$Me
5 X = CH$_2$OH
6 X = CH$_2$OTBMS



7 X = CH$_2$OH
8 X = CHO
9 X =





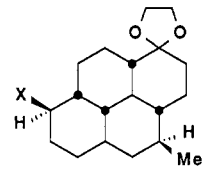
10 X = CH$_2$OTBMS
11 X = CHO
12 X = EtO$_2$C
13 X = HOCH$_2$ 
14 X = BzOCH$_2$ 

15

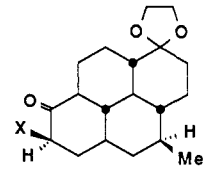
of the minor amount of erythro contaminent was most easily accomplished chromatographically at a later stage (compound **12**). Although higher enantioselectivity can be achieved using the phenmenthol controller group,[8] the menthol controller was selected for initial studies because it is relatively cheap and because the level of enantioselectivity is sufficiently high with menthol to allow unambiguous assignment of absolute configuration to the final product. Diester **4** was transformed into **6** (85% overall) by the following sequence: (1) reduction with $NaAl(CH_3OCH_2CH_2O)_2H_2$ (2.3 equiv) in ether at −40 °C for 1.5 h and (2) silylation with *tert*-butyldimethylchlorosilane (TBMS chloride) (1.05 equiv), triethylamine (1.2 equiv), and 4-(dimethylamino)-pyridine (0.4 equiv) in CH_2Cl_2 at 23 °C for 30 min. Conversion of **6** to the *E*-diene **9** was affected by the following sequence: (1) reduction to **7** (0.4 M $LiAlH_4$ in ether at 23 °C for 1.5 h, 90%); (2) oxidation of **7** to **8** (3 equiv of pyridinium dichromate (PDC) and 4A molecular sieves in CH_2Cl_2 at 23 °C for 30 min); and (3) Wittig coupling[10] of **8** with methylallyldiphenylphosphonium bromide (1.2 equiv) and KO-*t*-Bu (1.1 equiv) in THF at 0 °C for 45 min to give **9** (75% from **7**). Diene **9** underwent stereospecific internal Diels–Alder addition upon heating in toluene at 150 °C for 20 h to give the trans-fused adduct **10** in 90% yield.[11]

Desilylation of **10** (Bu_4NF, THF, 23 °C, 1.5 h) and oxidation with PDC (as for **8**) yielded **11** (82%) which upon treatment with triethyl lithio-4-phosphono-*E*-crotonate (Aldrich Co.) in THF at −78 °C initially and −78 to 23 °C over 1 h gave after chromatography on a 15-μm sg column (Yamamura Co.) (97:3 hexane-THF) pure *E,E*-diene ester **12** (70%). Reduction of **12** (2.2 equiv of diisobutylaluminum hydride in toluene at −20 °C for 10 min) gave **13** which was etherified (4 equiv of NaH, 1.4 equiv of benzyl bromide in dimethyl sulfoxide at 23 °C for 30 min) to afford *E,E*-diene benzyl ether **14** (89%).

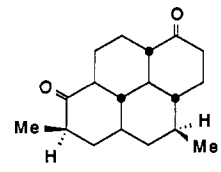
When **14** was heated in toluene solution (0.04 M) at 185 °C for 36 h internal Diels–Alder reaction occurred to give after sg chromatography (Waters Prep-500 instrument) 54% yield of the desired adduct **15**, along with 36% of a diastereomeric adduct arising from addition to the opposite face of the dienophilic bond.[12] Although evidence was obtained that this ratio could be improved by changing the terminal diene substituent this option has not yet been pursued. Hydrogenation of **15** (1 atm of H_2, Pd–C, ethanol, 23 °C, 4.5 h) produced **16**, $[\alpha]^{23}_D$ +11.9° (*c* 1.3, $CHCl_3$), mp 109–110 °C (80%), which was oxidized (PDC, as for **8**, 80%) to aldehyde **17**, $[\alpha]^{23}_D$ +15.7° (*c* 1.2, $CHCl_3$), mp 89–91 °C.



16 X = CH$_2$OH
17 X = CHO



18 X = H
19 X = Me



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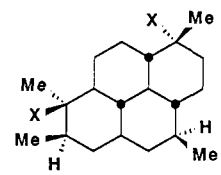

21 X = OH
22 X = OCOCF$_3$

Treatment of **17** with excess pyrrolidine in benzene at reflux (tosic acid as catalyst) for 10 h provided the corresponding enamine (90%) which underwent C=C cleavage to the corresponding nor ketone upon reaction with ruthenium tetroxide in CCl_4 at 0 °C for 5 min.[13] Addition to this ketone to a 1 M solution of sodium methoxide in methanol at 23 °C caused rapid (<2 min) epimerization to the more stable all trans-fused ketone **18**, $[\alpha]^{23}_D$ +12.3° (*c* 2.5, $CHCl_3$), mp 114–115 °C (75% yield). Reaction of **18** with 1.05 equiv of LDA (−78 °C, 15 min) followed by 5 equiv of methyl iodide (−78 to 23 °C over 20 min) produced a mixture of axial and equatorial α-methyl ketones (ratio 6:1, respectively) which upon treatment with 0.5 M sodium methoxide in 1:1 THF–methanol at 23 °C for 12 h gave in 90% yield the more stable epimer **19**, $[\alpha]^{23}_D$ +8.5° (*c* 2.6, $CHCl_3$), mp 168–170 °C. Keto ketal **19** was deketalized by exposure to 0.5 M HCl in 50% aqueous acetone to afford (>99%) **20**, $[\alpha]^{23}_D$ +7.5° (*c* 2.5, $CHCl_3$), mp 137–140 °C. Reaction of **20** with 4.8 equiv of methyllithium and 5 equiv of $CeCl_3$ in THF at −78 to −60 °C (1.5 h) and −60 to 0 °C (0.5 h) gave 92% yield of mainly the diaxial diol **21** which upon esterification with 3 equiv of trifluoroacetic anhydride and 5 equiv of pyridine (CH_2Cl_2, 0 °C, 20 min) provided bistrifluoroacetate **22** (95%).

The last step of the synthesis, introduction of the two isocyanide groups, was accomplished in a single biomimetic operation.[2] Thus,

(9) Analysis of the mixture containing **4** was carried out after conversion to the corresponding benzyl ester (by saponification followed by esterification with phenyldiazomethane) using HPLC on a silica (Du Pont Zorbax B 5830) column with 96:4 hexane–*tert*-butyl methyl ether. Elution times for the isomeric components were 7.1 min (erythro a, 9%), 10.1 min (erythro b, 2%), 21.2 min (*ent*-**4**, 17%), and 22.3 min (**4**, 72%). The assignments which are firmly based on previous work[8] were confirmed by the successful conversion of **4** to **1** (a proof of threo stereochemistry).

(10) Vedejs, E.; Fang, H. W. *J. Org. Chem.* **1984**, *49*, 210.

(11) In contrast free enone corresponding to ketal **9** undergoes internal Diels–Alder addition rapidly at 23 °C or below to form only the cis-fused adduct. The preference for trans specificity in the reaction **9** → **10** is likely due to steric interactions of the ketal unit which disfavor endo relative to exo addition. See also: Remizeuski, S. W.; Stouch, T. R.; Weinreb, S. *Tetrahedron* **1985**, *41*, 1173.

(12) The assignment of configuration to **15** follows clearly from its further conversion to the all-trans-fused ketone **18** (vide infra). The diastereomeric Diels–Alder product was transformed in a similar way to an α,β-cis-fused diastereomer of **18** which did not isomerize upon vigorous base treatment.

(13) Desai, M. C.; Chawla, H. P. S.; Dev, S. *Tetrahedron* **1982**, *38*, 379.

reaction of **22** with 15 equiv of trimethylsilyl cyanide (Aldrich Co.) and 20 equiv of titanium tetrachloride[14] (both freshly distilled) in CH_2Cl_2 at 23 °C for 3.5 h produced a mixture of four diastereomeric isocyanides (70% total yield) which were separated by thin-layer sg chromatography into the following components: diaxial diisocyanide (30%, least polar), diequatorial diisocyanide (15%, most polar), and a mixture of axial–equatorial diisocyanides (55%, intermediate polarity). The two axial–equatorial diisocyanides were separated by HPLC on a Waters Co. 5-μm spherical silica column using 96:4 hexane–*tert*-butyl methyl ether to give 7,20-diisocyanoadociane (**1**) and the less polar 7,20-bis-epi-diisocyanoadociane. Synthetic **1** so obtained was identical with authentic samples[15] by HPLC, sg TLC, 500-MHz ^{1}H NMR, infrared, and mass spectral comparison. The synthetic material had $[\alpha]^{23}_D$ +23.0° (*c* 0.27, $CHCl_3$) as compared to $[\alpha]^{23}_D$ +47.8° (*c* 0.23, $CHCl_3$) measured for the reference sample of naturally derived 7,20-diisocyanoadociane, a result in accord with the observed ca. 60% enantiomeric excess determined for the Michael product **4**, the first chiral intermediate. Since the absolute configuration of **4** (excess enantiomer) follows from the method of synthesis, the previously unknown absolute configuration of natural 7,20-diisocyanoadociane can now be defined as in **1**.

The simultaneous introduction of the two isocyano groups in this synthesis of **1** has the advantage of shortening the pathway of synthesis and also making available the various diastereomers of **1** as reference compounds. It is possible to adjust the synthetic scheme for separate introduction of the isocyanide groups with control of stereochemistry, such methodology having been developed in these laboratories.[16,17]

Supplementary Material Available: ^{1}H NMR, IR, UV, and mass spectral data for compounds **1**–**22** and for the 7,20-diastereomers of **1** (10 pages). Ordering information is given on any current masthead page.

(14) Sasaki, et al. (Sasaki, T.; Nakanishi, A.; Ohno, M. *J. Org. Chem.* **1981**, *46*, 5445) report a similar conversion of adamantyl chloride to the corresponding isocyanide.

(15) We are grateful to Drs. R. J. Wells and M. J. Garson for generously providing reference samples of native 7,20-diisocyanoadociane.

(16) Unpublished work of M. Ishiguro and A. Ghosh.

(17) This research was assisted financially by a grant from the National Science Foundation.

Intermediacy of 8-(*R*)-HPETE in the Conversion of Arachidonic Acid to Pre-Clavulone A by *Clavularia viridis*. Implications for the Biosynthesis of Marine Prostanoids

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Among the most surprising developments in the field of organic natural products in recent years was the discovery that a marine organism, the soft coral *Plexaura homomalla*, produces large amounts (ca. 1.8% of dry weight) of prostaglandin A_2 methyl ester acetate (**1**) or the 15-epimer (depending on subspecies).[1] Also unexpected was the finding that the biosynthesis of this substance in coral proceeds by a pathway which differs from that for formation of prostaglandins (PG's) in mammals (endoperoxide pathway).[2] Because of severe practical difficulties associated with biosynthetic research using *Plexaura homomalla*, progress in defining the biosynthetic pathway has been slow.[3] Recently, however, another family of prostanoids, the clavulones (exemplified by clavulone I, **2**), has been identified from the Okinawan soft coral *Clavularia viridis*,[4] which has proved to be much more amenable to biosynthetic studies.[5] It was shown by radiotracer experiments that a homogenate of *C. viridis* is able to convert arachidonic acid to a new eicosanoid, **3** (termed pre-clavulone A), which seems likely to be an intermediate on the pathway to **2**.[5] Because of the structural similarity of **3** and the plant regulator *cis*-jasmonic acid, it was suggested that the biosyntheses of these substances may be closely related and may involve pericyclic ring closure of a 2-oxidopentadienyl cation.[6] Strong evidence for this surmise is reported herein. A logical possibility for the biosynthesis of PGA_2 methyl ester acetate in *P. homomalla* is now apparent.

Incubation of arachidonic acid (2–3 mM) with an acetone powder[7] from *C. viridis* (7 mg/mL) for 1 h at 24 °C in 100 mM Tris buffer at pH 8.0 provided a more polar compound determined to be 8(*R*)-hydroperoxy-5,11,14(*Z*),9(*E*)-eicosatetraenoic acid (8(*R*)-HPETE),[8] in yields as high at 19% (remainder mainly arachidonic acid). Identification was made by comparison with authentic samples of (±)-8-HPETE[9] and, following reduction, of (±)-8-HETE (HPLC, IR, ^{1}H NMR, MS), and determination of absolute configuration.[10]

Neither arachidonic acid nor 8-HPETE was converted by acetone powder[7] or homogenate preparations[5,11] from *C. viridis*

(1) (a) Weinheimer, A. J.; Spraggins, R. L. *Tetrahedron Lett.* **1969**, 5185. (b) Schneider, W. P.; Hamilton, R. D.; Rhuland, C. E. *J. Am. Chem. Soc.* **1972**, *94*, 2122.

(2) (a) Corey, E. J.; Washburn, W. N.; Chen, J. C. *J. Am. Chem. Soc.* **1973**, *95*, 2054. (b) Corey, E. J.; Washburn, W. N. *Ibid.* **1974**, *96*, 934. (c) Corey, E. J.; Ensley, H. E.; Hamberg, M.; Samuelsson, B. *Chem. Commun.* **1975**, 277.

(3) These difficulties include, in addition to the obvious geographical problems, the extreme instabilty of enzyme preparations from *P. homomalla* and the self degradation of this coral even at −78 °C.

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(5) Corey, E. J.; Lansbury, P. T. Jr.; Yamada, Y. *Tetrahedron Lett.* **1985**, *26*, 4171. The absolute configuration of pre-clavulone A has not been established; it may be either **3** or the mirror image.

(6) (a) Vick, B. A.; Zimmerman, D. C. *Biochem. Biophys. Res. Commun.* **1983**, *111*, 470. (b) Vick, B. A.; Feng, P.; Zimmerman, D. C. *Lipids* **1980**, *15*, 468.

(7) The coral was collected off Ishigaki Island and kept at −78 °C until use. An acetone powder was prepared by homogenizing ca. 5 g of frozen coral in 250 mL of acetone at −20 °C. The milky suspension was decanted from residual skeletal matter and filtered with suction. The resulting off-white powder was washed with acetone and ether, then air dried, and used immediately. A sample of the acetone powder which was stored overnight at −20 °C was completely inactive.

(8) Recently it has been reported that arachidonic acid is converted to 8(*R*)-HPETE in the gorgonian coral *Pseudoplexaura porosa*: Bundy, G. L.; Nidy, E. G.; Epps, D. E.; Mizsak, S. A.; Wnuk, R. J., *J. Biol. Chem.* **1986**, *261*, 747.

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(10) The absolute configuration of 8-HPETE was determined by correlation with (*S*)-malic acid by the following sequence: (1) conversion to 8-HPETE methyl ester (CH_2N_2 in ether); (2) reduction (trimethyl phosphite in benzene at 25 °C for 10 min); (3) esterification with (−)-menthyl chloroformate in pyridine–methylene chloride containing 4-(dimethylamino)pyridine; (4) ozonolysis (O_3, CH_2Cl_2, −78 °C, 5 min) followed by oxidative treatment with peroxyacetic acid for 18 h at 20 °C; (5) esterification (CH_2N_2 in ether). The resulting *O*-menthyl carbonate derivative of methyl malate was compared by gas chromatography[8] with authentic standards prepared from (*S*)-malic acid and racemic malic acid. The coral-derived compound coeluted with the slower *R* standard indicating that the 8-HPETE from coral possesses the *R* configuration.

(11) A homogenate of *C. viridis* was prepared by blending ca. 5 g of frozen coral in 75 mL of 100 mM Tris buffer, pH 8.0, in a Waring blender for 1 min. at ca. 5 °C. The tan supernatant was used directly.

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