Enantioselective Synthesis of (+)- and (−)-Muricatacin through S_E2' Addition of Nonracemic γ-Silyloxy Allylic Stannanes to Aldehydes

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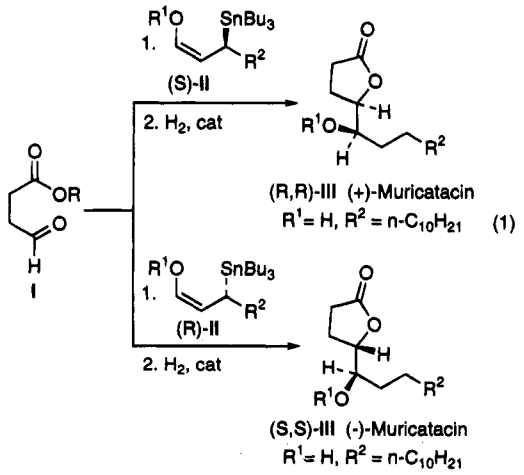
The acetogenins (*R,R*)-(+)- and (*S,S*)-(-)-muricatacin were synthesized through the highly stereoselective addition of γ-silyloxy allylic stannanes (*S*)-**6** and (*R*)-**6** to (*E*)-ethyl 3-formylpropenoate (**12**) in the presence of $BF_3{\cdot}OEt_2$. The resulting adducts (*R,R*)-**13** and (*S,S*)-**13** afforded the aforementioned acetogenins upon catalytic hydrogenation and subsequent deprotection–lactonization with aqueous HF. Interestingly, additions of stannanes **6** (racemic) to the saturated aldehydes RCH_2CH_2CHO (**8**, R = CO_2Et, R = CN, R = Cl) in the presence of $BF_3{\cdot}OEt_2$ afforded *ca.* 70:30 mixtures of *syn* and *anti* adducts **9a–c**. In contrast, the *n*-alkyl aldehyde **8** (R = n-C_4H_9) underwent highly selective *syn* addition (97:3) with the crotyl analogue **7** of stannane **6**.

The recent isolation and structure elucidation of muricatacin (**III**) from the seeds of the tropical fruit *Annona muricata* L.[1] has stimulated a great deal of attention,[2] no doubt stemming from the wide range of biological properties attributed to muricatacin and its more complex congeners.[3] Interestingly, both enantiomers of muricatacin are found in nature. The isolated material is a mixture of the two, with the (−)-(*R,R*) enantiomer predominant (ee of *ca.* 25% based on the optical rotation of synthetic material).[2,4]

Our synthetic plan, outlined in eq 1, entailed addition of a nonracemic γ-alkoxy allylic stannane **II** to a succinaldehyde derivative **I** followed by hydrogenation and lactonization. Related S_E2' additions are known to be stereospecific with respect to the stannane reagent and highly *syn* selective overall.[5] It was expected that the (*S*) reagent (*S*)-**II** would give rise to (*R,R*)-muricatacin and vice versa.



Our recent findings that TBS-protected stannanes such as **II** (R¹ = TBS) show improved *syn* selectivity in Lewis acid-promoted additions to aldehydes prompted our choice of (*S*)-**6** and (*R*)-**6** as the stannane reagents.[5b] These were synthesized by addition of Bu_3SnLi to tridecenal **1**,[6] followed by *in situ* oxidation of the intermediate alkoxide with diisopropyl azodicarboxylate.[7] The crude acyl stannane **2** was reduced with (*R*)-BINAL-H or (*S*)-BINAL-H to afford the (*S*)-α-hydroxy stannane (*S*)-**3** or the enantiomer (*R*)-**3**, respectively.[8] Treatment with TBSCl and imidazole led to the α-OTBS allylic stannanes (*S*)-**5** and (*R*)-**5**. ^1H NMR analysis of the *O*-methyl mandelate derivatives (*S*)-**4** and (*R*)-**4** of the hydroxy stannane precursors indicated an enantiomeric excess of >95% for each stannane reagent.[9]

Upon stirring with $BF_3{\cdot}OEt_2$ in CH_2Cl_2 at −78 °C, each of the α-silyloxy stannanes (*S*)-**5** and (*R*)-**5** smoothly isomerized to the γ-isomers (*S*)-**6** (88% yield) and (*R*)-**6** (95% yield). Alternatively, the γ-isomer (*R*)-**6** could be obtained directly from the crude α-hydroxy stannane (*R*)-**3** with TBSOTf and i-Pr_2NEt at 0 °C.[5b] Both procedures were equally efficient based on starting enal **1**.

The requisite succinic aldehyde ester **8** (R = CO_2Et) was prepared through ozonolysis of ethyl 4-pentenoate[10] and subsequent reductive workup with Me_2S. Addition

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(2) (a) Figadère, B.; Harmange, J-C.; Laurens, A.; Cavé, A. *Tetrahedron Lett.* **1991**, *32*, 7539. (b) Scholz, G.; Tochtermann, W. *Tetrahedron Lett.* **1991**, *32*, 5535. (c) Wang, Z-M.; Lian, X-L.; Sharpless, K. B.; Sinha, S. C.; Sinha-Bagchi, A.; Keinman, E. *Tetrahedron Lett.* **1992**, *33*, 6407.

(3) Rupprecht, J. K.; Hui, Y. H.; McLaughlin, J. L. *J. Nat. Prod.* **1990**, *53*, 237.

(4) A portion of this work has appeared in preliminary form: Marshall, J. A.; Welmaker, G. S. *Synlett* **1992**, 537.

(5) (a) *Cf.* Marshall, J. A.; Welmaker, G. S.; Gung, B. W. *J. Am. Chem. Soc.* **1991**, *113*, 647. (b) Marshall, J. A.; Welmaker, G. S. *J. Org. Chem.* **1992**, *57*, 7158.

(6) 2-Tridecenal (**1**) is available from Pflatz and Bauer. Our sample was prepared by Wittig-homologation of undecanal (Aldrich Chemical) with (carbomethoxymethylene)triphenylphosphorane followed by reduction and Swern oxidation: Omura, K.; Swern, D. *Tetrahedron* **1978**, *34*, 1651.

(7) We have previously employed 1,1'-(azodicarbonyl)dipiperidine (ADD) for this *in situ* oxidation.[5] *Cf.* Narasaka, K.; Morikawa, A.; Saigo, K.; Mukaiyama, T. *Bull. Chem. Soc. Jpn.* **1977**, *50*, 2773. We are grateful to Prof. Cava (Alabama) for suggesting azodicarboxylic esters as less expensive alternatives.

(8) Noyori, R.; Tomino, I.; Tanimoto, Y.; Nishizawa, M. *J. Am. Chem. Soc.* **1984**, *106*, 6709.

(9) The ee of the hydroxy stannane was calculated from the ^1H NMR spectra of the (*S*)- and (*R*)-*O*-methyl mandelates. *Cf.* Trost, B. M.; Belletire, J. L.; Godleski, S.; McDougal, P. G.; Balkovec, J. M.; Baldwin, J. J.; Christy, M. E.; Ponticello, G. S.; Varga, S. L.; Springer, J. P. *J. Org. Chem.* **1986**, *51*, 2370.

(10) Aldrich Chemical, Milwaukee, WI. *Cf.* (a) Peak, D. A.; Robinson, R.; Walker, J. J. *J. Chem. Soc.* **1936**, 733. (b) Battersby, A. R.; Hunt, E.; McDonald, E.; Moron, J. *J. Chem. Soc., Perkin Trans. 1* **1973**, 2917.

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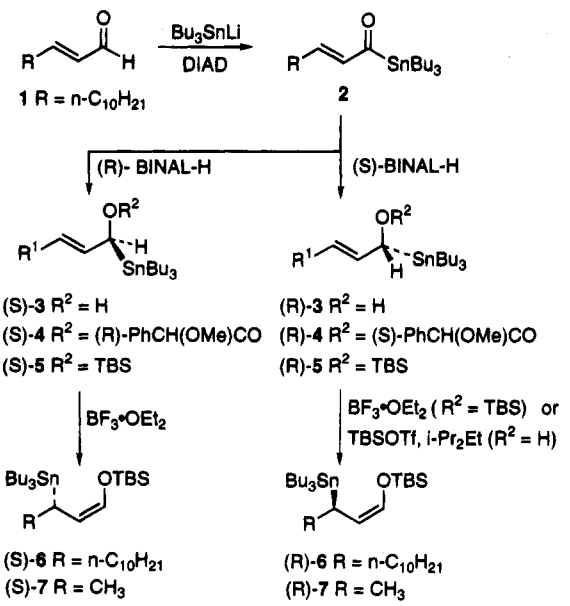
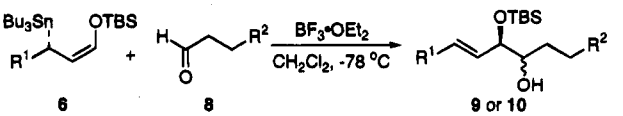


of stannane (*S*)-**6** to this aldehyde in the presence of BF_3•OEt_2 at −78 °C afforded the adduct **9a** in 84% yield as a 70:30 mixture of *syn* and *anti* diastereomers (Table 1, entry 1). This result was rather surprising, as we had previously obtained the adducts of the corresponding crotyl stannane **7** and heptanal as a 97:3 *syn:anti* mixture (entry 6). When the crotyl reagent was employed with the foregoing aldehyde ester, the *syn:anti* ratio increased to 88:12 (entry 2). Thus, it would appear that the diastereoselectivity of the addition is somewhat dependent on the nature of R^1 in the stannane reagent and even more dependent on the aldehyde β-substituent R^2.[11]

Suspecting that complexation between the BF_3 Lewis acid and the ester carbonyl may be responsible for the diminished stereoselectivity of the addition,[12] we examined the cyano aldehyde **8** (R^2 = CN).[13] Unfortunately, this addition fared no better. The *syn* and *anti* adducts **9b** were formed in a ratio nearly equal to that from the corresponding ester aldehyde (entry 3). Again, the crotyl stannane **7** showed a somewhat higher *syn:anti* selectivity (entry 4). Hoping to further decrease the presumed interaction of BF_3 with the aldehyde β-substituent, we next examined the β-chloro aldehyde **8** (R^2 = Cl).[14] However, no significant improvement in the *syn:anti* ratio of adducts **9c** was observed. These experiments suggest a through-space or dipole−dipole interaction between the β-substituent R^2 and the BF_3 complex of aldehydes **8** may cause decreased diastereoselectivity.[12]

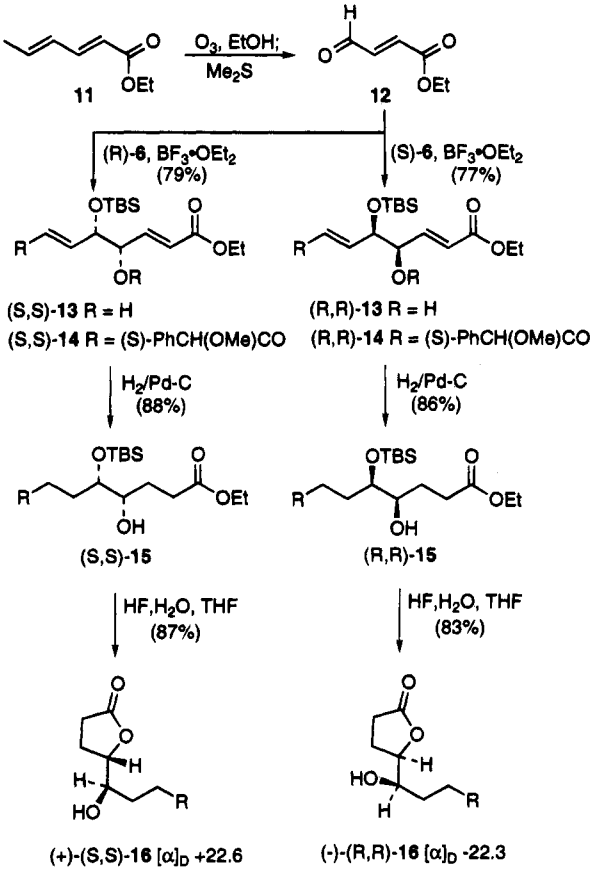
We have previously found that conjugated aldehydes give high ratios of *syn:anti* adducts with allyl stannanes.[5,15] We therefore turned our attention to the enal ester **12** as a possible aldehyde substrate. The (*E*)-double bond of **12** would also prohibit any through-space interaction of the ester carbonyl with the intermediate BF_3 complex of the aldehyde.

Table 1. BF_3-Promoted Addition of γ-Silyloxy Allylic Stannanes to β-Substituted Aldehydes



entry	R^1	R^2	adduct	yield, %	*syn:anti*[a]
1	n-$C_{10}H_{21}$	CO_2Et	9a[b]	84	70:30
2	CH_3	CO_2Et	10a[c]	82	88:12
3	n-$C_{10}H_{21}$	CN	9b[d]	80	68:32
4	CH_3	CN	10b[c]	75	82:18
5	n-$C_{10}H_{21}$	Cl	9c[d]	76	72:28
6	CH_3	n-C_4H_9	10d[e]	86	97:3[e]

[a] Ratios secured through integration of the ^1H NMR spectra of crude product mixtures. [b] The (*S*)-stannane (*S*)-**6** was employed. [c] The racemic stannane (*R,S*)-**7** was employed. [d] The racemic stannane (*R,S*)-**6** was employed. [e] Data from ref 5b.



Enal **12** was prepared by selective ozonolysis of ethyl sorbate (**11**) and reductive workup.[16] Addition of stannane (*R*)-**6** in the presence of BF_3•OEt_2 at −78 °C afforded the adduct (*S,S*)-**13** in 79% yield as a *ca.* 95:5 mixture of *syn* and *anti* adducts. As expected, the addition of stannane (*S*)-**6** to aldehyde **12** was equally selective. We were also able to carry out these additions with the α-silyloxy stannanes by pretreatment with BF_3•OEt_2 prior to aldehyde addition. Yields for both methods were comparable.

(11) We have found that the isopropyl analogue of silyloxy stannane **6** (R = *i*-Pr) fails to react with certain α-benzyloxy aldehydes in the presence of $MgBr_2$ under conditions where the related MOM or BOM derivatives afford adducts in high yield: Marshall, J. A.; Luke, G. P. *J. Org. Chem.* **1993**, *58*, 6229.

(12) An effect of this type was previously observed by Yamamoto *et al.* in the BF_3-promoted addition of tributyl crotylstannane to a γ-carbomethoxy aldehyde: Yamamoto, Y.; Yatagai, H.; Ishihara, Y.; Maeda, N.; Maruyama, R. *Tetrahedron* **1984**, *40*, 2239.

(13) Cyano aldehyde **8** (R^2 = CN) was prepared by ozonolysis of 4-pentenenitrile followed by reductive workup with Me_2S: Sumitomo, H.; Kobayashi, K. *J. Polym. Sci.*, Part A-1 **1972**, *10*, 2479. It was used without purification.

(14) Chloro aldehyde **8** (R^2 = Cl) was prepared by Swern oxidation[6] of 3-chloro-1-propanol: MacLeod, A. J.; Rossiter, J. J. *J. Chem. Soc., Perkin Trans. 1* **1983**, 717. It was used without purification.

(15) For a recent review: Marshall, J. A. *Chemtracts−Org. Chem.* **1992**, 75.

(16) Veysoglu, T.; Mitscher, L. A.; Swayze, J. K. *Synthesis* **1980**, 807.

The assigned stereochemistry of adducts (*S,S*)- and (*R,R*)-**13** is based on ample literature precedent.[5,15] The ee of these products was estimated to be *ca.* 95% or better from ^{1}H NMR analysis of the *O*-methyl mandelates **14**. Each of the allylic alcohol adducts was subjected to catalytic hydrogenation, affording the tetrahydro products (*S,S*)- and (*R,R*)-**15**. Concomitant silyl ether cleavage and lactonization with aqueous HF gave rise to the enantiomeric muricatacins (+)-(*S,S*)-**16** and (−)-(*R,R*)-**16**. The optical rotations and melting points of these samples were in close agreement with reported values.[2]

The foregoing syntheses illustrate the use of nonracemic γ-silyloxy stannanes as chiral reagents for the preparation of selectively monoprotected 1,2-diols. The work also uncovers an unexpected and intriguing effect of aldehyde β-substituents which can lower the diastereoselectivity of the addition. We further note that stereoselectivity can also be diminished through introduction of a long-chain alkyl group at the α position (R^1 in **6**; see Table 1). The origin of this effect has yet to be elucidated, but steric interactions with BF_3 in the aldehyde complex could be at least partially responsible.[17]

Experimental Section[18]

(*S*)-(*E*)-1-(Tri-*n*-butylstannyl)-2-tridecen-1-ol [(*S*)-3]. To a stirred, cooled (0 °C) solution of 0.85 mL (6.1 mmol) of HN(*i*-Pr)$_2$ in 20 mL of THF was added 2.4 mL (6.2 mmol) of 1.6 M *n*-BuLi in hexanes. The solution was stirred for 20 min at 0 °C and then 1.6 mL (5.9 mmol) of Bu_3SnH was introduced. The resulting solution was stirred for 40 min at 0 °C and then cooled to −78 °C. To this solution was added 1.0 g (5.1 mmol) of 2-tridecenal[6] in 3 mL of THF. The reaction mixture was stirred for 15 min at −78 °C and then 1.5 mL (7.6 mmol) of diisopropyl azodicarboxylate was added. The suspension was warmed to 0 °C and stirred for 1 h. The reaction mixture was then quenched with saturated aqueous NH_4Cl, the phases were separated, and the aqueous phase was extracted with ether. The combined organic layers were dried over $MgSO_4$, concentrated under reduced pressure, dissolved in hexanes, filtered, and again concentrated under reduced pressure to give the crude acyl stannane **2**, which was used immediately.

A solution of 10 mL (10 mmol) of 1.0 M $LiAlH_4$ in THF was added to 10 mL of THF with stirring, and then 10 mL (10 mmol) of 1.0 M EtOH in THF was added over 30 min. The reaction mixture was stirred for 30 min at ambient temperature. To this mixture was added a solution of 2.9 g (10 mmol) of (*R*)-1,1′-bi-2-naphthol in 20 mL of THF over 1 h. The milky white reaction mixture was heated to reflux for 1 h, allowed to cool to ambient temperature, and then cooled to −78 °C. To this suspension was added the crude acyl stannane **2** in 10 mL of THF over 1 h. The reaction mixture was stirred for 8 h at −78 °C and then quenched with MeOH, followed by saturated aqueous NH_4Cl. The phases were separated and the aqueous phase was treated with 3% HCl and extracted with ether. The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was diluted with 200 mL of hexanes and filtered, affording 2.8 g (97% recovery) of binaphthol, $[\alpha]_D$ +34 (*c* 1.0, THF), mp 207 °C; reported $[\alpha]_D$ +34 (*c* 1.0, THF), mp 208−210 °C.[8] [^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.98−7.87 (m), 7.39−7.12 (m), 5.02 (s).] The filtrate was concentrated under reduced pressure and the crude hydroxy stannane (*S*)-**3** was protected immediately. ^{1}H NMR analysis of the (*R*)-*O*-methyl mandelate derivative (*S*)-**4** showed a dr of 98:2.

(*S*)-(*E*)-1-[(*tert*-Butyldimethylsilyl)oxy]-1-(tri-*n*-butylstannyl)-2-tridecene [(*S*)-5]. To a stirred, cooled (0 °C) solution of crude hydroxy stannane (*S*)-**3** in 10 mL of CH_2Cl_2 was added 0.52 g (7.6 mmol) of imidazole, followed by 0.77 g (5.1 mmol) of TBSCl. The thick reaction mixture was stirred for 30 min and then quenched with saturated aqueous NH_4Cl and diluted with ether. The phases were separated and the aqueous phase was extracted with ether. The combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography through silica gel (elution with hexanes) afforded 1.4 g (45% from aldehyde **1**) of the α-silyloxy stannane (*S*)-**5**: $[\alpha]_D$ −53 (*c* 1.8, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.60 (dd, 1H, *J* = 15.1, 5.6 Hz), 5.32 (dt, 1H, *J* = 15.1, 6.9 Hz), 4.61 (d, 1H, *J* = 5.6 Hz), 1.98 (q, 2H, *J* = 6.9 Hz), 1.56−1.22 (m), 0.88 (s, 9H), 0.87 (t, 9H, *J* = 7.2 Hz), 0.86 (t, 3H, *J* = 7.3 Hz), 0.00 (6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 134.5, 122.2, 69.4, 32.5, 31.9, 30.1, 29.7, 29.7, 29.6, 29.4, 29.2, 29.2, 29.2, 27.5, 25.9, 22.7, 18.2, 14.1, 13.7, 9.1, −4.5, −5.2. Anal. Calcd for $C_{31}H_{66}OSiSn$: C, 61.89; H, 11.06. Found: C, 61.75; H, 11.11.

(*Z*)-(*S*)-1-[(*tert*-Butyldimethylsilyl)oxy]-3-(tri-*n*-butylstannyl)-2-tridecene [(*S*)-6]. To a stirred, cooled (-78 °C) solution of 0.10 g (0.17 mmol) of α-(silyl)oxystannane (*S*)-**5** in 2 mL of CH_2Cl_2 was added 0.22 μL (0.18 mmol) of BF_3·OEt_2. The solution was stirrred for 40 min at −78 °C and then quenched with saturated aqueous $NaHCO_3$ and warmed to room temperature. The phases were separated and the aqueous phase was extracted with ether. The combined organic extracts were washed with brine, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure. Chromatography (elution with hexanes) of the crude product gave 88 mg (88%) of the γ-(silyloxy) stannane (*S*)-**6**: $[\alpha]_D$ +115 (*c* 1.9, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.99 (d, 1 H, *J* = 5.7 Hz), 4.40 (dd, 1 H, *J* = 11.1, 5.7 Hz), 2.53 (m, 1H), 1.54−1.24 (m), 0.91 (s, 9H), 0.87 (t, 9 H, *J* = 7.12 Hz), 0.83 (t, 3 H, *J* = 7.3 Hz), 0.09 (6 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 134.1, 115.1, 33.3, 31.9, 30.5, 29.1, 29.1, 29.4, 29.1, 27.6, 27.2, 25.7, 25.7, 22.9, 22.7, 18.2, 14.1, 13.7, 8.9, −3.0, −5.2, −5.4. Anal. Calcd for $C_{31}H_{66}OSiSn$: C, 61.89; H, 11.06. Found: C, 61.81; H, 11.07.

Ethyl (2*E*,6*E*)-(4*R*,5*R*)-5-[(*tert*-Butyldimethylsilyl)oxy]-4-hydroxy-2,6-heptadecadienoate [(*R,R*)-13]. To a stirred, cooled (-78 °C) solution of 1.0 g (1.7 mmol) of α-stannane (*S*)-**5** in 5 mL of CH_2Cl_2 was added 0.31 mL (2.5 mmol) of BF_3·OEt_2. The resulting solution was stirred at −78 °C for 50 min and then a solution of 0.21 g (1.6 mmol) of (*E*)-3-formyl-2-propenoate (**12**)[16] in 2 mL of CH_2Cl_2 was introduced. The reaction mixture was stirred at −78 °C for 25 min, quenched with saturated aqueous $NaHCO_3$, diluted with ether, and allowed to warm to ambient temperature. The phases were separated and the aqueous phase was extracted with ether. The combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by flash chromatography through silica gel (elution with 10% ethyl acetate-hexanes) to afford 0.56 g (77%) of the coupled product (*R,R*)-**13**, which was shown to be a >95:5 mixture of *syn*:*anti* isomers by ^{1}H NMR analysis. $[\alpha]_D$ +14.1 (*c* 2.0, $CHCl_3$); IR (neat) 3499, 1725, 1660 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.88 (dd, 1 H, *J* = 15.7, 4.2 Hz), 6.09 (dd, 1 H, *J* = 15.7, 1.9 Hz), 5.64 (dt, 1 H, *J* = 15.4, 6.7 Hz), 5.38 (dd, 1 H, *J* = 15.4, 7.5 Hz), 4.17 (q, 2 H, *J* = 7.1 Hz), 4.06 (m, 1 H), 3.92 (t, 1 H, *J* = 6.7 Hz), 2.64 (d, 1 H, *J* = 4.8 Hz), 2.01 (q, 2 H, *J* = 6.7 Hz), 1.26 (t, 3 H, *J* = 7.1 Hz), 1.24 (m, 16 H), 0.86 (s, 9 H), 0.85 (t, 3 H, *J* = 7.0 Hz), 0.02 (6 H) [distinguishable peaks for the *anti* isomer are visible at 3.19, 3.09, and 2.38]; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.4, 146.5, 135.3, 128.8, 121.7, 76.9, 74.3, 60.3, 32.2, 31.9, 29.6, 29.6, 29.5, 29.3, 29.2, 29.0, 25.8, 22.7, 18.1, 14.2, 14.1, −3.9, −4.8. Anal. Calcd for $C_{25}H_{48}O_4Si$: C, 68.13; H, 10.98. Found: C, 68.23; H, 11.01. The ^{1}H NMR spectrum of the *O*-methyl mandelate derivative (*R,R*)-**14** showed *ca.* 3% of a diastereomeric product according to integration of signals at 6.90 and 6.70 ppm arising from the C-3 vinylic proton.

Ethyl (4*R*,5*R*)-5-[(*tert*-Butyldimethylsilyl)oxy]-4-hydroxyheptadecadienoate [(*R,R*)-15]. A stirred suspension of 0.50 g (1.1 mmol) of dienoate (*R,R*)-**13** and 0.50 g of 5% Pd on activated carbon in 20 mL of EtOH was placed under a H_2 atmosphere. The reaction mixture was stirred for 2 h and then filtered through Celite. The filtrate was concentrated and the crude product was purified by flash chromatography through

(17) *Cf.* Denmark, S. E.; Henke, B. R.; Weber, E. *J. Am. Chem. Soc.* **1987**, *109*, 2512.

(18) For typical experimental protocols, see ref 5a.

silica gel (elution with 5% ethyl acetate–hexanes) to afford 0.43 g (86%) of the hydrogenated product (*R,R*)-**15**. $[\alpha]_D$ −5.8 (*c* 2.1, $CHCl_3$); IR (neat) 3521, 1730 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 4.11 (q, 2 H, J = 7.1 Hz), 3.46 (m, 2 H), 2.45 (q, 2 H, J = 7.2 Hz), 2.17 (s, 1 H), 1.70 (q, 2 H, J = 7.4 Hz), 1.26–1.08 (m, 22 H), 1.23 (t, 3 H, J = 7.0 Hz), 0.88 (s, 9 H), 0.86 (t, 3 H, J = 6.9 Hz), 0.06 (6 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 177.8, 82.1, 74.6, 58.8, 33.1, 32.3, 30.1, 30.0, 30.0, 30.0, 29.9, 29.9, 29.7, 29.0, 26.2, 25.6, 24.0, 23.1, 18.8, 18.4, 14.5, −4.1, −4.1. Anal. Calcd for $C_{25}H_{52}O_4Si$: C, 67.51; H, 11.78. Found: C, 67.66; H, 11.81.

(−)-Muricatacin [(*R,R*)-16]. To a stirred solution of 80 mg (0.17 mmol) of the hydroxy ester (*R,R*)-**15** in 6 mL of 1:1 THF:H_2O was added 0.1 mL of 49% aqueous HF. The reaction mixture was stirred for 6 h at ambient temperature and then diluted with water and ether. The phases were separated and the aqueous phase was extracted with ether. The combined organic extracts were dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The product was purified by chromatography through silica gel (elution with 25% ethyl acetate–hexanes) to afford 43 mg (83%) of (−)-muricatacin. $[\alpha]_D$ −23.3 (*c* 1.8, $CHCl_3$); mp 67–68 °C; IR (neat) 3575, 1768 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 4.39 (dt, 1 H, J = 7.4, 4.5 Hz), 3.54 (m, 1 H), 2.59, 2.49 (ABX, 2 H, J_{AB} = 9.8 Hz, J_{AX} = 5.0 Hz, J_{BX} = 0.9 Hz), 2.25–2.05 (m, 3 H), 1.55–1.19 (m), 0.85 (t, 3 H, J = 6.9 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 177.3, 83.0, 73.6, 33.0, 31.9, 29.7, 29.7, 29.6, 29.5, 29.4, 28.7, 25.5, 24.1, 22.7, 14.1. Anal. Calcd for $C_{17}H_{30}O_3$: C, 71.79; H, 11.34. Found: C, 71.71; H, 11.33. Reported: $[\alpha]_D$ −22.9 ($CHCl_3$); mp 72 °C;[2b] $[\alpha]_D$ −23.1 (*c* 2.36, $CHCl_3$); mp 73–74 °C.[2c]

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Supplementary Material Available: Experimental procedures for **9a–c**, **10a,b**, (*R*)-**3**, (*R*)-**5**, (*R*)-**6**, (*S,S*)-**13**, (*S,S*)-**15**, and (*S,S*)-**16**, and selected ^1H NMR spectra (23 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.