complexes using phenyl substituents on the tellurolate gave, as soluble products, lanthanide complexes which retained alkali-metal halide salts. In addition, insoluble materials often formed which probably consist of higher order clusters, oligomers, or polymers.[2c,10] The use of 2,4,6-trisubstituted aryl substituents enabled isolation of soluble complexes (eq 1). The potassium salts of the aryl tellurolates react much more cleanly than do the analogous lithium salts because lithium halides tend to coordinate to the lanthanide products more readily, a feature commonly observed in organolanthanide chemistry.[11] The potassium salt of mesityl tellurolate can be prepared by the metathesis reaction of LiTeMes[12] with potassium *tert*-butoxide or by the recently reported reduction of the ditelluride[13] with potassium tris(*sec*-butyl)borohydride.[14] Solvent-free KTeMes can be isolated by drying under vacuum.[15]

The ytterbium(II) complex of this ligand is extremely air-sensitive and soluble in toluene, dimethoxyethane, and THF. The complex is crystallized in 85% yield from a cooled solution of toluene and THF as orange crystals and is found to be diamagnetic by magnetic susceptibility measurements made on a Gouy balance, becoming paramagnetic upon exposure to air. Elemental analysis confirmed that both tellurolate ligands substituted onto the complex, for a Yb:Te ratio of 1:2, with no halogens detected, was obtained.[8]

The complex was further characterized by ^{125}Te and ^{171}Yb NMR.[16] The ^{125}Te spectrum, in d_8-THF (Figure 1a), showed a single resonance at −270 ppm, shifted 26 ppm downfield from the resonance of KTeMes. The ^{171}Yb nucleus has a single resonance, which can be observed (Figure 1b) at +526 ppm. Both resonances are somewhat broad ($\Delta w_{1/2}$ = 60–125 Hz), possibly due, in the ^{125}Te case, to unresolved coupling to ytterbium [^{173}Yb nucleus (16% abundant, $I = {}^5/_2$) and ^{171}Yb nucleus (14% abundant, $I = {}^1/_2$)] or to rapid ligand or solvent exchange occurring in solution at room temperature. Low-temperature NMR studies on the diglyme adduct of this Yb(II) complex show that solvent exchange may be occurring, but no ligand exchange via tellurolates bridging to form dimer or cluster species[2b,18] is evident even at −60 °C. The simplicity of all the NMR spectra,[8] as well as the lack of tellurolate ligand exchange seen at low temperature, suggests a monomeric structure for these complexes.

Complexes can be similarly synthesized using Sm(II) and Eu(II), which are paramagnetic in the divalent state, as well as complexes of analogous selenolate ligands.[19] The complex Sm(TeMes)$_2$THF$_2$ (**2**) is isolated in approximately 67% yield as dark green crystals.[20] Elemental analysis confirms the formulation of complete substitution of the halide anions by the tellurolate ligands. These samarium tellurolate and selenolate compounds have magnetic moments of approximately 3.1 μ_B, consistent with Sm(II).[21] The selenolate complexes can be prepared but are not as soluble as the tellurolate congeners.[19]

Preliminary results on the thermal decomposition of these divalent lanthanide complexes suggest that they possess the correct stoichiometry to act as precursors to rare earth monochalcogenides. Pyrolysis of the Yb(II) complex occurs in refluxing toluene or at 250–300 °C in vacuo to produce a black insoluble char[22a] and releases volatile organotelluride byproducts. The byproducts, studied by ^{125}Te NMR, display a resonance at +253 ppm in d_6-benzene corresponding to dimesityl monotelluride (TeMes$_2$).[13] The formation of TeMes$_2$ as the major pyrolysis byproduct is expected upon deposition of LnTe from these divalent complexes (eq 2), and analogous species have been observed in the pyrolytic decomposition of precursors to other metal chalcogenides.[2a] Annealing the char obtained from low-temperature pyrolysis of **1** at 900 °C for 24 h under argon yields a crystalline powder containing YbTe as seen by its X-ray powder diffraction pattern.[22b] These data suggest that decomposition to lanthanide tellurides is proceeding at low temperatures.

$$\mathrm{Ln(TeMes)_2THF_{2-3}} \xrightarrow{\Delta} \mathrm{LnTe} + \mathrm{TeMes_2} \qquad (2)$$

This method utilizing molecular precursors and milder reaction conditions appears promising in the preparation of rare earth monochalcogenides. It affords the advantages of purification of the soluble precursors by conventional organometallic techniques prior to thermal decomposition and an oxygen-free, lower-temperature pyrolysis. The synthesis of the precursor complexes, the first divalent lanthanide complexes of the lower chalcogenide ligands, adds a new class of compounds to those known for lanthanides in this lower oxidation state. Further studies utilizing higher temperatures following deposition of rare earth monochalcogenides to determine crystallinity of the phases obtained from these organometallic precursors are continuing.

Acknowledgment. We thank Dr. Alan Benesi of Pennsylvania State University for his advice in obtaining multinuclear NMR spectra. A.R.S thanks the Shell Oil Foundation for a graduate fellowship. We also thank Dr. M. Steigerwald for helpful and informative discussions.

(10) Barbash, Y. V.; Skrypnik, Y. G.; Shevchuk, I. A.; Korotkova, Z. G. *J. Anal. Chem. USSR (Engl. Transl.)* **1979**, *34*, 1163.
(11) Watson, P. L.; Whitney, J. F.; Harlow, R. L. *Inorg. Chem.* **1981**, *20*, 3271.
(12) Lange, L.; DuMont, W. W. *J. Organomet. Chem.* **1985**, *286*, C1.
(13) Akiba, M.; Lakshmikanthan, M. V.; Jen, K. Y.; Cava, M. P. *J. Org. Chem.* **1984**, *49*, 4819.
(14) Bonasia, P. J.; Arnold, J. *J. Chem. Soc., Chem. Commun.* **1990**, 1299.
(15) ^{1}H NMR data for KTeMes (d_8-THF): δ 6.56 (s, 2 H), 2.45 (s, 6 H), 2.01 (s, 3 H). ^{125}Te NMR (d_8-THF): δ −296 ppm (referenced to Me$_2$Te; δ = 0 ppm).
(16) Spectrometer frequencies (Bruker AM 300) were 94.69 and 52.525 MHz for ^{125}Te and ^{171}Yb, respectively.
(17) *NMR and the Periodic Table*; Harris, R. K., Mann, B. E., Eds.; Academic Press: London, 1978; Chapter 12, p 383.
(18) Avent, A. G.; Edelman, M. A.; Lappert, M. F.; Lawless, G. A. *J. Am. Chem. Soc.* **1989**, *111*, 3423.
(19) Bianconi, P. A.; Strzelecki, A. R.; Helsel, B. A.; Utz, T.; Lin, M. C. To be submitted for publication.
(20) Spectral data for Sm(TeMes)$_2$THF$_2$ (**2**): ^{1}H NMR (d_8-THF, 300 MHz) δ 7.51 (s, 4 H), 4.45 (s, 12 H), 3.61 (br, THF), 1.76 (br, THF), 1.46 (s, 6 H); ^{13}C{^{1}H} NMR δ 132.9, 130.0, 120.9 (aromatics, ipso carbon missing), 68.4 (THF), 41.4 (*o*-CH$_3$), 22.5 (THF), 21.5 ppm (*p*-CH$_3$). Anal. Calcd for SmTe$_2$C$_{26}$H$_{38}$O$_2$: Sm, 19.1; Te, 32.4; C, 39.6; H, 4.9. Found: Sm, 19.1; Te, 31.8; C, 40.2; H, 4.9.
(21) Evans, D. F.; Fazakerley, G. V.; Phillips, R. F. *J. Chem. Soc. A* **1971**, 1931.
(22) (a) Char yield = 29%; theoretical char yield for complete decomposition of **1** to YbTe is 35%. (b) X-ray powder diffraction peaks at d = 3.16, 2.24, 1.84, 1.58, 1.42, 1.31, and 1.12 Å correspond to cubic YbTe. (J.C.P.D.S. X-ray Powder Data File, 18-1468, p 1040.)

New Evidence Supporting a Radical Mechanism of the Inactivation of General Acyl-CoA Dehydrogenase by a Metabolite of Hypoglycin

Ming-tain Lai and Hung-wen Liu*

Department of Chemistry
University of Minnesota
Minneapolis, Minnesota 55455

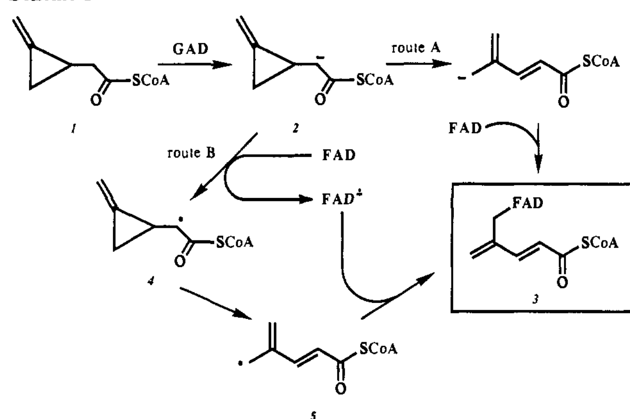
Received December 20, 1991

General acyl-CoA dehydrogenase (GAD) is a FAD-dependent enzyme which catalyzes the conversion of a medium-chain fatty acyl-CoA to the corresponding α,β-enolyl-CoA product.[1] When GAD is exposed to (methylenecyclopropyl)acetyl-CoA (MCPA-CoA, **1**), a metabolite of hypoglycin A that causes Jamaican vomiting sickness,[2] time-dependent inactivation ensues with concomitant bleaching of the active-site FAD.[3] This inhibition

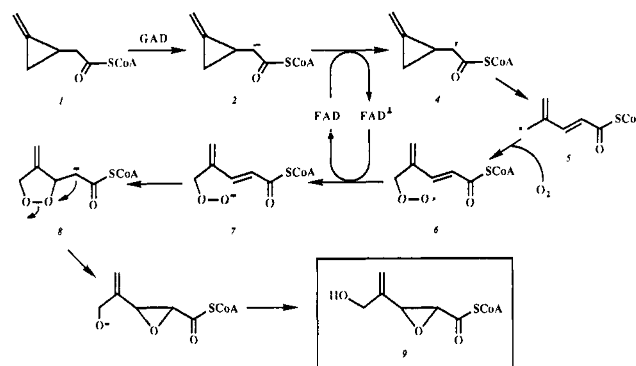
(1) (a) Thorpe, C.; Matthews, R. G.; Williams, C. H. *Biochemistry* **1979**, *18*, 331. (b) Ghisla, S.; Thorpe, C.; Massey, V. *Biochemistry* **1984**, *23*, 3154. (c) Pohl, B.; Raichle, T.; Ghisla, S. *Eur. J. Biochem.* **1986**, *160*, 109.
(2) (a) Tanaka, K. In *Handbook of Clinical Neurology*; Vinken, P. J., Bruyn, G. W., Eds.; Elsevier-North Holland: Amsterdam, 1979; Vol. 37, Chapter 17, p 511. (b) Tanaka, K.; Ikeda, Y. In *Fatty Acid Oxidation; Clinical, Biochemical, and Molecular Aspects*; Tanaka, K., Coates, P. M., Eds.; Alan R. Liss, Inc.: New York, 1990; p 167.

0002-7863/92/1514-3160$03.00/0 © 1992 American Chemical Society

Scheme I



Scheme II



is widely believed to proceed via a C_α deprotonation (**2**), followed by ring fragmentation and then covalent modification of the flavin coenzyme (**3**) (Scheme I, route A).[3] However, we have recently found that this inactivation is nonstereospecific, since the partition ratios for (1*R*)- and (1*S*)-MCPA-CoA are nearly identical.[4] In light of the rearrangement of an α-cyclopropyl radical to the straight-chain alkyl radical as an extremely facile process,[5] such nonstereospecific inactivation may be envisaged as a spontaneous ring fragmentation induced by a transient α-cyclopropyl radical **4**. This explanation supports a one-electron oxidation pathway (Scheme I, route B) as opposed to the anion-induced ring cleavage mechanism (Scheme I, route A).[6] Since a partition ratio of ca. 3 has been found for this inactivation,[4] it is obvious that GAD is capable of turning over the latent inhibitor, prior to being inactivated via a course similar to that of inactivation. These mechanistic ambiguities may thus be resolved if the turnover product(s) can be isolated and characterized. Reported in this paper are our results on the isolation and structural elucidation of a major turnover product from the enzymatic incubation of MCPA-CoA, and the mechanistic implication for the inactivation of GAD by this inhibitor.

The inactivation was conducted aerobically by mixing the purified enzyme (0.6 μmol)[7] with 7 molar equiv of chemically synthesized MCPA-CoA[4] in 50 mM potassium phosphate buffer (pH 7.6) at room temperature. The incubation was continued for 15 min to ensure complete inactivation, and the resulting mixture, without further treatment, was loaded in batches onto an HPLC Partisil-C_{18} column (4.5 × 250 mm) and was eluted with 30% methanol in 50 mM potassium phosphate buffer (pH 5.3). The major peak with a retention time of 4.3 min, which was absent in the control, prepared concurrently with boiled enzyme, was collected.[8] After removal of methanol in vacuo, the pooled fractions were repurified and desalted by reversed-phase chromatography (eluting with water and then methanol)[9] and then concentrated. The ^{1}H-NMR spectrum of this product, measured with a sample which was repeatedly dissolved in ^2H_2O and lyophilized prior to analysis, displayed four sets of resonances at δ 5.35 and 5.34 (1 H each), 3.99 and 3.96 (1 H each), 3.80 (1 H), and 3.68 (1 H), in addition to those of the coenzyme A.[10] While the disappearance of the characteristic signals for the structure of MCPA-CoA at δ 1.62, 1.27 and 1.06 (the cyclopropyl hydrogens), and 2.57 and 2.42 (the side-chain methylene hydrogens)[4c] clearly indicated the destruction of the cyclopropyl group, the chemical shifts of those new peaks observed for the product strongly suggested the retention of the terminal methylene moiety and the presence of a highly oxygenated skeleton in its structure. Although no coupling was found in the COSY analysis, a TOCSY experiment[11] with a mixing time of 80 ms clearly revealed the correlation between the resonances of δ 5.35/5.34 and 3.99/3.96, as well as δ 3.80 and 3.68. Owing to the scarcity of the sample, the chemical shifts of the carbon signals were obtained by a ^{13}C–^{1}H–detected HMQC (heteronuclear multiple quantum coherence) experiment,[11] in which four pertinent peaks appearing at δ 114.0, 56.8, 56.4, and 56.0 were found to be the corresponding carbons bearing the δ 5.35/5.34, 3.99/3.96, 3.80, and 3.68 protons. The structure of a CoA ester (**9**) was established on the basis of these results. The assigned structure is consistent with data obtained from GC–MS analysis where the turnover product (**9**) was hydrolyzed, followed by hydride reduction and subsequent acetylation to afford the expected diacetate ($(M + 1)^+$ 215, isobutane; $(M + 18)^+$ 232, ammonia).[12] In addition, the proposed structure is further supported by comparison of the NMR signal pattern with that of the corresponding methyl ester.[13]

The identification of **9** as the major turnover product of this inactivation strongly supports the intermediacy of a ring-opened

(3) (a) Ghisla, S.; Wenz, A.; Thorpe, C. In *Enzyme Inhibitors*; Brodbeck, U., Ed.; Verlag Chemie: Weinheim, Germany, 1980; p 43. (b) Wenz, A.; Thorpe, C.; Ghisla, S. *J. Biol. Chem.* **1981**, *256*, 9809. (c) Ghisla, S.; Melde, K.; Zeller, H. D.; Boschert, W. In *Fatty Acid Oxidation; Clinical, Biochemical, and Molecular Aspects*; Tanaka, K., Coates, P. M., Eds.; Alan R. Liss, Inc.: New York, 1990; p 185.

(4) (a) Lenn, N. D.; Shih, Y.; Stankovich, M. T.; Liu, H.-w. *J. Am. Chem. Soc.* **1989**, *111*, 3065. (b) Lai, M.-t.; Liu, H.-w. *J. Am. Chem. Soc.* **1990**, *112*, 4034. (c) Lai, M.-t.; Liu, L.-d.; Liu, H.-w. *J. Am. Chem. Soc.* **1991**, *113*, 7388.

(5) (a) Griller, D.; Ingold, K. U. *Acc. Chem. Res.* **1980**, *13*, 317. (b) Stubbe, J. *Biochemistry* **1988**, *27*, 3893 and references cited therein. (c) Newcomb, M.; Glenn, A. G. *J. Am. Chem. Soc.* **1989**, *111*, 275.

(6) An alternate pathway has lately been put forward in which the inactivation is ascribed to the formation of a tightly bound complex between FAD and the inhibitor, instead of formation of the covalent adduct **3** (Tserng, K.-Y.; Jin, S.-J.; Hoppel, C. L. *Biochemistry* **1991**, *30*, 10755).

(7) Thorpe, C. *Methods Enzymol.* **1981**, *71*, 366.

(8) Except for two small humps at 8.3 and 10.8 min, other peaks having retention times of 3.9, 5.5, and 12.5 min have been identified as free CoA, FAD, and MCPA-CoA, respectively. Assuming that these two unknown species are also derived from MCPA-CoA, integration of these peaks indicated that ester **9** accounts for more than 60% of the turnover products.

(9) Eberhard, A. *Chromatogram* **1987**, *8*, 10.

(10) The UV spectrum of this compound is that of the coenzyme A with a maximal absorption at 260 nm. ^{1}H NMR (^2H_2O) of the purified turnover product: δ 8.50, 8.21 (1 H each; s; adenine H's), 6.11 (1 H; d, *J* = 6.0; ribose anomeric H), *5.35, 5.34* (1 H each; br s; =CH_2), 4.95–4.88 (1 H; buried under ^{2}HOH peak), 4.70, 4.53, (1 H each; s; ribose H's), 4.18 (2 H; s; ribose CH_2O), 3.99 (2 H; s), *3.99, 3.96* (1 H each; s), *3.80* (1 H; d, *J* = 1.6), 3.79 (1 H; m), *3.68* (1 H; d, *J* = 1.6), 3.50 (1 H; m), 3.39 (2 H; t, *J* = 11), 3.28 (2 H; t, *J* = 11), 2.99 (2 H; m), 2.37 (2 H; m), 0.83, 0.70 (3 H each; s; Me's); the chemical shifts of signals other than the resonances assigned to CoA are shown in italics.

(11) For a good review of COSY, TOCSY, and HMQC experiments, see: Martin, G. E.; Zektzer, A. S. In *Two-Dimensional NMR Methods for Establishing Molecular Connectivity*; VCH Publishers: New York, 1988. The fact that no correlation was found by the COSY experiment may be attributed to the weak coupling between peaks.

(12) Direct MS measurements failed to detect the molecular ion of **9**. The major peaks of its high-resolution FAB-MS at 866.0141 and 887.9980 are clusters of the (CoA + Na^+ + $2K^+$) and (CoA + $2Na^+$ + K^+) charge complexes, calculated for $C_{21}H_{34}N_7O_{16}P_3SK_2Na$ (866.0167) and $C_{21}H_{33}N_7O_{16}P_3SK_2Na_2$ (887.9987), respectively.

(13) ^{1}H NMR ($CDCl_3$) of the methyl ester of **9**: δ 5.39, 5.38 (1 H each; br s; =CH_2), 4.12, 4.06 (1 H each; AB quartet, *J* = 13.0; CH_2OH), 3.79 (3 H; s; OMe), 3.70, 3.57 (1 H each; d, *J* = 1.7; epoxide H's), 1.54 (1 H; br s; OH). The minor mismatching of the chemical shifts between the signals of **9** and those of the methyl ester standard may be attributed to the structural variation of the ester moieties and the difference of the solvents used for spectral measurements. The methyl ester standard was prepared from (*E*)-methyl 3-(tributylstannyl)acrylate by coupling with protected 2-iodoallyl alcohol (Stille, J. K.; Groh, B. L. *J. Am. Chem. Soc.* **1987**, *109*, 813) followed by epoxidation.

radical **5** which, after recombination with the flavin semiquinone, leads to covalent modification of FAD (Scheme I, route B). Since the reactions of carbon radicals, particularly cyclopropylcarbinyl and homoallylic species, with molecular oxygen are well documented,[14] the inactivation derailment may be envisioned as trapping the acyclic radical **5** with O_2 to form a transient peroxy radical **6** which, upon reduction by one-electron transfer from the active-site-bound flavin semiquinone, gives rise to a peroxy anion **7**. Since the partition ratio of this inactivation is approximately 3, reacting with oxygen instead of coupling with the flavin coenzyme is clearly a more facile process for the ring-opened radical intermediate **5**. As depicted in Scheme II, this reroute is culminated by an intramolecular epoxidation[15] converting **7** via a 1,2-dioxolanylcarbinyl anion **8** to the observed turnover product **9**.[16] The mechanistic insights derived from this study provide highly convincing evidence sustaining our early notion that inactivation of GAD by MCPA-CoA is likely to proceed through a radical mechanism. These results may also be extrapolated to suggest that GAD is capable of mediating one-electron oxidation-reduction.

Acknowledgment. We thank Dr. Vikram Roongta for his assistance with NMR measurements. This work was supported by a National Institutes of Health grant (GM 40541). H.-w.L. also thanks the National Institutes of Health for a Research Career Development Award (GM 00559).

(14) (a) Nakamura, E.; Inubushi, T.; Aoki, S.; Machii, D. *J. Am. Chem. Soc.* **1991**, *113*, 8980. (b) Beckwith, A. L. J. *Tetrahedron* **1981**, *37*, 3073. (c) Porter, N. A. In *Free Radicals in Biology*; Pryor, W. A., Ed.; Academic Press: New York, 1980; Vol. IV, p 261. (d) Beckwith, A. L. J.; Ingold, K. U. In *Rearrangements in Ground and Excited States*; de Mayo, P., Ed.; Academic Press: New York, 1980.

(15) (a) Clark, C.; Hermans, P.; Meth-Cohn, O.; Moore, C.; Taljaard, H. C.; van Vuuren, G. *J. Chem. Soc., Chem. Commun.* **1986**, 1378. (b) Rontani, J.-F. *Tetrahedron Lett.* **1991**, 6551. (c) Dowd, P.; Ham, S. W. *J. Am. Chem. Soc.* **1991**, *113*, 9403.

(16) An alternate mechanism is also conceivable involving an intramolecular cyclization of **6** to produce a 1,2-dioxolanylcarbinyl radical (Feldman, K. S.; Simpson, R. E. *J. Am. Chem. Soc.* **1989**, *111*, 4878) and then a one-electron reduction to give the corresponding anion **8**.

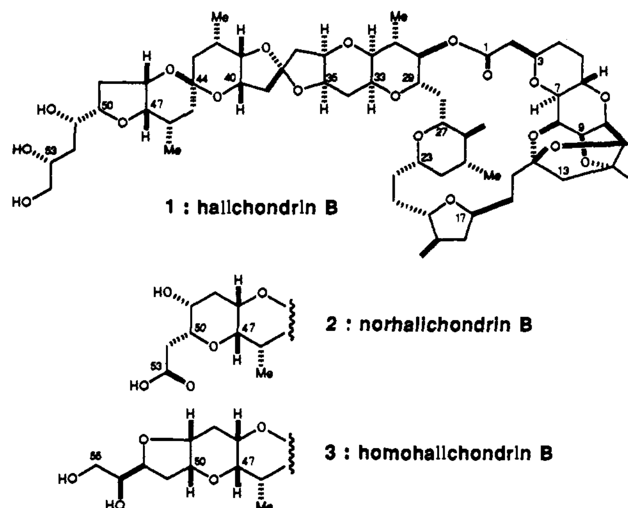
Total Synthesis of Halichondrin B and Norhalichondrin B

Thomas D. Aicher, Keith R. Buszek, Francis G. Fang, Craig J. Forsyth, Sun Ho Jung, Yoshito Kishi,* Michael C. Matelich, Paul M. Scola, Denice M. Spero, and Suk Kyoon Yoon

Department of Chemistry, Harvard University 12 Oxford Street, Cambridge, Massachusetts 02138

Received December 20, 1991

Halichondrins are a class of polyether macrolides isolated originally from the marine sponge *Halichondria okadai* Kadota.[1,2] Halichondrins, especially halichondrin B and homohalichondrin B, exhibit extraordinary in vitro and in vivo antitumor activity. However, the very limited supply of halichondrins from natural sources has prevented further evaluation of their potential clinical application thus far. Their intriguing and challenging structural features, coupled with this fact, encouraged synthetic efforts toward this class of natural products.[3,4] In this paper, we report the first total synthesis of halichondrin B and norhalichondrin B, which has, we believe, potential to meet the demand.



Scheme I outlines the synthesis of the right half of the halichondrin Bs. We planned to form the C-21–C-22 bond[5] via a Horner–Emmons reaction, followed by conjugate reduction. We were concerned with double-bond isomerization from the C-19 exocyclic to the C-19–C-20 endocyclic position in this process. This transformation was accomplished via the preparation of the aldehyde from the primary alcohol **3**[6,7] by Dess–Martin oxidation,[8] Horner–Emmons reaction under carefully controlled conditions, and the conjugate reduction of the resulting enone by the Stryker reagent,[9] without double-bond isomerization. Hydride reduction of the resulting saturated ketone yielded approximately a 1:1 mixture of the two possible diastereomers. As the stereochemistry of diastereomeric alcohols could not be firmly established at this stage, both diastereomers were transformed separately into the corresponding mesylates and used for the next coupling reaction. However, it is important to note that the two diastereomeric alcohols were readily interconvertible via the Mitsunobu reaction.[10]

(1) (a) Uemura, D.; Takahashi, K.; Yamamoto, T.; Katayama, C.; Tanaka, J.; Okumura, Y.; Hirata, Y. *J. Am. Chem. Soc.* **1985**, *107*, 4796-4798. (b) Hirata, Y.; Uemura, D. *Pure Appl. Chem.* **1986**, *58*, 701-710.

(2) A recent publication (Bai, R.; Paull, K. D.; Herald, C. L.; Malspeis, L.; Pettit, G. R.; Hamel, E. *J. Biol. Chem.* **1991**, *266*, 15882-15889) implies that halichondrin B and homohalichondrin B are isolated from *Axinella* sponges.

(3) For the synthetic work from this laboratory, see: (a) Aicher, T. D.; Kishi, Y. *Tetrahedron Lett.* **1987**, *28*, 3463-3466. (b) Aicher, T. D.; Buszek, K. R.; Forsyth, C. J.; Fang, F. G.; Jung, S. H.; Kishi, Y.; Scola, P. M. *Tetrahedron Lett.*, in press. (c) Buszek, K. R.; Forsyth, C. J.; Fank, F. G.; Jung, S. H.; Kishi, Y.; Scola, P. M.; Yoon, S. K. *Tetrahedron Lett.*, in press. (d) Fang, F. G.; Kishi, Y.; Matelich, M. C.; Scola, P. M. *Tetrahedron Lett.*, in press.

(4) For the synthetic work from other laboratories, see: (a) Kim, S.; Salomon, R. G. *Tetrahedron Lett.* **1989**, *30*, 6279-6282. (b) Cooper, A. J.; Salomon, R. G. *Tetrahedron Lett.* **1990**, *31*, 3813-3816. (c) Burke, S. D.; Buchanan, J. L.; Rovin, J. D. *Tetrahedron Lett.* **1991**, *32*, 3961-3964.

(5) The numbering adopted in this paper corresponds to that of halichondrins.

(6) This substance was synthesized from 2-deoxy-L-arabinose diethyl thioacetal 4,5-acetonide (Wong, M. Y. H.; Gray, G. R. *J. Am. Chem. Soc.* **1978**, *100*, 3548) in 47% overall yield in 13 steps: (1) $AcOH/H_2O$/room temperature. (2) TBDPSiCl/imidazole. (3) $I_2/NaHCO_3/H_2O$/acetone. (4) Ac_2O/pyridine/room temperature. (5) $CH_2{=}CHCH_2TMS/BF_3{\cdot}OEt_2/CH_3CN/0$ °C. (6) (a) 9-BBN; (b) H_2O_2. (7) $MMTrCl/Et_3N/CH_2Cl_2$. (8) K_2CO_3/MeOH. (9) Swern oxidation. (10) MeOH/PPTS. (11) Tebbe reagent (Tebbe, F. N.; Parshall, G. W.; Reddy, G. S. *J. Am. Chem. Soc.* **1978**, *100*, 3611-3613. Cannizzo, L. F.; Grubbs, R. H. *J. Org. Chem.* **1985**, *50*, 2386-2397). (12) PvCl/pyridine. (13) TBAF.

(7) Satisfactory spectroscopic data (^1H and ^{13}C NMR, HRMS, MS, IR, UV, $[\alpha]_D$) were obtained for all new compounds reported in this paper.

(8) Dess, D. B.; Martin, J. C. *J. Org. Chem.* **1983**, *48*, 4155-4156.

(9) (a) Mahoney, W. S.; Brestensky, D. M.; Stryker, J. M. *J. Am. Chem. Soc.* **1988**, *110*, 291-293. (b) Mahoney, W. S.; Stryker, J. M. *J. Am. Chem. Soc.* **1989**, *111*, 8818-8823. (c) We are indebted to Professor Stryker for a sample of this reagent.

(10) For a review on this reaction, see: Mitsunobu, O. *Synthesis* **1981**, 1-28.

 © 1992 American Chemical Society