Parallel, Stereoselective Syntheses of both Enantiomers of Muricatacin and Their Sulfur and Nitrogen Relatives Using the Silyloxy Diene-Based Methodology

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Introduction

A prominent objective of our laboratory is to develop flexible, chemically uniformed methodology to assemble diverse collections of chiral nonracemic bioactive molecules and variants thereof to be used to discover potential therapeutic candidates of novel or improved functional profiles.[1] To this end, we recently introduced a homogeneous triad of nucleophilic reactants, namely, 2-[(*tert*-butyldimethylsilyl)oxy]furan (hereafter TBSOF), 2-[(*tert*-butyldimethylsilyl)oxy]thiophene (TBSOT), and *N*-(*tert*-butoxycarbonyl)-2-[(*tert*-butyldimethylsilyl)oxy-]pyrrole (TBSOP), whose application in synthesis has been thoroughly pursued and demonstrated.[2−4] In order for this chemistry to further enlarge the synthetic horizons, we envisaged preparing both enantiomers of muricatacin, (*R*,*R*)- and (*S*,*S*)-**1a**,[5,6] and their sulfur and nitrogen relatives, (*R*,*R*)- and (*S*,*S*)-**1b** and (*R*,*R*)- and (*S*,*S*)-**1c**, moving from the above-mentioned silyloxy dienes according to a chemically uniformed reaction protocol, using both enantiomers of glyceraldehyde acetonide [(*R*)- and (*S*)-**2**] as the chiral sources.

Muricatacin, an acetogenin derivative that shows cytotoxic activity against certain human tumor cell lines,[7] has been isolated from the seeds of *Annona muricata*,[5] and remarkably, the natural compound comprises both (−)-muricatacin [(*R*,*R*)-**1a**] and its enantiomer (+)-muricatacin [(*S*,*S*)-**1a**].[8]

Results and Discussion

The retrosynthetic analysis of the muricatacin targets, outlined in Scheme 1, simply entailed diastereoselective coupling of TBSOF, TBSOT, and TBSOP to suitably protected glyceraldehyde derivative **A** to form unsaturated adducts **B**, and subsequent saturation of the double bond within **B** and oxidative sacrifice of the C-7 carbon atom to aldehydes **C**, followed by final Wittig elongation/hydrogenation maneuver. The Lewis acid-promoted conjugate Mukaiyama-aldol addition of the silyloxy diene reagents to chiral α-alkoxy aldehydes proved to be highly 4,5-*syn* selective, with α-*R*-configured aldehydes forming 4*R* adducts and vice versa.[2−4] It was thus expected that D-glyceraldehyde (*R*)-**2** would produce (4*R*,5*R*)-configured muricatacin derivatives, while L-glyceraldehyde (*S*)-**2** would furnish (4*S*,5*S*) congeners.

For the (*R*,*R*)-muricatacin series, the three parallel syntheses commenced with (+)-(*R*)-glyceraldehyde acetonide (*R*-**2**), which was coupled to TBSOF, TBSOT, and TBSOP under BF_3 etherate (TBSOF and TBSOT) or $SnCl_4$ assistance (TBSOP).[9] Under optimal conditions (Scheme 2), 4,5-*syn*-configured adducts **3a**−**c** preferentially formed, contaminated by only marginal amounts of the corresponding 4,5-*anti* diastereoisomers that were easily separated by flash chromatography on silica gel. The de values ranged from 88% for **3a** to 82% for **3b** to 89% for **3c**.[10] At this point of the synthesis, it was necessary to saturate the double bond within **3** and protect the free hydroxyl at C-5 before fission of the C-6−C-7 carbon−carbon bond. Thus, compounds **3a**−**c** were subjected to sequential catalytic hydrogenation (H_2, Pd

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(8) Muricatacin is probably a product of oxidative fission of the various monotetrahydrofuranic acetogenins in the plant (ref 6b).

(9) For each coupling reaction, the choice of the optimum protocol (Lewis acid activator, solvent, temperature) resulted from previous extensive work in our laboratory (see ref 2).

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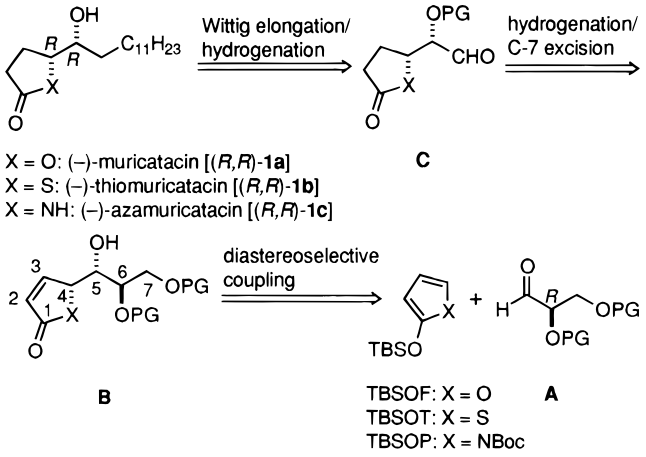
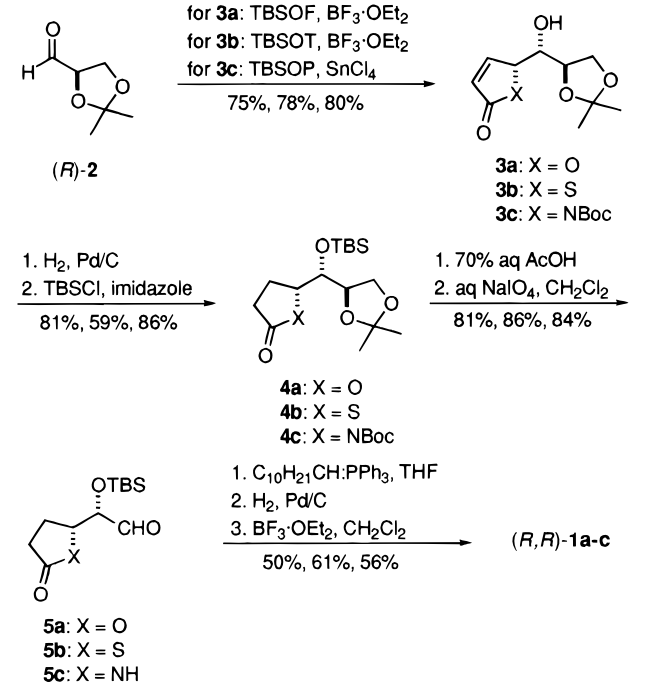
Scheme 1. Retrosynthetic Analysis of (*R,R*)-Muricatacin and Its Congeners Using the Silyloxy Diene Methodology[a]



[a] PG = protective groups.

Scheme 2. Synthesis of (*R,R*)-Muricatacin Derivatives[a]

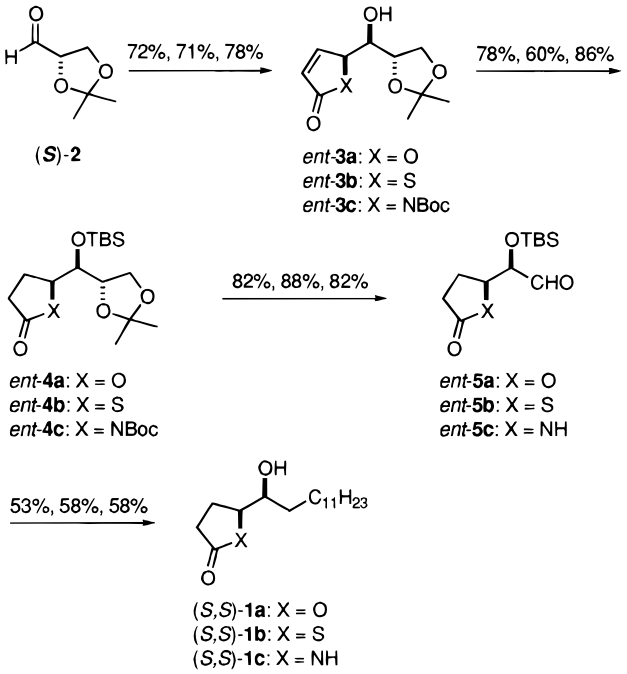


[a] The yields quoted refer to oxygen, sulfur, and nitrogen derivatives, respectively.

on carbon) and protection of the OH function as TBS ether (TBSCl, imidazole, DMF) to afford seven-carbon intermediates **4a**–**c** in excellent isolated yields.[11]

The oxidative removal of the C-7 carbon atom within **4a**–**c** to generate the six-carbon aldehydes **5a**–**c** was effected by cleaving of the terminal acetonide (70% aqueous AcOH, 50 °C) followed by fission of the diol so formed by $NaIO_4$-impregnated wet silica in CH_2Cl_2. The sequences afforded configurationally stable compounds **5a**–**c** in high yields, which were used as such in the next stages of the syntheses. There remained to carry out suitable elongations on **5a**–**c** in order to complete the elaboration of the muricatacin side chains. Indeed, Wittig olefination of aldehydes **5a**–**c** in THF with the appropriate C_{11} ylide (undecylphosphonium bromide/BuLi) gave rise to the corresponding unsaturated compounds, which were quickly transformed to muricatacin derivatives (*R,R*)-**1a**–**c** by catalytic hydrogenation (Pd on carbon, THF) followed by BF_3 etherate-promoted desilylation[12] (50%, 61%, and 56% yields for the three reactions). The overall yields from (*R*)-**2** were 25%, 24%, and 32%, respectively, over eight steps.

Scheme 3. Synthesis of (*S,S*)-Muricatacin Derivatives[a]



[a] Reaction conditions, see Scheme 2. The yields quoted refer to oxygen, sulfur, and nitrogen derivatives, respectively.

The synthetic paths to (+)-muricatacin enantiomers from L-glyceraldehyde (*S*)-**2** (Scheme 3) were similar to those of their (4*R*,5*R*)-configured counterparts and proceeded uneventfully to afford, first, adducts *ent*-**3a**–**c**, which were then transformed to target compounds (*S,S*)-**1a**–**c** via the respective intermediates *ent*-**4a**–**c** and *ent*-**5a**–**c**. Corroborating the reliability of the strategy, (+)-muricatacin [(*S,S*)-**1a**] and its sulphur and nitrogen relatives, (*S,S*)-**1b** and (*S,S*)-**1c**, were thus prepared in 24%, 22%, and 32% overall yields, respectively, from L-glyceraldehyde (*S*)-**2**.

In conclusion, what we have reported is a concise, diastereoselective synthesis of both enantiomers of muricatacin and their sulfur and nitrogen relatives that uses readily available D- and L-glyceraldehyde acetonides as the sole sources of chirality. In the course of this investigation, TBSOF, TBSOT, and TBSOP have emerged as a modular triad of reactants that features uniform

(10) The relative (and hence absolute) configuration of the key 4,5-*syn*-configured adducts **3a**–**c** was unambiguously determined by single-crystal X-ray analysis. **3a**: Casiraghi, G.; Colombo, L.; Rassu, G.; Spanu, P.; Gasparri Fava, G.; Ferrari Belicchi, M. *Tetrahedron* **1990**, *46*, 5807–5824. **3b**: Gasparri Fava, G.; Ferrari Belicchi, M.; Pelosi, G.; Zanardi, F.; Casiraghi, G.; Rassu, G. *J. Chem. Crystallogr.* **1996**, *26*, 509–513. **3c**: Rassu, G.; Casiraghi, G.; Spanu, P.; Pinna, L.; Gasparri Fava, G.; Ferrari Belicchi, M.; Pelosi, G. *Tetrahedron: Asymmetry* **1992**, *3*, 1035–1048. The configuration of the respective 4,5-*anti* congeners was judged as such on the basis of clean base-promoted C-4 epimerization experiments.

(11) We were unsuccessful in obtaining the intended derivatives **4a**–**c** by adopting the reverted maneuver (protection, then reduction), since unwanted epimerization at C-4 occurred under the basic conditions of the TBS-protection protocol.

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reactivity and wide, confident applicability. The transformations disclosed herein promise to elevate the synthetic utility of the title heterocyclic silyloxy dienes for the preparation of constitutionally and chirally diverse compounds, both individuals and ensembles, equipped with a variety of oxygen, sulfur, and nitrogen combinations.

Experimental Section[13]

Materials. 2,3-*O*-Isopropylidene-D-glyceraldehyde [(*R*)-**2**] was prepared from D-mannitol (Aldrich) according to the literature.[14] The preparation of 2,3-*O*-isopropylidene-L-glyceraldehyde [(*S*)-**2**] was carried out starting with 5,6-*O*-isopropylidene-L-gulonic acid 1,4-lactone (Fluka) following a known protocol.[15] 2-[(*tert*-Butyldimethylsilyl)oxy]furan (TBSOF) was obtained from 2-furaldehyde (Aldrich) following a reported method.[2m] 2-[(*tert*-Butyldimethylsilyl)oxy]thiophene (TBSOT) was prepared from thiophene (Aldrich) according to the method in a precedent paper.[2h] The synthesis of *N*-(*tert*-butoxycarbonyl)-2-[(*tert*-butyldimethylsilyl)oxy]pyrrole (TBSOP) was carried out starting with pyrrole (Aldrich) according to a precedent protocol.[2c] Undecyltriphenylphosphonium bromide was obtained from 1-bromoundecane (Aldrich) and triphenylphosphine according to a standard protocol. The gummy salt was thoroughly dried under vacuum (P_2O_5) prior to use.

6,7-*O*-Isopropylidene-2,3-dideoxy-D-*arabino*-hept-2-enonic Acid 1,4-Lactone (3a). General Procedure. To a solution of TBSOF (3.05 mL, 15.4 mmol) in anhydrous CH_2Cl_2 (60 mL) under argon atmosphere was added 2,3-*O*-isopropylidene-D-glyceraldehyde [(*R*)-**2**] (2.60 g, 20 mmol), and the resulting mixture was cooled to −80 °C. BF_3 etherate (1.89 mL, 15.4 mmol), cooled to the same temperature, was added dropwise to the stirring solution, and the reaction was allowed to proceed for 6 h at −80 °C. The reaction was then quenched at −80 °C by the addition of saturated aqueous $NaHCO_3$, and after ambient temperature was reached, the mixture was extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were washed with brine, dried ($MgSO_4$), filtered, and concentrated in vacuum to give a solid crude residue, which was subjected to flash chromatographic purification (3:2 hexanes/EtOAc). There were obtained 2.47 g (75%) of pure **3a** along with 0.16 g (5%) of the corresponding epimer 4-*epi*-**3a**.

Compound **3a**: white crystals; mp 125 °C; $[\alpha]^{20}_D$ +69.6 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.59 (dd, J = 5.8, 1.7 Hz, 1H), 6.17 (dd, J = 5.8, 1.9 Hz, 1H), 5.27 (m, 1H), 4.18 (m, 2H), 4.05 (m, 1H), 3.67 (m, 1H), 2.94 (d, J = 6.6 Hz, 1H), 1.42 (s, 3H), 1.37 (s, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 176.4, 154.3, 122.1, 109.8, 84.2, 75.5, 72.9, 67.1, 26.7, 25.1. Anal. Calcd for $C_{10}H_{14}O_5$: C, 56.07; H, 6.59. Found: C, 55.94; H, 6.71.

Compound 4-*epi*-**3a**: an oil; $[\alpha]^{20}_D$ −79.4 (*c* 0.6, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.61 (dd, J = 5.6, 1.5 Hz, 1H), 6.22 (dd, J = 5.6, 2.0 Hz, 1H), 5.20 (ddd, J = 4.7, 2.0, 1.5 Hz, 1H), 4.0 - 4.2 (m, 3H), 3.97 (dd, J = 7.1, 4.7 Hz, 1H), 2.60 (bs, 1H), 1.45 (s, 3H), 1.37 (s, 3H). Anal. Calcd for $C_{10}H_{14}O_5$: C, 56.07; H, 6.59. Found: C, 56.39; H, 6.40.

6,7-*O*-Isopropylidene-4-thio-2,3,4-trideoxy-D-*arabino*-hept-2-enonic Acid 1,4-Thiolactone (3b). The title compound was prepared according to the procedure described for **3a**, employing 2.71 g (12.6 mmol) of TBSOT, 2.13 g (16.4 mmol) of D-glyceraldehyde (*R*)-**2**, and 1.55 mL (12.6 mmol) of BF_3 etherate in CH_2Cl_2 (50 mL) at −80 °C for 4 h. After flash chromatographic purification (1:1 hexanes/EtOAc), thiolactone **3b** was recovered in 78% yield (2.26 g), along with the corresponding epimer 4-*epi*-**3b** (0.23 g, 8% yield).

Compound **3b**: an oil; $[\alpha]^{20}_D$ +67.0 (*c* 2.5, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.54 (dd, J = 6.1, 2.9 Hz, 1H), 6.31 (dd, J = 6.1, 1.9 Hz, 1H), 4.91 (m, 1H), 3.8−4.2 (m, 4H), 2.74 (bs, 1H), 1.41 (s, 3H), 1.32 (s, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 199.6, 156.7, 133.4, 110.0, 78.1, 72.9, 67.1, 58.4, 26.7, 24.9. Anal. Calcd for $C_{10}H_{14}O_4S$: C, 52.16; H, 6.13. Found: C, 52.24; H, 6.01.

(13) For general experimental procedures, see ref 2m.
(14) Schmid, C. R.; Bryant, J. D. *Org. Synth.* **1995**, *72*, 6−13.
(15) Hubschwerlen, C.; Specklin, J.-L.; Higelin, J. *Org. Synth.* **1995**, *72*, 1−5.

Compound 4-*epi*-**3b**: an oil; $[\alpha]^{20}_D$ −58.0 (*c* 2.7, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68 (dd, J = 6.0, 2.7 Hz, 1H), 6.37 (dd, J = 6.0, 2.1 Hz, 1H), 4.76 (ddd, J = 5.1, 2.7, 2.1 Hz, 1H), 3.9−4.2 (m, 4H), 3.33 (bs, 1H), 1.44 (s, 3H), 1.37 (s, 3H). Anal. Calcd for $C_{10}H_{14}O_4S$: C, 52.16; H, 6.13. Found: C, 52.21; H, 6.20.

4-[(*tert*-Butoxycarbonyl)amino]-6,7-*O*-isopropylidene-2,3,4-trideoxy-D-*arabino*-hept-2-enonic Acid 1,4-Lactam (3c). The above procedure described for **3a** was here adopted, with slight modifications concerning the Lewis acid promoter ($SnCl_4$ instead of BF_3 etherate) and the solvent (Et_2O instead of CH_2Cl_2). Starting from 2.45 g (8.2 mmol) of TBSOP, 1.39 g (10.7 mmol) of D-glyceraldehyde (*R*)-**2**, and 0.97 mL (8.2 mmol) of $SnCl_4$ in anhydrous Et_2O (50 mL) for 5 h at −80 °C, there was obtained a crude product, which was purified by crystallization from CH_2Cl_2/hexane to furnish 2.06 g (80%) of pure **3c**, accompanied by 0.12 g (4.7% yield) of its diastereoisomer 4-*epi*-**3c**, which was obtained in a pure form by flash chromatography of the mother liquor residue (1:1 hexanes/EtOAc).

Compound **3c**: white solid; mp 138−140 °C; $[\alpha]^{20}_D$ +197.6 (*c* 0.83, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 (dd, J = 6.3, 2.1 Hz, 1H), 6.13 (dd, J = 6.3, 1.5 Hz, 1H), 4.81 (dt, J = 5.7, 2.4 Hz, 1H), 4.09 (ddd, J = 6.0, 5.7, 3.9 Hz, 1H), 4.01 (q, J = 6.0, 1H), 3.94 (dd, J = 8.1, 6.0 Hz, 1H), 3.86 (dd, J = 8.1, 6.0 Hz, 1H), 3.63 (d, J = 3.9 Hz, 1H), 1.57 (s, 9H), 1.37 (s, 3H), 1.32 (s, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 168.9, 150.9, 148.2, 126.9, 109.2, 83.8, 75.6, 72.6, 66.4, 65.6, 28.0 (3 C), 26.4, 25.1. Anal. Calcd for $C_{15}H_{23}NO_6$: C, 57.50; H, 7.40; N, 4.47. Found: C, 57.31; H, 7.35; N, 4.32.

Compound 4-*epi*-**3c**: white solid; mp 118−120 °C; $[\alpha]^{20}_D$ −120.0 (*c* 0.8, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.29 (dd, J = 6.3, 2.1 Hz, 1H), 6.16 (dd, J = 6.3, 2.0 Hz, 1H), 4.97 (q, J = 2.1 Hz, 1H), 4.20 (m, 1H), 4.15 (td, J = 6.6, 2.2 Hz, 1H), 4.03 (m, 2H), 3.49 (d, J = 6.6 Hz, 1H), 1.56 (s, 9H), 1.46 (s, 3H), 1.37 (s, 3H). Anal. Calcd for $C_{15}H_{23}NO_6$: C, 57.50; H, 7.40; N, 4.47. Found: C, 57.30; H, 7.55; N, 4.31.

6,7-*O*-Isopropylidene-2,3-dideoxy-L-*arabino*-hept-2-enonic Acid 1,4-Lactone (*ent*-3a). The title compound was prepared according to the synthetic protocol described for its enantiomer **3a** by employing L-glyceraldehyde (*S*)-**2** in place of (*R*)-**2**. Starting with TBSOF (2.85 g, 14.4 mmol), pure *ent*-**3** was obtained (2.22 g, 72%) as colorless crystals: mp 123 °C; $[\alpha]^{20}_D$ −68.9 (*c* 1.0, $CHCl_3$). ^{1}H and ^{13}C NMR spectra fully coincided with those of its enantiomeric counterpart **3a**. Anal. Calcd for $C_{10}H_{14}O_5$: C, 56.07; H, 6.59. Found: C, 55.88; H, 6.70.

6,7-*O*-Isopropylidene-4-thio-2,3,4-trideoxy-L-*arabino*-hept-2-enonic Acid 1,4-Thiolactone (*ent*-3b). The above procedure to **3b** was adopted, employing L-glyceraldehyde (*S*)-**2** in place of (*R*)-**2**. Starting with 2.71 g (12.6 mmol) of TBSOT, thiolactone *ent*-**3b** was obtained (2.06 g, 71%) as an oil: $[\alpha]^{20}_D$ −65.9 (*c* 2.4, $CHCl_3$). ^{1}H and ^{13}C NMR spectra were in perfect agreement with those of enantiomeric thiolactone **3b**. Anal. Calcd for $C_{10}H_{14}O_4S$: C, 52.16; H, 6.13. Found: C, 52.34; H, 6.09.

4-[(*tert*-Butoxycarbonyl)amino]-6,7-*O*-isopropylidene-2,3,4-trideoxy-L-*arabino*-hept-2-enonic Acid 1,4-Lactam (*ent*-3c). The above procedure to **3c** was followed by replacing (*R*)-**2** with (*S*)-**2**. Starting with 2.0 g (6.72 mmol) of TBSOP, there was obtained a crude product that was crystallized from CH_2Cl_2/hexane to afford 1.64 g (78%) of lactam *ent*-**3c** as a white solid: mp 135−136 °C; $[\alpha]^{20}_D$ −195.66 (*c* 0.4, $CHCl_3$). ^{1}H and ^{13}C NMR spectra were in perfect agreement with those of enantiomeric lactam **3c**. Anal. Calcd for $C_{15}H_{23}NO_6$: C, 57.50; H, 7.40; N, 4.47. Found: C, 57.39; H, 7.63; N, 4.28.

5-*O*-(*tert*-Butyldimethylsilyl)-6,7-*O*-isopropylidene-2,3-dideoxy-D-*arabino*-heptonic Acid 1,4-Lactone (4a). General Procedure. Palladium on carbon (10%, 0.3 g) was added to a solution of α,β-unsaturated lactone **3a** (2.4 g, 11.2 mmol) in anhydrous THF (60 mL) in the presence of a small amount of NaOAc (0.09 g) at room temperature. The reaction vessel was evacuated by aspirator and thoroughly purged with hydrogen (three times), and the resulting heterogeneous mixture was stirred under a balloon of hydrogen. After 24 h, the hydrogen was evacuated, the catalyst filtered off, and the filtrate concentrated under vacuum to give a crude residue that was subjected to flash chromatographic purification (3:2 EtOAc/hexanes). There was obtained 2.2 g (90%) of saturated lactone as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.77 (td, J = 7.5, 2.1 Hz, 1H),

4.14 (m, 2H), 4.01 (m, 1H), 3.53 (bs, 1H), 3.35 (bs, 1H), 2.5−2.7 (m, 2H), 2.31 (m, 2H), 1.41 (s, 3H), 1.35 (s, 3H). The saturated lactone was subjected to 5-*O*-TBS protection. Thus, TBSCl (4.4 g, 29.1 mmol) and imidazole (2.0 g, 29.1 mmol) were sequentially added to a solution of the saturated lactone (2.1 g, 9.7 mmol) in anhydrous DMF (15 mL) under stirring at room temperature. After 24 h, further portions of TBSCl (1.4 g, 9.28 mmol) and imidazole (0.63 g, 9.3 mmol) were added, and the resulting solution was allowed to stir for an additional 12 h. The reaction was then quenched with 5% aqueous citric acid and the resulting mixture extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were dried ($MgSO_4$) and concentrated under vacuum to afford a crude residue that was purified by flash chromatography (1:1 hexanes/EtOAc). Protected lactone **4a** (2.9 g, 90%) was obtained as a colorless oil: $[\alpha]^{20}_D$ −9.5 (*c* .0.6, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.60 (dt, J = 6.6, 3.6 Hz, 1H), 4.13 (m, 1H), 4.06 (dd, J = 8.1, 6.3 Hz, 1H), 3.87 (dd, J = 8.1, 6.9 Hz, 1H), 3.78 (dd, J = 6.0, 3.6 Hz, 1H), 2.51 (m, 2H), 2.21 (m, 2H), 1.41 (s, 3H), 1.33 (s, 3H), 0.89 (s, 9H), 0.13 (s, 6H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 176.5, 109.0, 81.2, 76.3, 74.3, 66.6, 28.4, 26.5, 25.8 (3C), 27.2, 23.6, 18.1, −4.0 (2C). Anal. Calcd for $C_{16}H_{30}O_5Si$: C, 58.15; H, 9.15. Found: C, 58.20; H, 9.09.

5-*O*-(*tert*-Butyldimethylsilyl)-6,7-*O*-isopropylidene-4-thio-2,3,4-trideoxy-D-*arabino*-heptonic Acid 1,4-Thiolactone (4b). The above hydrogenation procedure to **4a** was employed, with unsaturated thiolactone **3b** (2.20 g, 9.55 mmol), 10% Pd on carbon (270 mg), and NaOAc (85 mg) in dry THF (50 mL). After flash chromatographic purification (1:1 EtOAc:hexanes), the saturated thiolactone intermediate (2.0 g, 90% yield) was obtained as white crystals: mp 118-120 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.25 (ddd, J = 7.5, 7.0, 3.9 Hz, 1H), 4.09 (m, 1H), 3.95 (m, 2H), 3.77 (dd, J = 7.2, 3.9 Hz, 1H), 2.91 (d, J = 3.6 Hz, 1H), 2.5−2.8 (m, 2H), 2.1−2.5 (m, 2H), 1.42 (s, 3H), 1.34 (s, 3H). This intermediate was subjected to the same protection protocol as that utilized to afford **4a**, employing 2 × 3.88 g (2 × 25.77 mmol) of TBSCl and 2 × 1.75 g (2 × 25.77 mmol) of imidazole in anhydrous DMF (30 mL) for 48 h. After flash chromatography (7:3 hexanes/EtOAc), protected thiolactone **4b** (1.93 g, 65%) was obtained as an oil: $[\alpha]^{20}_D$ −57.3 (*c* 3.3, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.14 (ddd, J = 9.9, 5.7, 4.8 Hz, 1H), 4.02 (m, 2H), 3.93 (dd, J = 5.4, 4.8 Hz, 1H), 3.84 (m, 1H), 2.61 (m, 2H), 2.29 (m, 1H), 2.09 (m, 1H), 1.42 (s, 3H), 1.33 (s, 3H), 0.89 (s, 9H), 0.13 (s, 3H), 0.12 (s, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 207.8, 109.2, 77.8, 74.7, 66.4, 54.9, 42.3, 28.5, 26.5, 25.8 (3 C), 25.1, 18.3, −3.6, −3.9. Anal. Calcd for $C_{16}H_{30}O_4SSi$: C, 55.45; H, 8.73. Found: C, 55.39; H, 8.88.

4-[(*tert*-Butoxycarbonyl)amino]-5-*O*-(*tert*-butyldimethylsilyl)-6,7-*O*-isopropylidene-2,3,4-trideoxy-D-*arabino*-heptonic Acid 1,4-Lactam (4c). The above hydrogenation procedure to transform **3a** into **4a** was adopted, with unsaturated lactam **3c** (2.0 g, 6.38 mmol), 10% Pd on carbon (210 mg), and NaOAc (88 mg) in dry THF (30 mL). After flash chromatographic purification (6:4 hexanes:EtOAc), there was obtained a saturated lactam intermediate (1.85 g, 92%) as a white solid: mp 99−103 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.31 (ddd, J = 5.7, 5.4, 3.9 Hz, 1H), 4.05 (m, 2H), 3.97 (ddd, J = 5.5, 4.8, 1.2 Hz, 1H), 3.69 (q, J = 5.7 Hz, 1H), 3.54 (d, J = 6.3 Hz, 1H), 2.71 (dt, J = 17.1, 10.5 Hz, 1H), 2.32 (ddd, J = 17.7, 6.0, 4.8 Hz, 1H), 2.10 (m, 2H), 1.48 (s, 9H), 1.36 (s, 3H), 1.30 (s, 3H). This intermediate was subjected to the same protection protocol as that utilized to afford **4a**, employing 2 × 2.65 g (2 × 17.58 mmol) of TBSCl and 2 × 1.20 g (2 × 17.62 mmol) of imidazole in dry DMF (20 mL) for 48 h. After flash chromatographic purification (7:3 hexanes/EtOAc), protected lactam **4c** (2.37 g, 94%) was obtained as a pale yellow oil: $[\alpha]^{20}_D$ +21.3 (*c* 0.8, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.14 (ddd, J = 8.1, 3.6, 1.2 Hz, 1H), 4.04 (dd, J = 8.4, 3.3 Hz, 1H), 4.02 (dd, J = 8.4, 6.3 Hz, 1H), 3.90 (m, 1H), 3.66 (dd, J = 8.1, 6.3 Hz, 1H), 2.51 (m, 1H), 2.33 (m, 1H), 2.11 (m, 1H), 1.93 (m, 1H), 1.46 (s, 9H), 1.24 (s, 3H), 1.20 (s, 3H), 0.80 (s, 9H), 0.07 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 174.4, 149.8, 109.8, 82.3, 75.2, 71.1, 68.6, 60.2, 31.8, 29.4, 28.0 (3 C), 26.2, 25.4 (3 C), 24.9, 17.6, −4.2, −5.0. Anal. Calcd for $C_{21}H_{39}NO_6Si$: C, 58.71; H, 9.15; N, 3.26. Found: C, 58.79; H, 9.20; N, 3.12.

5-*O*-(*tert*-Butyldimethylsilyl)-6,7-*O*-isopropylidene-2,3-dideoxy-L-*arabino*-heptonic Acid 1,4-Lactone (*ent*-4a). The above hydrogenation−protection procedure to **4a** was adopted with 2.2 g (10.27 mmol) of unsaturated lactone *ent*-**3a** to afford protected lactone *ent*-**4a** (2.6 g, 78%) as an oil: $[\alpha]^{20}_D$ +11.3 (*c* 1.2, $CHCl_3$); ^{1}H and ^{13}C NMR spectra fully coincided with those of its enantiomer **4a**. Anal. Calcd for $C_{16}H_{30}O_5Si$: C, 58.15; H, 9.15. Found: C, 58.22; H, 9.20.

5-*O*-(*tert*-Butyldimethylsilyl)-6,7-*O*-isopropylidene-4-thio-2,3,4-trideoxy-L-*arabino*-heptonic Acid 1,4-Thiolactone (*ent*-4b). The above hydrogenation−protection procedure to **4b** was adopted with 2.0 g (8.69 mmol) of unsaturated thiolactone *ent*-**3b** to afford protected thiolactone *ent*-**4b** (1.8 g, 60%) as an oil: $[\alpha]^{20}_D$ +61.2 (*c* 2.5, $CHCl_3$); ^{1}H and ^{13}C NMR spectra fully coincided with those of its enantiomer **4b**. Anal. Calcd for $C_{16}H_{30}O_4SSi$: C, 55.45; H, 8.73. Found: C, 55.30; H, 8.90.

4-(*tert*-Butoxycarbonyl)amino]-5-*O*-(*tert*-butyldimethylsilyl)-6,7-*O*-isopropylidene-2,3,4-trideoxy-L-*arabino*-heptonic Acid 1,4-Lactam (*ent*-4c). The above hydrogenation−protection procedure to **4c** was adopted, with 2.20 g (7.0 mmol) of unsaturated lactam *ent*-**3c**, to afford saturated and protected lactam *ent*-**4c** (2.6 g, 86%) as an oil: $[\alpha]^{20}_D$ −24.4 (*c* 1.8, $CHCl_3$); ^{1}H and ^{13}C NMR spectra fully coincided with those of its enantiomer **4c**. Anal. Calcd for $C_{21}H_{39}NO_6Si$: C, 58.71; H, 9.15; N, 3.26. Found: C, 58.60; H, 9.29; N, 3.18.

2-*O*-(*tert*-Butyldimethylsilyl)-4,5-dideoxy-D-*threo*-hexuronic Acid 6,3-Lactone (5a). General Procedure. Protected lactone **4a** (2.8 g, 8.5 mmol) was dissolved in 10 mL of 70% aqueous acetic acid, and the resulting solution was allowed to react at 50 °C. The reaction was monitored by TLC and was judged complete after 8 h. The solution was then quenched with saturated $NaHCO_3$, and the resulting mixture was extracted with EtOAc (3 × 30 mL). The combined organic layers were dried ($MgSO_4$) and concentrated to give a crude residue that was purified by flash chromatography (9:1 EtOAc/MeOH). There was obtained a pure terminal diol intermediate (2.34 g, 95%) as a white solid: mp 81−83 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.68 (td, J = 7.2, 4.2 Hz, 1H), 3.86 (m, 4H), 2.85 (bs, 1H), 2.56 (m, 2H), 2.17 (m, 3H), 0.91 (s, 9H), 0.15 (s, 6H). This partially deprotected lactone was then dissolved in CH_2Cl_2 (16 mL) and treated with a 0.65 M aqueous $NaIO_4$ solution (16 mL) and chromatography grade SiO_2 (16 g). The resulting heterogeneous mixture was vigorously stirred at room temperature until complete consumption of the starting material (about 20 min, monitoring by TLC). The slurry was filtered under suction and the silica thoroughly washed with CH_2Cl_2 and EtOAc. The filtrates were evaporated to afford aldehyde **5a** (1.77 g, 85%) as colorless crystals: mp 60−61 °C; $[\alpha]^{20}_D$ −97.8 (*c* 2.7, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.67 (d, J = 1.3 Hz, 1H), 4.88 (ddd, J = 8.1, 5.4, 2.6 Hz, 1H), 4.04 (dd, J = 2.6, 1.3 Hz, 1H), 2.57 (m, 2H), 2.37 (m, 1H), 2.19 (m, 1H), 0.95 (s, 9H), 0.12 (s, 6H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 201.9, 176.5, 79.6, 79.2, 27.7, 25.5 (3 C), 23.2, 18.0, −4.7, −5.2. Anal. Calcd for $C_{12}H_{22}O_4Si$: C, 55.78; H, 8.58. Found: C, 55.65; H, 8.63.

2-*O*-(*tert*-Butyldimethylsilyl)-3,4,5-trideoxy-3-thio-D-*threo*-hexuronic Acid 6,3-Thiolactone (5b). The title compound was prepared following the two-step procedure described to transform **4a** into **5a**, starting with 1.90 g (5.48 mmol) of protected thiolactone **4b**. The first deprotection step afforded 1.60 g (95% yield) of a partially deprotected thiolactone as white crystals: mp 77−79 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.13 (m, 1H), 3.92 (m, 1H), 3.69 (m, 3H), 2.92 (bs, 2H), 2.57 (m, 2H), 2.20 (m, 1H), 2.00 (m, 1H), 0.86 (s, 9H), 0.11 (s, 3H), 0.10 (s, 3H). This intermediate was transformed into aldehyde **5b** by the same oxidative protocol as that used to afford **5a**. **5b** (1.29 g, 90%) was obtained as an oil: $[\alpha]^{20}_D$ −109.8 (*c* 1.1, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.50 (d, J = 1.5 Hz, 1H), 4.06 (m, 1H), 3.98 (dd, J = 6.9, 1.8 Hz, 1H), 2.50 (m, 2H), 2.20 (m, 1H), 2.00 (m, 1H), 0.82 (s, 9H), 0.03 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 208.0, 201.9, 79.9, 53.4, 42.0, 28.5, 25.8 (3 C), 18.3, −3.5, −3.9. Anal. Calcd for $C_{12}H_{22}O_3SSi$: C, 52.52; H, 8.08. Found: C, 52.56; H, 8.21.

2-*O*-(*tert*-Butyldimethylsilyl)-3,4,5-trideoxy-3-amino-D-*threo*-hexuronic Acid 6,3-Lactam (5c). The title compound was prepared following the two-step procedure described to transform **4a** into **5a**, starting with 2.30 g (5.35 mmol) of protected lactam **4c**. The first deprotection step afforded 1.44 g (93%) of a partially deprotected lactam as white crystals: mp 94−96 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.20 (bs, 2H), 3.91 (m, 1H), 3.74 (m, 1H), 3.5−3.7 (m, 3H), 3.32 (m, 2H), 2.17 (m, 1H), 1.95 (m, 1H), 0.90 (s, 9H), 0.12 (s, 3H), 0.11 (s, 3 H). This intermediate was transformed into aldehyde **5c** (1.15 g, 90%)

as an oil: $[\alpha]^{20}_D$ −64.5 (*c* 2.2, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 9.65 (s, 1H), 6.62 (bs, 1H), 3.91 (m, 2H), 2.25 (m, 3H), 2.02 (m, 1H), 0.94 (s, 9H), 0.12 (s, 3H), 0.11 (s, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 202.2, 178.2, 80.3, 55.2, 29.5, 25.6 (3 C), 22.5, 18.0, −4.6, −5.1. Anal. Calcd for $C_{12}H_{23}NO_3Si$: C, 55.99; H, 9.01; N, 5.44. Found: C, 56.08; H, 9.12; N, 5.31.

2-*O*-(*tert*-Butyldimethylsilyl)-4,5-dideoxy-L-*threo*-hexuronic Acid 6,3-Lactone (*ent*-5a). The above two-step procedure to **5a** was adopted, with 2.5 g (7.56 mmol) of lactone *ent*-**4a**, to afford 1.6 g (82%) of pure aldehyde *ent*-**5a** as a glassy solid: $[\alpha]^{20}_D$ +96.3 (*c* 2.4, $CHCl_3$). ^1H and ^{13}C NMR spectra fully coincided with those of its enantiomer **5a**. Anal. Calcd for $C_{12}H_{22}O_4Si$: C, 55.78; H, 8.58. Found: C, 55.70; H, 8.61.

2-*O*-(*tert*-Butyldimethylsilyl)-3,4,5-trideoxy-3-thio-L-*threo*-hexuronic Acid 6,3-Thiolactone (*ent*-5b). The above two-step procedure to **5b** was adopted, with 1.7 g (4.90 mmol) of thiolactone *ent*-**4b**, to afford 1.19 g (88%) of pure aldehyde *ent*-**5b** as an oil: $[\alpha]^{20}_D$ +107.3 (*c* 1.1, $CHCl_3$). ^1H and ^{13}C NMR spectra fully coincided with those of its enantiomer **5b**. Anal. Calcd for $C_{12}H_{22}O_3SSi$: C, 52.52; H, 8.08. Found: C, 52.48; H, 7.89.

2-*O*-(*tert*-Butyldimethylsilyl)-3,4,5-trideoxy-3-amino-L-*threo*-hexuronic Acid 6,3-Lactam (*ent*-5c). The above two-step procedure to **5c** was adopted, with 2.5 g (5.82 mmol) of lactam *ent*-**4c**, to afford 1.23 g (82%) of pure aldehyde *ent*-**5c** as an oil: $[\alpha]^{20}_D$ +65.8 (*c* 2.1, $CHCl_3$). ^1H and ^{13}C NMR spectra fully coincided with those of its enantiomer **5c**. Anal. Calcd for $C_{12}H_{23}NO_3Si$: C, 55.99; H, 9.01; N, 5.44. Found: C, 55.75; H, 9.12; N, 5.60.

(−)-Muricatacin [(*R*,*R*)-1a]. General Procedure. *n*-Butyllithium (7.2 mL of a 1.6 M solution in hexanes, 11.5 mmol) was added to a solution of undecyl triphenylphosphonium bromide (5.9 g, 11.9 mmol) in anhydrous THF (30 mL) at −80 °C. After 3 h, aldehyde **5a** (1.7 g, 6.58 mmol), previously dissolved in 30 mL of anhydrous THF, was added to this red-orange solution at −80 °C. The resulting solution was allowed to warm to room temperature, and after 3 days, the reaction was concentrated under vacuum, poured into water, and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were dried ($MgSO_4$) and concentrated to provide a crude residue that was purified by flash chromatography (8:2 hexanes/EtOAc). There was obtained a 9:1 *Z*/*E* mixture of an olefin intermediate (1.57 g, 60%) as an oil: ^1H NMR (300 MHz, $CDCl_3$, *Z*-isomer) δ 5.52 (m, 1H), 5.39 (t, *J* = 8.7 Hz, 1H), 4.51 (dd, *J* = 8.7, 4.2 Hz, 1H), 4.45 (m, 1H), 2.56 (ddd, *J* = 17.5, 10.2, 7.5 Hz, 1H), 2.43 (ddd, *J* = 17.5, 9.6, 6.3 Hz, 1H), 2.0−2.3 (m, 4H), 1.26 (m, 16H), 0.87 (m, 12H), 0.07 (s, 3H), 0.05 (s, 3H). A solution of this unsaturated compound (1.5 g, 3.78 mmol) in dry THF (30 mL) was subjected to catalytic hydrogenation with 10% Pd on carbon (124 mg) in the presence of NaOAc (52 mg) at room temperature for 24 h. The catalyst was then removed by filtration and the filtrate concentrated to give a crude residue, which was subjected to flash chromatographic purification (8:2 hexanes/EtOAc). This material (1.4 g, 3.51 mmol, 93%) was dissolved in dry $CHCl_3$ (20 mL), and BF_3 etherate (0.86 mL, 7.02 mmol) was added dropwise to the stirring solution at ambient temperature. After 8 h, the reaction was quenched with solid $NaHCO_3$, and the resulting mixture was concentrated under vacuum to afford a crude residue, which was purified by flash chromatography (6:4 hexanes/EtOAc). There was obtained pure muricatacin [(*R*,*R*)-**1a**] (0.9 g, 90%) as colorless crystals: mp 71−73 °C; $[\alpha]^{20}_D$ −23.1 (*c* 1.5, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 4.42 (td, *J* = 7.2, 4.5 Hz, 1H), 3.58 (m, 1H), 2.63 (ddd, *J* = 17.7, 9.9, 5.4 Hz, 1H), 2.54 (dt, *J* = 17.7, 9.0, 1H), 2.0−2.3 (m, 2H), 1.86 (d, *J* = 5.7 Hz, 1H), 1.4−1.6 (m, 2H), 1.1−1.4 (m, 20H), 0.87 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 177.2, 82.9, 73.7, 33.0, 31.9, 29.6 (3 C), 29.5 (3 C), 29.3, 28.7, 25.4, 24.1, 22.7, 14.1. Anal. Calcd for $C_{17}H_{32}O_3$: C, 71.79; H, 11.34. Found: C, 71.75; H, 11.41. Reported data: mp 72 °C; $[\alpha]^{24}_D$ −22.9 (*c* 1.1, $CHCl_3$) (ref 6a); mp 73−74 °C, $[\alpha]_D$ −23.14 (*c* 2.36, $CHCl_3$) (ref 6c); mp 67−68 °C, $[\alpha]_D$ −23.3 (*c* 1.8, $CHCl_3$) (ref 6d).

(−)-Thiomuricatacin [(*R*,*R*)-1b]. The above procedure to (*R*,*R*)-**1a** was adopted, starting with aldehyde **5b** (1.27 g, 4.62 mmol). An unsaturated intermediate formed as a 9:1 *Z*/*E* isomeric mixture (1.24 g, 65%) as an oil: ^1H NMR (300 MHz, $CDCl_3$, *Z* isomer) δ 5.54 (dt, *J* = 11.4, 6.9 Hz, 1H), 5.29 (bt, *J* = 11.4 Hz, 1H), 4.49 (t, *J* = 8.1 Hz, 1H), 3.88 (bq, *J* = 8.1 Hz, 1H), 2.62 (ddd, *J* = 16.8, 9.3, 5.1 Hz, 1H), 2.53 (ddd, *J* = 16.8, 9.9, 7.2 Hz, 1H), 1.9−2.3 (m, 2H), 1.68 (m, 2H), 1.2−1.4 (m, 16H), 0.87 (m, 12H), 0.07 (s, 3H), 0.03 (s, 3H). Hydrogenation and BF_3 etherate-promoted deprotection of this intermediate finally gave a crude residue, which was subjected to flash chromatographic purification (8:2 hexanes/EtOAc) to furnish pure thiomuricatacin [(*R*,*R*)-**1b**] (0.84 g, 94%) as colorless crystals: mp 40−42 °C; $[\alpha]^{20}_D$ −39.1 (*c* 1.1, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 3.98 (ddd, *J* = 7.5, 6.3, 4.8 Hz, 1H), 3.77 (ddd, *J* = 8.8, 4.8, 4.5 Hz, 1H), 2.73 (ddd, *J* = 16.8, 7.5, 5.4 Hz, 1H), 2.56 (ddd, *J* = 16.8, 9.0, 7.8 Hz, 1H), 2.32 (dddd, *J* = 13.2, 7.8, 6.3, 5.4 Hz, 1H), 2.17 (dddd, *J* = 13.2, 9.0, 7.5, 7.5 Hz, 1H), 1.71 (bs, 1H), 1.50 (m, 2H), 1.1−1.4 (m, 20H), 0.88 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 208.0, 74.3, 56.9, 42.0, 36.4, 31.9, 29.6, 29.5, 29.4 (3C), 29.3, 28.9, 28.5, 25.6, 22.6, 14.1. Anal. Calcd for $C_{17}H_{32}O_2S$: C, 67.95; H, 10.73. Found: C, 67.90; H, 10.78.

(−)-Azamuricatacin [(*R*,*R*)-1c]. The above procedure to (*R*,*R*)-**1a** was adopted, starting with aldehyde **5c** (1.0 g, 3.89 mmol). An unsaturated intermediate formed as a 9:1 *Z*/*E* isomeric mixture (0.92 g, 60%) as an oil: ^1H NMR (300 MHz, $CDCl_3$, *Z*-isomer) δ 5.75 (bs, 1H), 5.53 (m, 1H), 5.24 (m, 1H), 4.20 (t, *J* = 8.7 Hz, 1H), 3.52 (m, 1H), 2.32 (m, 2H), 2.05 (m, 2H), 1.69 (m, 1H), 1.27 (m, 17H), 0.88 (m, 12H), 0.06 (s, 3H), 0.03 (s, 3H). Hydrogenation and BF_3 etherate-promoted deprotection of this intermediate finally gave a crude residue, which was subjected to flash chromatographic purification (9:1 EtOAc/MeOH) to furnish pure azamuricatacin [(*R*,*R*)-**1c**] (0.61 g, 93%) as a white solid: mp 63−65 °C; $[\alpha]^{20}_D$ −13.3 (*c* 0.3, MeOH); $[\alpha]^{20}_D$ −9.2 (*c* 0.4, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 6.30 (bs, 1H), 3.54 (q, *J* = 7.0 Hz, 1H), 3.38 (m, 1H), 2.37 (m, 2H), 2.26 (bs, 1H), 2.16 (m, 1H), 1.78 (m, 1H), 1.47 (m, 2H), 1.2−1.4 (m, 20H), 0.88 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 178.2, 75.5, 59.1, 33.5, 31.9, 30.3, 29.6 (3 C), 29.5 (3 C), 29.3, 25.3, 23.8, 22.7, 14.1. Anal. Calcd for $C_{17}H_{33}NO_2$: C, 72.04; H, 11.73; N, 4.94. Found: C, 72.10; H, 11.75; N, 4.81.

(+)-Muricatacin [(*S*,*S*)-1a]. The above three-step procedure to (*R*,*R*)-**1a** was adopted, with aldehyde *ent*-**5a** (1.5 g, 5.8 mmol), to afford pure muricatacin [(*S*,*S*)-**1a**] (0.87 g, 53%) as a white solid: mp 73−74 °C; $[\alpha]^{20}_D$ +23.0 (*c* 1.6, $CHCl_3$); ^1H and ^{13}C NMR spectra fully coincided with those of its enantiomeric counterpart (*R*,*R*)-**1a**. Anal. Calcd for $C_{17}H_{32}O_3$: C, 71.79; H, 11.34. Found: C, 71.53; H, 11.45. Reported data: mp 65 °C, $[\alpha]^{25}_D$ +25 (*c* 1.7, MeOH) (ref 6b); mp 73−74 °C, $[\alpha]_D$ +23.02 (*c* 1.26, $CHCl_3$) (ref 6c); mp 67−68 °C, $[\alpha]_D$ +22.6 ($CHCl_3$) (ref 6d); mp 72 °C, $[\alpha]_D$ +23.6 (*c* 1.50, $CHCl_3$) (ref 6e); mp 65−66 °C, $[\alpha]^{23}_D$ +23.6 (*c* 1.6, $CHCl_3$) (ref 6f).

(+)-Thiomuricatacin [(*S*,*S*)-1b]. The above three-step procedure to (*R*,*R*)-**1b** was adopted, with aldehyde *ent*-**5b** (1.1 g, 4.0 mmol), to afford pure thiomuricatacin [(*S*,*S*)-**1b**] (0.7 g, 58%) as a glassy solid: $[\alpha]^{20}_D$ +36.2 (*c* 1.8, $CHCl_3$). ^1H and ^{13}C NMR spectra fully coincided with those of its enantiomeric counterpart (*R*,*R*)-**1b**. Anal. Calcd for $C_{17}H_{32}O_2S$: C, 67.95; H, 10.73. Found: C, 67.85; H, 10.82.

(+)-Azamuricatacin [(*S*,*S*)-1c]. The above three-step procedure to (*R*,*R*)-**1c** was adopted, with aldehyde *ent*-**5c** (1.0 g, 3.89 mmol), to afford pure azamuricatacin [(*S*,*S*)-**1c**] (0.64 g, 58%) as a white solid: mp 63−64 °C; $[\alpha]^{20}_D$ +14.0 (*c* 0.4, MeOH); $[\alpha]^{20}_D$ +10.3 (*c* 0.4, $CHCl_3$). ^1H and ^{13}C NMR spectra fully coincided with those of its enantiomeric counterpart (*R*,*R*)-**1c**. Anal. Calcd for $C_{17}H_{33}NO_2$: C, 72.04; H, 11.73; N, 4.94. Found: C, 71.95; H, 11.81; N, 4.90.

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