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Structural Determination of (−)-SCH 64874 and Hirsutellomycin by Semisynthesis

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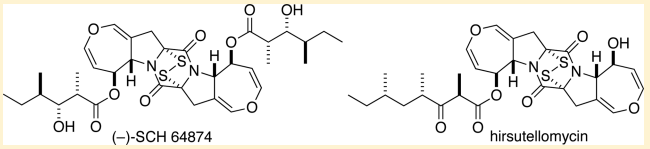
Supporting Information

ABSTRACT: The structure of a C_2-symmetric epidithiodiketopiperazine alkaloid, SCH 64874, was determined by semisynthesis. The relative stereochemistry of the β-hydroxy carboxylic acid chain having three chiral centers was determined by comparison of the NMR data of the four possible diastereomeric β-hydroxy carboxylic acid fragments with those of SCH 64874. Condensation of the (−)-deacetylaranotin core with two enantiomeric β-hydroxy carboxylic acids revealed the relative stereochemistry of SCH 64874. The relative stereochemistry of the β-keto carboxylic acid chain of the analogous alkaloid hirsutellomycin was determined in a stepwise manner. The C4′−C6′ *syn* relationships were predicted by comparing the NMR data of the corresponding ester fragments with that of hirsutellomycin. The relative stereochemistry of the whole molecule, including the epimerizable C2′ stereocenter, was determined by introduction of four possible side chains into the bisdethiodi(methylthio)deacetylaranotin core. We found that the stereochemistry of C2′ converged with that of the thermodynamically stable form influenced by the core structure.



INTRODUCTION

Epidithiodiketopiperazine (ETP) alkaloids have attracted considerable attention because of their unique structures possessing a sulfur-bridged diketopiperazine core and intriguing biological activities.[1] Among them, seven-membered dihydrooxepine-fused pyrrolidine/ETPs such as (−)-acetylaranotin (**1**),[2] (−)-emethallicin A (**2**),[3] and (−)-MPC1001 (**3**)[4] have been thoroughly investigated for the last few decades, since they exhibit fascinating biological activities (Figure 1). In spite of these attractive features, synthetic difficulties and a scarcity of natural compounds prevented this class of compounds from being further studied even in terms of their structural determination.

(−)-SCH 64874 (**4**),[5] isolated from the organic extract of the fermentation broth of an unidentified fungus, is one such compound that has been investigated due to its fascinating biological activities. This compound displays potent epidermal growth factor receptor antagonist activity. Although Hegde and co-workers presumed the structure of **4** to possess a (−)-deacetylaranotin (**5**) core, the absolute stereochemistry of the molecule and relative stereochemistry of the side chain remain unknown. Hirsutellomycin (**6**),[6] which had been isolated from the submerged cultures of the entomopathogenic fungus *Hirsutella kobayasii* BCC 1660 by former colleagues of one of the authors of this paper (M.I.) at the BIOTEC, Thailand, was reported to possess potent antituberculosis capabilities.[6] However, only the planar structure was investigated, and further biological activities have not yet been studied; this is due to the exhaustion of the supply of natural samples, and because the strain of *H. kobayashi* which produced **6** ceased to be in production. For accelerating further medical and biochemical investigations on these promising compounds, structural determination based on a synthetic approach is unavoidable. In this paper, we describe the semisynthesis of **4**

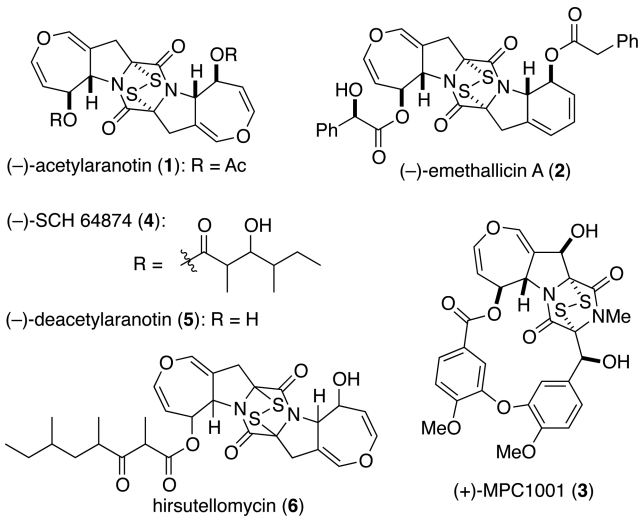


Figure 1. Epidithiodiketopiperazines (ETPs).

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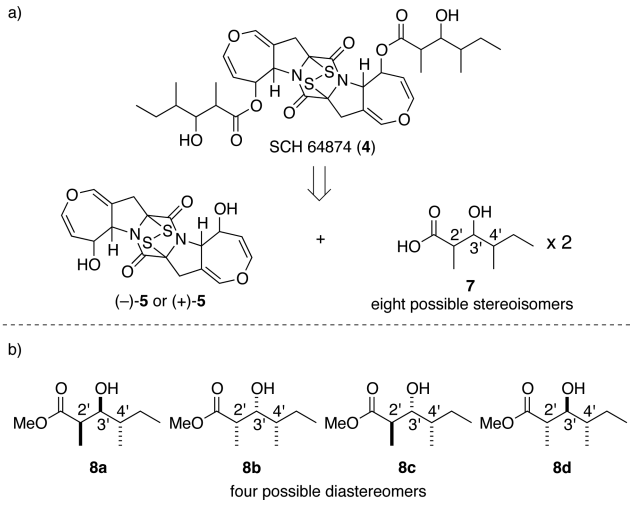
and **6**, aiming at the elucidation of the structure of these compounds.

RESULTS AND DISCUSSION

Structural Determination of SCH 64874. We designed a strategy for the semisynthesis of structurally unidentified SCH 64874 (**4**) so that synthetic efforts would become as efficient as possible (Scheme 1). Considering the C_2 symmetry,[5] **4** can be

Scheme 1. Strategy for Structural Determination of SCH 64874 (4)

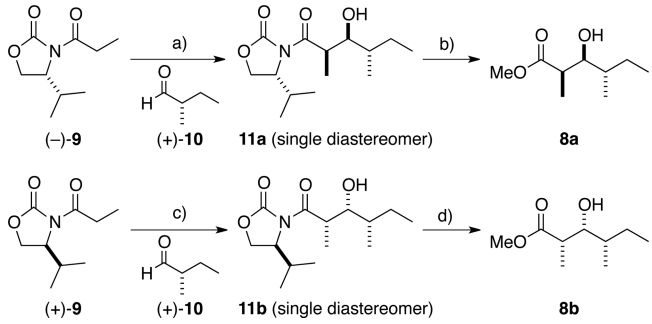


divided into (−)- or (+)-**5** and the two equivalent carboxylic acids **7**, which should be one of the eight possible stereoisomers (Scheme 1a). Due to the limited availability of (−)-**1**, a precursor of (−)-**5**, by the fermentation and isolation process, we used the following efficient strategy to semisynthesize (−)-**4** using a minimum amount of the deacetylaranotin core (−)-**5**. Thus, we tried to predict the relative stereochemistry of carboxylic acid **7** by comparing the NMR spectra of four possible diastereomeric esters **8a**−**d** with those of the corresponding side chain of the natural compound (Scheme 1b). Then, condensation of (−)-**5** with two enantiomers of carboxylic acid **7** possessing the predicted relative stereochemistry should reveal the relative stereochemistry between the aranotin core and the side chain and should reveal the absolute stereochemistry of **4** by comparing the optical rotation with the natural compound.

Esters **8a** and **8b** were synthesized using the Evans aldol reaction (Scheme 2).[7] Treatment of (−)-**9** with *n*-Bu_2BOTf[8]/Et_3N, followed by addition of aldehyde (+)-**10**,[9] afforded aldol product **11a** as a single diastereomer. The chiral auxiliary was removed by methanolysis to give ester **8a**.[10] Similarly, a combination of the boron enolate prepared from (+)-**9** and (+)-**10** afforded aldol product **11b**,[7] which was converted to ester **8b**[7] by methanolysis.

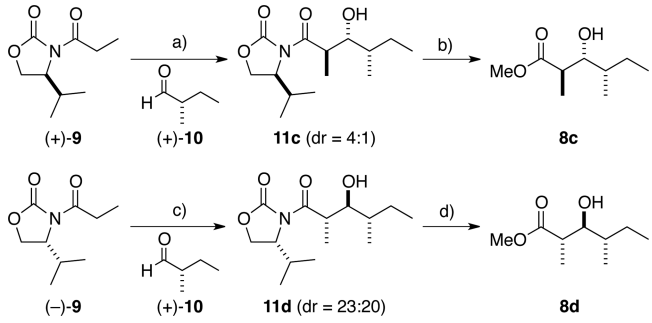
Conversely, esters **8c**[11] and **8d** were synthesized by a non-Evans *anti*-type aldol reaction (Scheme 3).[12] Treatment of (+)-**9** with *n*-Bu_2BOTf/*i*-Pr_2NEt, followed by addition of (+)-**10** in the presence of $SnCl_4$, afforded aldol product **11c** as a 4:1 diastereomeric mixture. After the separation of the minor diastereomer, the chiral auxiliary was removed by methanolysis to furnish ester **8c**. Ester **8d** was also synthesized via aldol product **11d** by the same protocol starting from (−)-**9**.

Scheme 2. Synthesis of Esters 8a and 8b[a]



[a]Reagents and conditions: (a) *n*-Bu_2BOTf, Et_3N, CH_2Cl_2, −78 to 0 °C then (+)-**10**, −78 to 0 °C, 63% (single diastereomer); (b) NaOMe, MeOH, 0 °C, 91%; (c) *n*-Bu_2BOTf, Et_3N, CH_2Cl_2, −78 to 0 °C; (+)-**10**, −78 to 0 °C, 83% (single diastereomer); (d) NaOMe, MeOH, 0 °C, 81%.

Scheme 3. Synthesis of Esters 8c and 8d[a]



[a]Reagents and conditions: (a) *n*-Bu_2BOTf, *i*-Pr_2NEt, CH_2Cl_2, −78 to 0 °C; (+)-**10**, $SnCl_4$, −78 to 0 °C, dr = 4:1; separation, 47%; (b) NaOMe, MeOH, 0 °C, 82%; (c) *n*-Bu_2BOTf, *i*-Pr_2NEt, CH_2Cl_2, −78 to 0 °C; (+)-**10**, $SnCl_4$, −78 to 0 °C, dr = 23:20; separation, 36%; (d) NaOMe, MeOH, 0 °C, 64%.

With the requisite diastereomers **8a**−**d** in hand, a careful NMR analysis was performed to predict the relative stereochemistry of the side chain of the natural product. Initially, differences in ^{13}C NMR chemical shifts between the side chains of **4** and each of the diastereomers **8a**−**d** were calculated (Figure 2). Differences between the ^{13}C NMR spectra of **4** and those of **8a**−**c** were smaller than those of **8d**. Next, we compared their ^1H NMR spectra to that of **4** (Figure 3). It was observed that the ^1H NMR spectrum of **8a** was very close to that of **4**, whereas that of **8b**−**d** had a big difference regarding the 3′ and/or 5′ position. These results clearly indicated that the relative stereochemistry of the side chains of **4** corresponds to that of **8a**.

Finally, both carboxylic acid (−)-**13** and its enantiomer were introduced onto the (−)-deacetylaranotin (**5**) core to determine the relative and absolute stereochemistry of **4**. THP-protected *β*-hydroxy carboxylic acids (−)-**13** and (+)-**13** were prepared from **11a** and **11e**,[13] respectively, by THP protection followed by the removal of the chiral auxiliary (Scheme 4).

The (−)-deacetylaranotin (**5**) core was prepared from (−)-acetylaranotin (**1**), which was isolated from fermentation broth of *Aspergillus terrreus* BCC 4480. Treatment of **1** with a weak acid (0.9% aq. HCl in MeOH) afforded (−)-**5** without the loss of the disulfide bridge (Scheme 5).[14] (−)-Diol **5** was condensed with two carboxylic acids (−)-**13** using WSCD·

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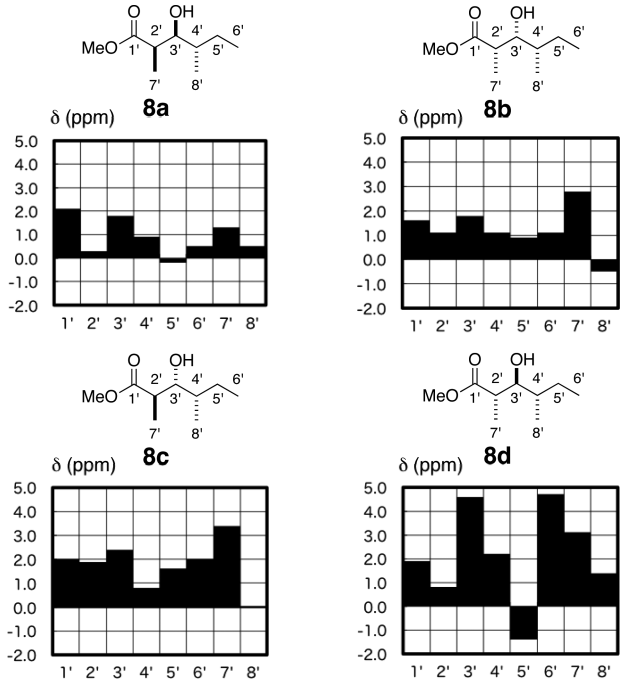


Figure 2. Comparative study of ^{13}C NMR data (100 MHz, $CDCl_3$).

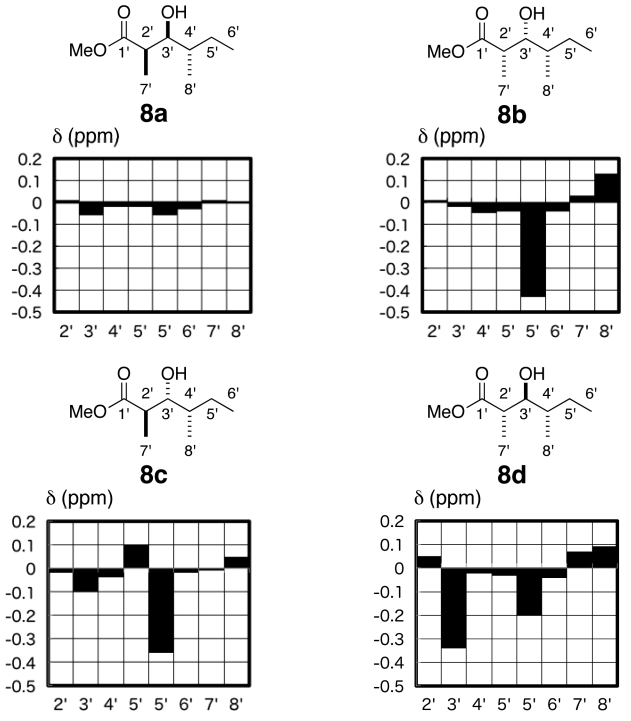
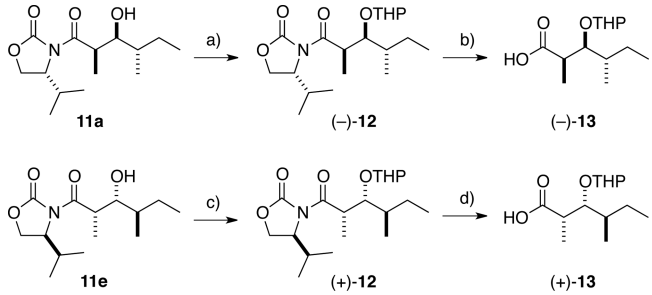


Figure 3. Comparative study of ^{1}H NMR data (400 MHz, $CDCl_3$).

HCl/DMAP to give diester **14** in moderate yield. Finally, the THP groups were removed by a careful treatment with PPTS[15] to obtain **15**. In addition, **17** was also derived from (−)-**5** and two (+)-**13** fragments by the same protocol.

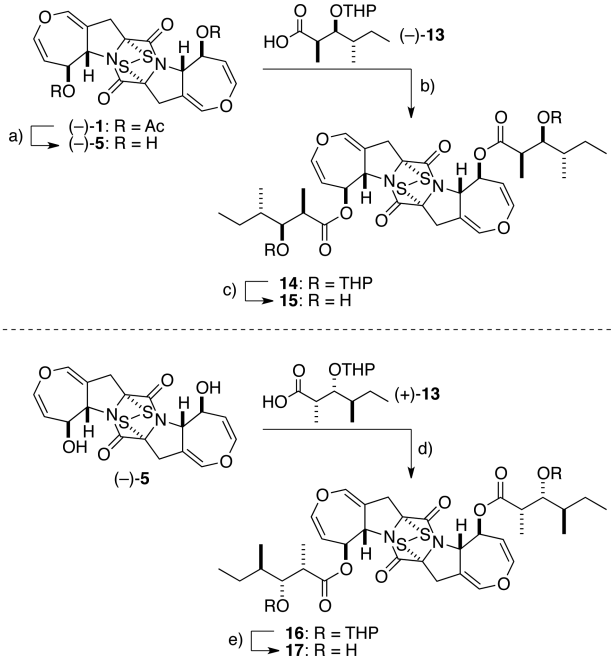
The difference between the chemical shifts in the ^{13}C and ^{1}H NMR spectra of **4** and synthetic compounds **15** and **17** (Figure 4) clearly demonstrated that the NMR profile of **17** completely matched with **4**, indicating that the relative stereochemistry of **4** was that described in **17**. In addition, the negative optical rotation of synthetic **17** matched with that of natural **4** ($[\alpha]_D^{29}$ = −169° (c = 0.141, $CHCl_3$), lit. $[\alpha]_D^{29}$ = −301.1° (solvent and concentration were not reported)),[5] strongly suggesting that the absolute configuration of **4** should be that of **17**.[16]

Scheme 4. Synthesis of Carboxylic Acids (−)-13 and (+)-13[a]



[a]Reagents and conditions: (a) DHP, $TsOH·H_2O$, CH_2Cl_2, rt, 90%; (b) $LiOH·H_2O$, H_2O_2, THF-H_2O (7:2), 0 °C to rt, 82%; (c) DHP, $TsOH·H_2O$, CH_2Cl_2, rt, 76%; (d) $LiOH·H_2O$, H_2O_2, THF-H_2O (7:2), 0 °C to rt, 84%.

Scheme 5. Synthesis of two Candidates of SCH 64874 (4)[a]



[a]Reagents and conditions: (a) 0.9% aq. HCl in MeOH, rt, 72%; (b) (−)-**13** WSCD·HCl, DMAP, CH_2Cl_2, rt, 42%; (c) PPTS, MeOH-CH_2Cl_2, rt, 66%; (d) (+)-**13** WSCD·HCl, DMAP, CH_2Cl_2, rt, 38%; (e) PPTS, MeOH-CH_2Cl_2, rt to 40 °C, 86%.

Structural Determination of Hirsutellomycin. The focus of our investigation then moved onto the structural determination of hirsutellomycin (**6**) by semisynthesis. Due to the unavailability of natural hirsutellomycin (**6**), our only means of determining its structure was chemical synthesis. Our own analysis of the NMR spectra (^{1}H NMR, ^{13}C NMR, DEPTs, COSY, HMQC, and HMBC) provided by the isolation chemists agreed with the reported planar structure of **6**. The close resemblance of the NMR data obtained for natural hirsutellomycin (**6**) with those of acetylaranotin and SCH 64874 (**17**) suggested that **6** shares the same relative configuration of it is deacetylaranotin core. Unfortunately, due to a lack of data regarding its optical rotation, it was impossible to determine the absolute stereochemistry of **6**.

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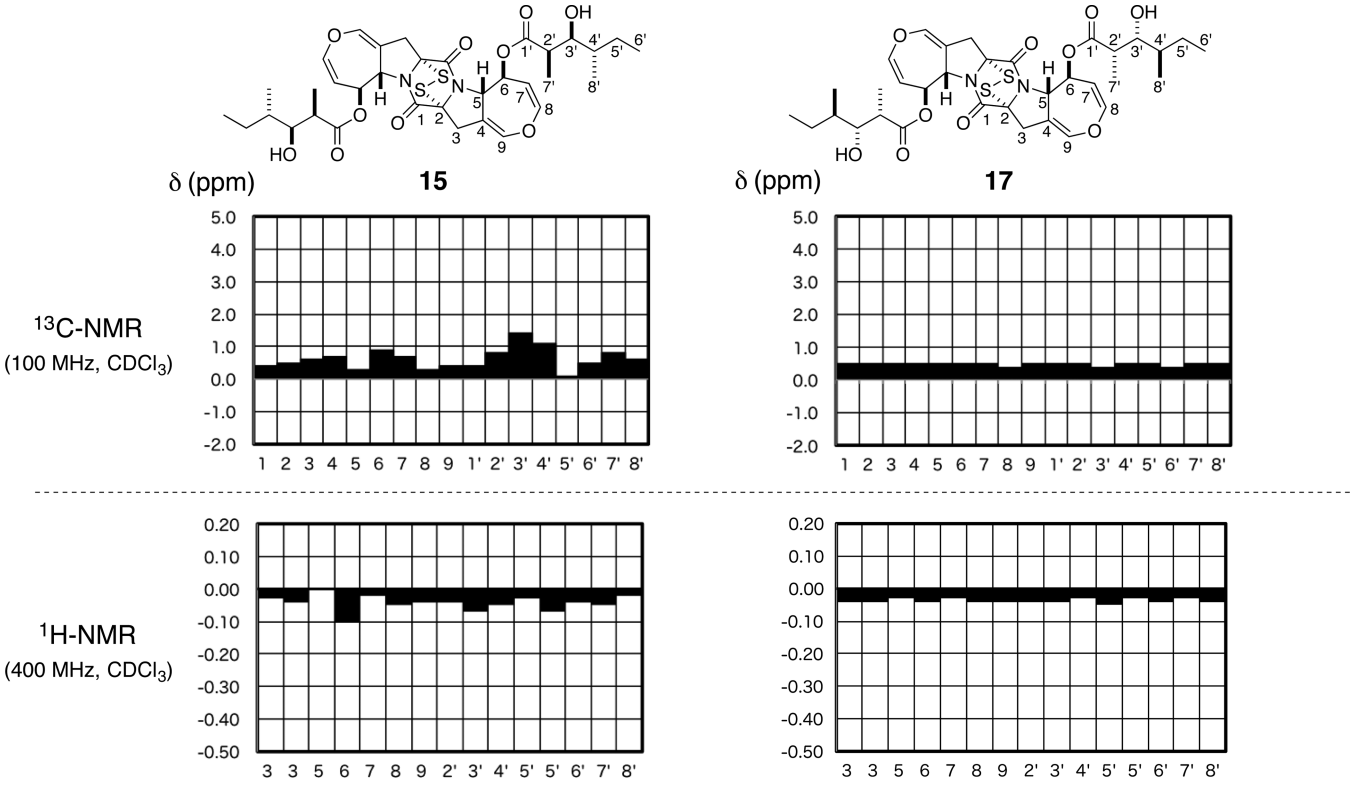
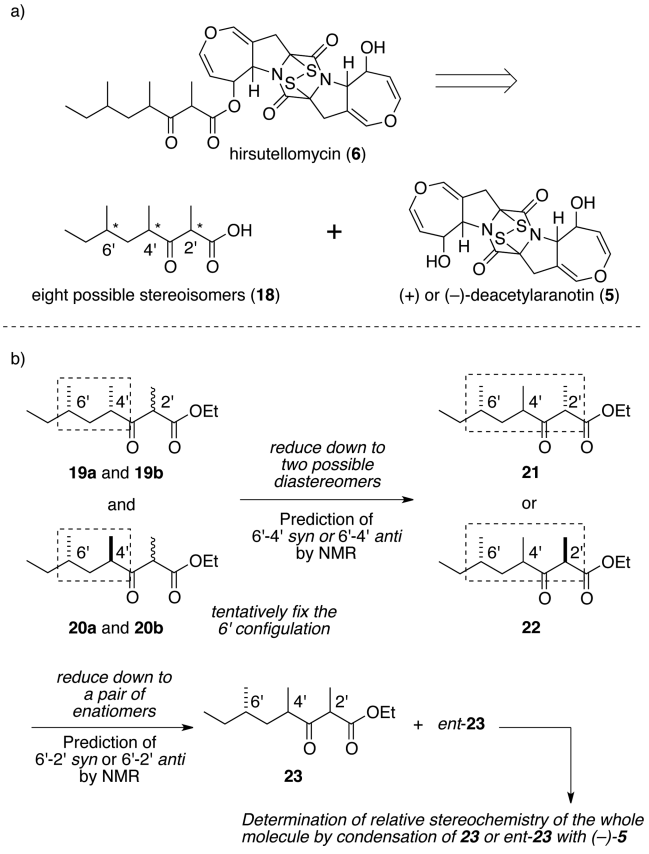


Figure 4. Comparative study of NMR data.

However, the fact that all of the analogous fungal epipolythiodiketopiperazines, including **1**, **2**, **3**, **17**, aranotin, and apoaranotin, contain (−)-deacetylaranotin-like (dihydroxepine-containing) cores, while not containing its antipode, strongly suggests that hirsutellomycin (**6**) should also have a (−)-deacetylaranotin core. Based on this hypothesis, we planned a semisynthesis strategy similar to the one used for SCH 64874 using a (−)-deacetylaranotin (**5**).

We planned an efficient strategy for the semisynthesis of the structurally unidentified compound **6** (Scheme 6). A disconnection in the ester moiety of **6** gives a *β*-keto carboxylic acid fragment **18** (Scheme 6a). In order to avoid the tedious preparation of the eight possible enantiomers of **18**, we used Professor Kishi's Universal NMR Data Base concept[17] to try to predict the relative stereochemistry C6′−C4′ using simple ester fragments. The concept states that the stereoelectronic interactions and the spectroscopic properties between the structural clusters in a molecule depend on the substituents that are connected either directly to or with a one-methylene bridge that does not depend on the rest of the molecule.[17] Thus, the absolute configuration of C6′ was tentatively fixed to be *S*, and the relative configuration between C6′−C4′ was predicted by comparing the NMR data of the ethyl esters **19** and **20** with the corresponding part of the ester chain of the natural compound **6** (Scheme 6b). This would reduce the four possible diastereomers down to just two (**21** or **22**). The prediction of the relative stereochemistry between C2′ and C6′ would further reduce the possibility down to just one diastereomer and its enantiomer. Finally, a condensation of the naturally occurring (−)-deacetylaranotin core with **23** and *ent*-**23** revealed the diastereomeric relationship between the side chain and the deacetylaranotin core, respectively, which could be used to determine the relative stereochemistry of **6**.

Scheme 6. Strategy for Structural Determination of Hirsutellomycin (6)



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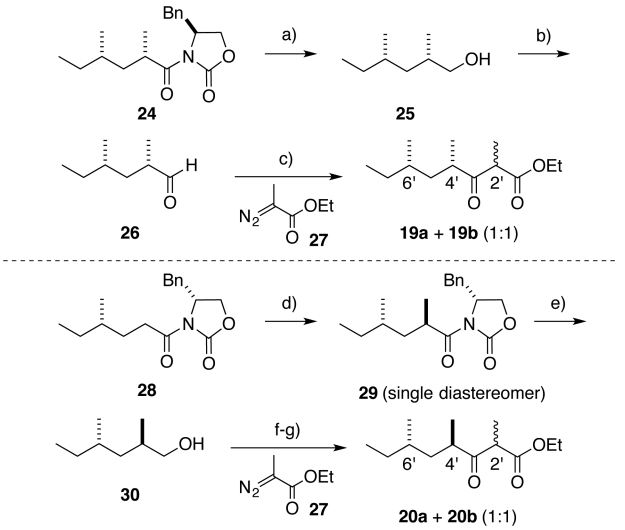
Esters **19** and **20** were prepared as diastereomeric mixtures regarding the C2′position from the known compounds of **24**[18] and **28**,[19] respectively (Scheme 7). Removal of the

Scheme 7. Synthesis of β-Keto Esters 19 and 20.[a]



[a]Reagents and conditions: (a) $LiBH_4$, THF-MeOH, 0 °C to rt; (b) SO_3·Py, Et_3N, CH_2Cl_2-DMSO, 0 °C; (c) **27**, $SnCl_2$, CH_2Cl_2, rt, 24% (3 steps, **19a**:**19b** = 1:1); (d) NaHMDS, THF,−78 °C; MeI, 71% (single diastereomer); (e) $LiBH_4$, THF-MeOH, 0 °C to rt; (f) SO_3·Py, Et_3N, CH_2Cl_2-DMSO, 0 °C to rt; (g) **27**, $SnCl_2$, CH_2Cl_2, rt, 20% (3 steps, **20a**:**20b** = 1:1).

oxazolidinone with $LiBH_4$ provided alcohol **25**, which was then subjected to Parikh−Doering oxidation[20] to give aldehyde **26**. Treatment of aldehyde **26** with diazoester **27** afforded the desired 4′,6′-*syn* ethyl ester **19a** and **19b** as a 1:1 diasteromiric mixture.[21] On the other hand, diastereoselective methylation of **28** gave **29** as a single diastereomer. As described in the synthesis of **19**, **29** was converted to a 1:1 diastereomeric mixture of 4′,6′-*anti* ethyl ester **20a** and **20b**.

A comparison between the ^1H NMR spectra of **6** with those of **19** and **20** suggested that the relative configurations between C-4′ and C-6′ of the natural product would be *syn* (Figure 5).[22] As such, a signal corresponding to the C-5′ position of **6** (1.7−1.8 ppm) was also observed for **19** (1.6−1.8 ppm). In contrast,

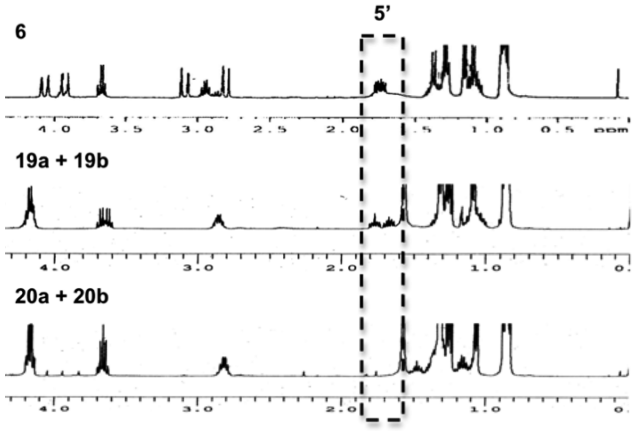
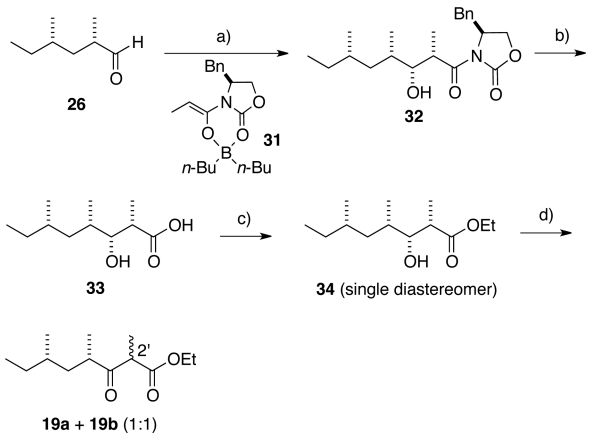


Figure 5. Comparative study of ^1H NMR spectrum (400 MHz, $CDCl_3$).

the signals on the C-5′ of **20** appeared far from those of **19** and **6** (1.48 and 1.25 ppm, respectively).

Next, we attempted to predict the relative stereochemistry between the C4′,6′, and C2′ positions by the stereoselective synthesis of esters **19a** (C2′-C6′ *syn*) and **19b** (C2′-C6′ *anti*) and the comparison of their NMR data. However, as the stereochemistry of the C2′ position was easily epimerized and giving a 1:1 mixture of the diastereomers, we abandoned this strategy (Scheme 8). An attempt was made to prepare **19a** by

Scheme 8. Trial for the Synthesis of β-Keto Ester 19a[a]

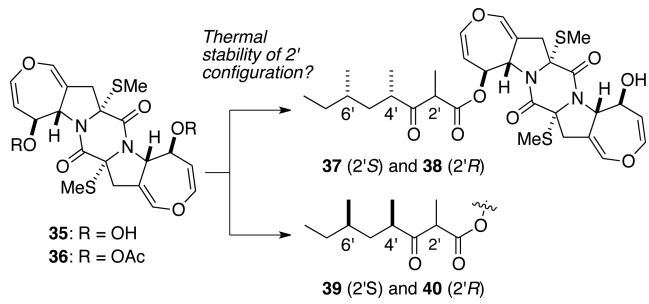


[a]Reagents and conditions: (a) **31**, −78 to 0 °C; separation, 65% (3 steps from **24**); (b) LiOH·H_2O, H_2O_2, THF, 0 °C to rt, 86%; (c) K_2CO_3, EtI, acetone, 50 °C, 89%; (d) Dess−Martin periodinane, CH_2Cl_2, 0 °C, 90% (**19a**:**19b** = 1:1).

first using the aldol reaction of the aldehyde **26** with a boron enolate **31** to give the aldol **32**[23] as the sole product. After the removal of the chiral auxiliary through basic hydrolysis, the resultant carboxylic acid was converted to an ethyl ester **34** under alkylation conditions. Unfortunately, the oxidation of the hydroxyl group with a Dess−Martin periodinane[24] gave a 1:1 mixture of **19a** and **19b**.

The revised strategy is depicted in Scheme 9. We considered that the stereochemistry on the side chain of C2′ was strongly

Scheme 9. Strategy for Determination of Relative Configuration



affected by the core skeleton, and so a thermodynamically more stable compound should exist. With this hypothesis, we planned to synthesize a series of compounds **37**−**40** by introduction of four possible diastereoisomers of side chains on the core skeleton and examine their thermodynamic stability. We chose the more abundant and easily available bisdethiodi-(methylthio) deacetylaranotin **35**[25] (from **36**) instead of the

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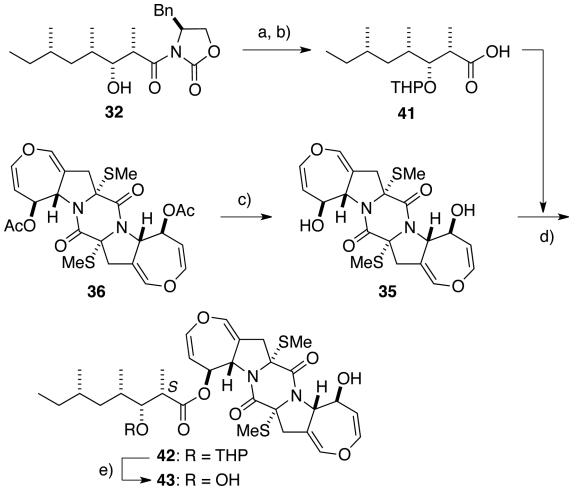
(−)-deacetylaranotin (**5**) as the core skeleton for this synthesis. In addition to elucidating the relationship between C4′,6′, and C2′, we hoped to obtain information on the relative stereochemistry between the core skeleton and the side chain.

Scheme 10 illustrates one example of introduction of side chain fragments onto the core skeleton **35**. The aldol product

Scheme 10. Introduction of the Side Chain Fragments[a]



[a]Reagents and conditions: (a) DHP, PPTS, CH_2Cl_2, rt; (b) LiOH·H_2O, H_2O_2, THF-H_2O, 0 °C to rt, 89% (2 steps); (c) K_2CO_3, MeOH, rt, quant.; (d) **41**, WSCD·HCl, DMAP, CH_2Cl_2, reflux, 36%; (e) PPTS, MeOH-CH_2Cl_2, 40 °C, 78%.

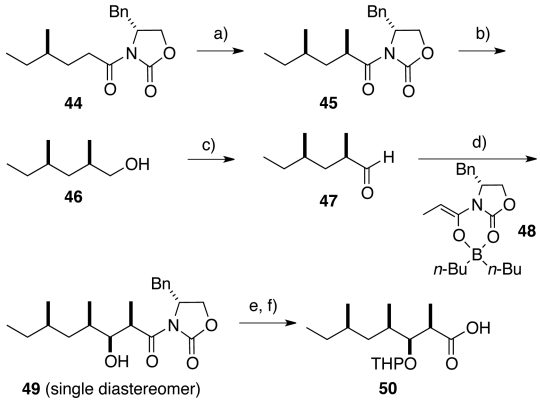
32 was converted into a carboxylic acid **41** via protection of hydroxyl group and hydrolysis of chiral auxiliary. Treatment of diacetate **36** with K_2CO_3 in MeOH produced alcohol **35**, which was condensed with carboxylic acid **41** to give the ester **42** in moderate yield. Acidic deprotection of THP group[15] gave *β*-hydroxy ester **43**.

Other carboxylic acids that were required to synthesize **38**, **39**, and **40** were synthesized by standard transformations. For example, the preparation of **50** started with the diastereoselective methylation of **44**[26] to give **45**,[27] which was subsequently converted to the aldehyde **47** through the removal of the chiral auxiliary and a Parikh−Doering oxidation[20] (Scheme 11). After the stereoselective aldol reaction of the aldehyde **47** with a boron enolate **48**, the resulting aldol **49** was protected by a THP group,[15] and the oxazolidinone was removed so as to furnish the carboxylic acid **50**.

Having prepared these carboxylic acids, these compounds were condensed with the core skeleton **35** through the same protocol used to obtain ester **43** (vide supra). The configurational stability of the C2′ position of the resultant esters was then carefully inspected (Scheme 12).

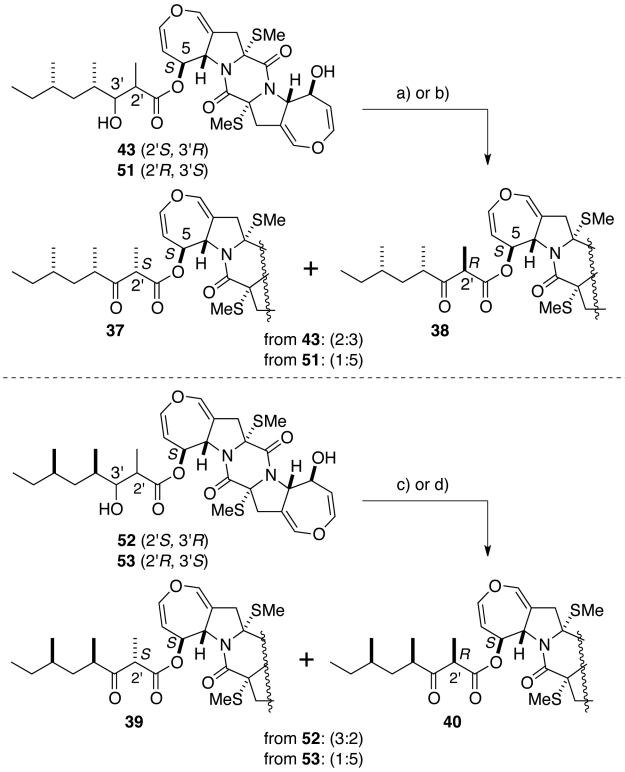
In all of the cases, the C2′ stereochemistry was epimerized so as to preferentially provide the C2′(*R*) isomer during the Dess−Martin oxidation. Although esters **38** and **40** were partially epimerized, the C2′(*R*) configuration of esters **37** and **39** tended to easily epimerize the C2′(*S*) isomers of **38** and **40**. These results indicated that the compounds **38** and **40** were more thermodynamically stable than **37** and **39**, respectively. Consequently, we predicted that the relative configurations of the C2′ and C5 positions of hirsutellomycin (**6**) are (*R*,*S*) or (*S*,*R*), respectively.

Scheme 11. Synthesis of Carboxylic Acid 50[a]



[a]Reagents and conditions: (a) NaHMDS, THF, −78 °C; MeI, 85% (single diastereomer); (b) $LiBH_4$, THF-MeOH, 0 °C to rt; (c) SO_3·Py, Et_3N, CH_2Cl_2-DMSO, 0 °C; (d) **48**, −78 to 0 °C, 45% (3 steps); (e) DHP, PPTS, CH_2Cl_2, rt; (f) LiOH·H_2O, H_2O_2, THF-H_2O, 0 °C to rt, 65% (2 steps).

Scheme 12. Thermal Stability of 2′ Configuration[a]



[a]Reagents and conditions: (a) DMP, CH_2Cl_2, 0 °C, 34% (from **43**, **37**:**38** = 2:3); (b) DMP, CH_2Cl_2, 0 °C, 67% (from **51**, **37**:**38** = 1:5); (c) DMP, CH_2Cl_2, 0 °C, 48% (from **52**, **39**:**40** = 3:2); (d) DMP, CH_2Cl_2, 0 °C, 37% (from **53**, **39**:**40** = 1:5).

The relative configuration between the C4′,6′, and C2′ positions on the side chain was also predicted by comparing the ^{13}C NMR spectra of **6** and the model compounds **38** and **40** (Figure 6). By judging the degree of deviation between the model compounds and **6**, we predicted that the relative configuration of the side chain of **6** might be **38**.

At this stage, we were ready to determine the relative configuration of hirsutellomycin (**6**) through the semisynthesis

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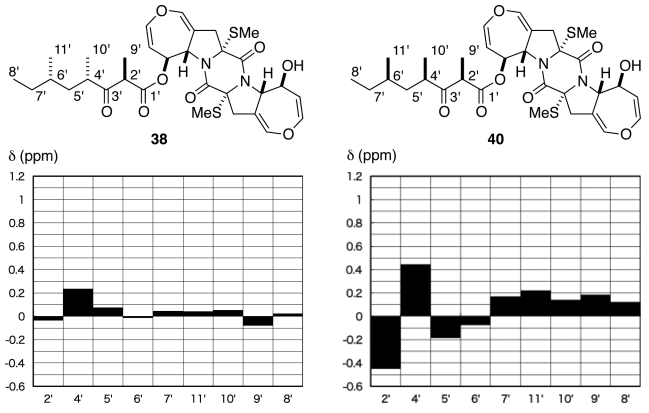
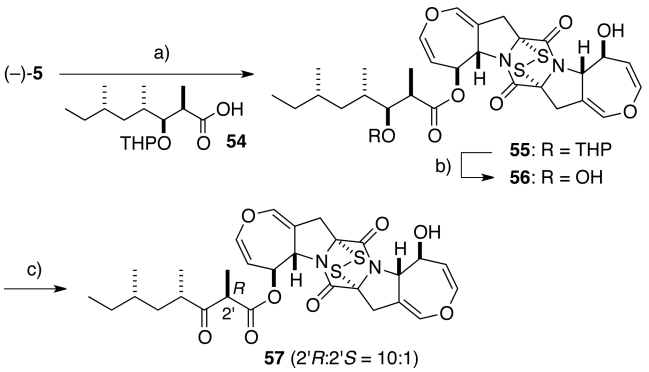


Figure 6. Comparative study of ^{13}C NMR data (150 MHz, $CDCl_3$).

of the predicted structure **56**. The synthesis of **57** commenced with the condensation of (−)-**5** with the carboxylic acid **54** to provide ester **55** in a 21% yield (Scheme 13). A careful

Scheme 13. Synthesis of β-Keto Ester 57[a]



[a]Reagents and conditions: (a) WSCD·HCl, DMAP, CH_2Cl_2, reflux, 21%; (b) PPTS, MeOH-CH_2Cl_2, 50 °C; (c) DMP, CH_2Cl_2, 0 °C, 58% (3 steps, dr 2′*R*:2′*S* = 10:1; this reaction was carried out once again by using recovered SM).

deprotection of the THP group using PPTS[15] produced the β-hydroxy ester **56**. Finally, the Dess−Martin oxidation of the hydroxyl group in **55** gave the β-keto ester **57** as a 10:1 diastereomeric mixture. The ^1H- and ^{13}C NMR spectra of the synthesized compound **57** were completely identical with those of the natural compound **6**.[6] From this result, therefore, we believe the relative configuration of hirsutellomycin (**6**) to be that of **57**.

CONCLUSION

In conclusion, we accomplished to semisynthesize (−)-SCH 64874 (**4**) and hirsutellomycin (**6**) from (−)-deacetylaranotin (**5**). Based on these semisyntheses, we were able to determine the relative configurations of **4** and **6**. During the structural determination of **6**, we found that the configuration of the active methine moiety in the side chain of **6** depended on that of the core skeleton. These results are expected to be useful for both synthetic and biological studies of these compounds and their related derivatives as well as compounds that possess a β-keto ester functionality.

EXPERIMENTAL SECTION

General Remarks. Materials were obtained from commercial suppliers and used without further purification unless otherwise mentioned. Anhydrous MeOH, Et_3N, and DIPEA were dried and distilled according to the standard protocols. Column chromatography was performed on silica gel 60N (spherical neutral, 63-210 μm), and flash column chromatography was performed on silica gel 60N (spherical neutral, 40−50 μm). Preparative TLC and analytical TLC were performed on glass plates precoated with a 0.25 mm thickness of silica gel. All melting points were determined on a melting point apparatus and are uncorrected. NMR spectra were recorded on a 400, 500, and 600 MHz spectrometer. Chemical shifts for ^1H NMR are reported in parts per million (ppm) downfield from tetramethylsilane as the internal standard and coupling constants are in Hertz (Hz). The following abbreviations are used for spin multiplicity: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, and br = broad. Chemical shifts for ^{13}C NMR are reported in ppm, relative to the central line of a triplet at 77.0 ppm for deuteriochloroform. IR spectra were measured on a FTIR spectrometer. Mass spectra were recorded on a EI or ESI-TOF MS spectrometer. Optical rotations were measured on a polarimeter. The structures of compounds **S1**−**S9** are indicated in the Supporting Information.

Search for Acetylaranotin-Producing Fungal Strains. To find acetylaranotin-producing fungal strains, 10 strains of *Aspergillus terreus*, deposited in the BIOTEC Culture Collection (BCC), were fermented in small scale (250 mL), and their extracts were analyzed by ^1H NMR ($CDCl_3$). Four strains produced acetylaranotion (**1**) and bisdethiodi-(methylthio) acetylaranotin (**36**). In all cases, the efficacy of the production of **1** was poor. Although not quantitative, the results suggested that strain BCC 4480 was the most suitable acetylaranotin producer. This fungus was isolated from a soil sample collected in Thailand and identified by Prof. Leka Manoch, and it was deposited in the BCC on August 27, 1998.

Fermentation of *Aspergillus terreus* BCC 4480 and Isolation of 1 and 36. The fungus BCC 4480 was fermented in Czapek−Dox broth (CZB; sucrose 30.0 g/L, $NaNO_3$ 3.0 g/L, K_2HPO_4 1.0 g/L, $MgSO_4·7H_2O$ 0.5 g/L, KCl 0.5 g/L, $FeSO_4·7H_2O$ 0.1 g/L; 200 × 250 mL) at 25 °C for 35 days under static conditions. The cultures were filtered to separate broth (filtrate) and mycelia (residue). The broth (ca. 50 L) was extracted with EtOAc (3 × 50 L) to obtain a brown gum (10.4 g, broth extract). The wet mycelia were macerated in MeOH (5 L, rt, 3 days) and filtered. H_2O (300 mL) and hexanes (1.5 L) were added to the filtrate, and the layers were separated. The aqueous MeOH (bottom) layer was partially concentrated by evaporation, and the residue was extracted with EtOAc. The combined EtOAc solution was concentrated under reduced pressure to obtain a brown gum (1.37 g, mycelial extract). The broth extract was fractionated by column chromatography on Sephadex LH-20 (MeOH), and the fractions containing target compounds were further separated by silica gel column chromatography (MeOH-CH_2Cl_2) and preparative HPLC using a reversed-phase column (MeOH/H_2O = 45:55) to furnish **1** (10 mg) and **36** (56 mg). The mycelial extract was also fractionated by similar chromatographic procedures to furnish **1** (13 mg) and **36** (323 mg). Additional samples of **1** and **36** were obtained by repetition of these fermentation/isolation procedures.

*(+)-(4S)-Oxazolidinone (+)-**9**.* A flame-dried 100 mL two-necked flask was charged with (4*S*)-(−)-4-isopropyl-2-oxazolidinone (1.28 g, 9.90 mmol) and dry THF (15 mL) under Ar. To the solution was added *n*-BuLi (7.22 mL, 1.51 M in *n*-hexane, 10.9 mmol) dropwise at −78 °C. After stirring for 10 min at −78 °C, *n*-propionyl chloride (1.04 mL, 11.9 mmol) was added, and the reaction mixture was warmed to room temperature. After stirring for 2.5 h at room temperature, aqueous NH_4Cl was added. The resulting mixture was extracted with CH_2Cl_2 eight times. The combined organic extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure to give a crude material, which was purified by flash column chromatography (hexanes-EtOAc = 3:1) to afford (+)-**9** (1.75 g, 9.43 mmol, 95%) as a pale yellow oil. R_f = 0.38 (hexanes-EtOAc = 5:1); $[\alpha]_D^{30}$ +90 (*c* 1.42, $CHCl_3$); IR (neat, cm^{-1}): 2966,

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1785, 1700, 1389, 1375, 1248, 1205, 1073, 1026, 758, 700; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.43 (ddd, J = 8.4, 4.0, 3.6 Hz, 1H), 4.27 (dd, J = 9.2, 8.4 Hz, 1H), 4.21 (dd, J = 9.2, 3.6 Hz, 1H), 3.04−2.84 (m, 2H), 2.44−2.30 (m, 1H), 1.17 (t, J = 7.2 Hz, 1H), 0.92 (d, J = 6.8 Hz, 3H), 0.88 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.0, 154.1, 63.3, 58.3, 29.0, 28.3, 17.9, 14.6, 8.4; HRMS (ESI) m/z: calcd for $C_9H_{15}NO_3Na$ 208.0944 [M + Na^+], found 208.0937.

*(−)-(4R)-Oxazolidinone (−)-**9**.* A flame-dried 50 mL two-necked flask was charged with (4*R*)-(−)-4-isopropyl-2-oxazolidinone (1.29 g, 10.0 mmol) and dry THF (15 mL) under Ar. To the solution was added *n*-BuLi (6.67 mL, 1.65 M in *n*-hexane, 11.0 mmol) at −78 °C. After stirring for 10 min at −78 °C, propionyl chloride (1.05 mL, 12.0 mmol) was added, and the reaction mixture was warmed to room temperature. After stirring for 3 h at room temperature, aqueous NH_4Cl was added to the reaction mixture. The resulting mixture was extracted with CH_2Cl_2 eight times. The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated under reduced pressure to give a crude material, which was purified by flash column chromatography (hexanes-EtOAc = 3:1) to afford oxazolidinone (−)-**9** (1.77 g, 9.53 mmol, 95%) as a pale yellow oil. R_f = 0.80 (hexanes-EtOAc = 1:1); $[\alpha]_D^{24}$ −81.6 (*c* 1.75, $CHCl_3$); IR (neat, cm^{-1}): 2966, 1784, 1703, 1389, 1375, 1248, 1208, 1072, 1026, 773, 700; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.47−4.40 (m, 1H), 4.27 (dd, J = 8.8, 8.4 Hz, 1H), 4.21 (dd, J = 8.8, 3.6 Hz, 1H), 3.04−2.84 (m, 2H), 2.45−2.33 (m, 1H), 1.17 (dd, J = 7.2, 5.6 Hz, 3H), 0.92 (d, J = 6.8 Hz, 3H), 0.88 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.9, 154.0, 63.3, 58.3, 29.0, 28.3, 17.8, 14.5, 8.3; LRMS (EI) m/z: 185 [M^+]; HRMS (ESI) m/z: calcd for $C_9H_{15}NO_3Na$ 208.0944 [M + Na^+], found 208.0938.

*(−)-(2R,3S,4S)-Aldol Product **11a**.*[7] A flame-dried 50 mL two-necked flask was charged with oxazolidinone (−)-**9** (300 mg, 1.62 mmol) and dry CH_2Cl_2 (4.4 mL) under Ar. To the solution was added *n*-Bu_2BOTf (4.0 mL, 0.75 M in CH_2Cl_2, 3.0 mmol) at −78 °C. After stirring for 10 min, Et_3N (553 μL, 3.97 mmol) was added dropwise. The solution was stirred for 1 h at −78 °C and for 100 min at 0 °C, then recooled to −78 °C. To the resulting mixture was slowly added a solution of (*S*)-2-methylbutanal ((+)-**10**) (1.17 mL, 16.2 mmol) in dry CH_2Cl_2 (1.2 mL). After stirring for 2 h at −78 °C and for 30 min at 0 °C, the reaction was quenched with pH 6.86 phosphate buffer (5.0 mL) and MeOH (5.0 mL), followed by 34% H_2O_2 (2.4 mL). The mixture was vigorously stirred at 0 °C for 30 min. The aqueous layer was extracted with CH_2Cl_2 three times. The combined organic extracts were washed with $NaHCO_3$, dried over $MgSO_4$, filtered, and concentrated under reduced pressure to give a crude material, which was purified by flash column chromatography (hexanes-EtOAc = 7:3) to afford aldol product **11a** (275 mg, 1.01 mmol, 63%) as a white solid. R_f = 0.31 (hexanes-EtOAc = 3:1); m.p.: 98−101 °C (hexanes-$CHCl_3$, white needle); $[\alpha]_D^{24}$ −70 (*c* 0.80, CH_2Cl_2); IR (ATR, cm^{-1}): 3463, 2963, 1764, 1684, 1387, 1372, 1238, 1206, 777, 705, 640; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.47 (dt, J = 8.4, 3.2 Hz, 1H), 4.29 (dd, J = 9.6, 8.4 Hz, 1H), 4.22 (dd, J = 9.6, 3.2 Hz, 1H), 4.01−3.93 (m, 1H), 3.63−3.58 (m, 1H), 3.11−3.07 (m, 1H), 2.42−2.28 (m, 1H), 1.87−1.73 (m, 1H), 1.55−1.50 (m, 1H), 1.24−1.12 (m, 1H), 1.23 (d, J = 7.2 Hz, 3H), 0.93 (d, J = 7.6 Hz, 3H), 0.91 (t, J = 8.0 Hz, 3H), 0.89 (d, J = 6.8 Hz, 3H), 0.85 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.4, 153.4, 74.5, 63.3, 58.2, 39.3, 36.7, 28.3, 25.1, 17.9, 14.70, 14.67, 10.8, 10.0; LRMS (EI) m/z: 272 [M + H^+]; HRMS (ESI) m/z: calcd for $C_{14}H_{25}NO_4Na$ 294.1676 [M + Na^+], found 294.1679.

The Structure of 11a Was Confirmed by the Following Procedure. A screw cap test tube was charged with **11a** (60 mg, 0.22 mmol) and dry Et_2O (0.8 mL). To the solution was added $LiBH_4$ (10 mg, 0.442 mmol) at −42 °C. After stirring for 14 h at room temperature, aqueous NH_4Cl was added at 0 °C. The resulting mixture was extracted with CH_2Cl_2 three times. The combined organic extracts were washed with brine, dried over $NaSO_4$, filtered, and concentrated under reduced pressure to give a crude material, which was purified by silica gel column chromatography (hexanes-EtOAc = 3:1) to afford **S1** (20.1 mg, 0.137 mmol, 62%) as a white solid. R_f = 0.36 (hexanes-EtOAc = 1:1); m.p.: 80−81 °C (hexanes-EtOAc, white needle); $[\alpha]_D^{26}$ −6.1 (*c* 0.14, $CHCl_3$); IR (neat, cm^{-1}): 3353, 2964, 2933, 2877, 1748, 1463, 1384, 1144, 1074, 1032, 973; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.82−3.68 (m, 2H), 3.56−3.50 (m, 1H), 2.00 (d, J = 4.4 Hz, 2H), 1.90−1.80 (m, 1H), 1.80−1.68 (m, 1H), 1.28−1.10 (m, 1H), 0.98 (d, J = 8.8 Hz, 3H), 0.93 (t, J = 7.6 Hz, 3H), 0.83 (d, J = 6.8 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 77.4, 67.9, 37.7, 36.0, 25.2, 14.9, 10.8, 8.7. Spectral data matched the reported data of **S1**.[28]

*(+)-(2S,3R,4S)-Aldol Product **11b**.*[7] A flame-dried 50 mL two-necked flask was charged with oxazolidinone (+)-**9** (300 mg, 1.62 mmol) and dry CH_2Cl_2 (4.4 mL) under Ar. To the solution was added *n*-Bu_2BOTf (4.0 mL, 0.75 M in CH_2Cl_2, 3.0 mmol) at −78 °C. After stirring for 10 min, Et_3N (553 μL, 3.97 mmol) was added dropwise. The solution was stirred for 1 h at −78 °C and for 100 min at 0 °C, then recooled to −78 °C. To the resulting mixture was slowly added a solution of (*S*)-2-methylbutanal ((+)-**10**) (1.17 mL, 16.2 mmol) in dry CH_2Cl_2 (1.2 mL). After stirring for 2 h at −78 °C and for 1 h at 0 °C, the reaction was quenched with pH 6.86 phosphate buffer (5.0 mL) and MeOH (5.0 mL), followed by 34% H_2O_2 (2.4 mL). The mixture was vigorously stirred at 0 °C for 30 min. The aqueous layer was extracted with CH_2Cl_2 three times. The combined organic extracts were washed with $NaHCO_3$, dried over $MgSO_4$, filtered, and concentrated under reduced pressure to give a crude material, which was purified by flash column chromatography (hexanes-EtOAc = 7:3) to afford aldol product **11b** (364 mg, 1.34 mmol, 83%) as a white solid. R_f = 0.23 (hexanes-EtOAc = 3:1); m.p.: 80−81 °C (hexanes-$CHCl_3$, white needle); $[\alpha]_D^{23}$ +74 (*c* 0.80, CH_2Cl_2); IR (ATR, cm^{-1}): 3531, 2963, 1766, 1681, 1381, 1209, 988, 957, 780, 706; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.47 (ddd, J = 8.0, 3.6, 3.6 Hz, 1H), 4.29 (dd, J = 9.6, 8.0 Hz, 1H), 4.22 (dd, J = 9.6, 3.6 Hz, 1H), 4.00 (qd, J = 7.2, 3.2 Hz, 1H), 3.67 (ddd, J = 7.2, 4.0, 3.2 Hz, 1H), 2.75 (d, J = 4.0 Hz, 1H), 2.35 (m, 1H,), 1.55−1.40 (m, 2H), 1.26 (d, J = 7.2 Hz, 3H), 1.20−1.05 (m, 1H), 0.98 (d, J = 6.8 Hz, 3H), 0.92 (d, J = 6.8 Hz, 3H), 0.90 (t, J = 7.2 Hz, 3H), 0.89 (d, J = 6.8 H, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.9, 153.4, 74.7, 63.3, 58.2, 39.7, 37.0, 28.3, 25.6, 17.9, 14.7, 14.6, 11.5, 11.2; LRMS (EI) m/z: 272 [M + H^+]; HRMS (ESI) m/z: calcd for $C_{14}H_{25}NO_4Na$ 294.1676 [M + Na^+], found 294.1674. Spectral data matched the reported data.[7]

*(+)-(2R,3R,4S)-Aldol Product **11c**.*[12] A flame-dried 30 mL two-necked flask was charged with oxazolidinone (+)-**9** (185 mg, 1.00 mmol) and dry CH_2Cl_2 (2.0 mL) under Ar. To the solution were added DIPEA (200 μL, 1.15 mmol) and *n*-Bu_2BOTf (330 mg, 1.20 mmol) at 0 °C. After stirring for 75 min, the solution was cooled to −78 °C. In a separate flame-dried 30 mL two-necked flask, (*S*)-2-methylbutanal ((+)-**10**) (108 μL, 1.50 mmol) was placed, to which was added a solution of $SnCl_4$ (88 μL, 0.75 mmol) in 2.0 mL of dry CH_2Cl_2. The resulting mixture was stirred for 5 min and transferred to the enol borate solution via cannula with aid of additional CH_2Cl_2 (1.0 mL). After stirring for 3 h, the reaction was quenched with MeOH-34% H_2O_2 aq. (5:1, 6.0 mL). Stirring was continued at −78 °C for another 10 min, after which time the solution was warmed to 0 °C and stirred for 30 min. To the solution was added water, and the aqueous layer of the resulting mixture was extracted twice with ether. The combined organic extracts were washed with saturated $NaHCO_3$ and brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure to give a crude material, which was purified by flash column chromatography (hexanes-EtOAc = 3:1) to afford aldol product **11c** (127 mg, 0.468 mmol, 47%) as a white solid. R_f = 0.20 (hexanes-EtOAc = 3:1); $[\alpha]_D^{28}$ +64 (*c* 0.82, CH_2Cl_2); IR (ATR, cm^{-1}): 3463, 2961, 1757, 1702, 1371, 1221, 1208, 775, 712; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.44 (ddd, J = 8.4, 3.6, 3.6 Hz, 1H), 4.28 (dd, J = 9.2, 8.4 Hz, 1H), 4.23 (dd, J = 9.2, 3.6 Hz, 1H), 4.06 (dq, J = 8.4, 6.8 Hz, 1H), 3.62 (ddd, J = 10.0, 8.4, 3.6 Hz, 1H), 2.51 (d, J = 10.0 Hz, 1H), 2.48−2.37 (m, 1H), 1.60−1.41 (m, 2H), 1.37−1.24 (m, 1H), 1.13 (d, J = 7.6 Hz, 3H), 0.98−0.88 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.2, 154.7, 77.6, 63.4, 59.0, 40.4, 37.0, 28.5, 26.7, 18.0, 14.7, 14.6, 12.2, 11.8; LRMS (EI) m/z: 271 [M^+]; HRMS (ESI) m/z: calcd for $C_{14}H_{25}NO_4Na$ 294.1676 [M + Na^+], found 294.1681.

*(−)-(2R,3S,4S)-Oxazolidinone **11d**.*[12] A flame-dried 30 mL two-necked flask was charged with oxazolidinone (−)-**9** (370 mg, 2.00 mmol) and dry CH_2Cl_2 (4.0 mL) under Ar. To the colorless solution were added DIPEA (400 μL, 2.30 mmol) and *n*-Bu_2BOTf (660 mg,

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2.40 mmol) at 0 °C. After stirring for 50 min, the solution was cooled to −78 °C. In a separate flame-dried 30 mL two-necked flask, (*S*)-2-methylbutanal ((+)-**10**) (108 μL, 1.50 mmol) was placed, to which was added a solution of $SnCl_4$ (176 μL, 1.50 mmol) in 4.0 mL of dry CH_2Cl_2. After stirring for 5 min, the solution was transferred to the enol borate solution via cannula with aid of additional CH_2Cl_2 (2.0 mL). After stirring for 6 h, the reaction was quenched with MeOH-34% H_2O_2 aq. (5:1, 12 mL). Stirring was continued at −78 °C for another 10 min, after which time the solution was warmed to 0 °C and stirred for 30 min. To the solution was added water, and the aqueous layer was extracted twice with ether. The combined organic extracts were washed with saturated $NaHCO_3$ and brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure to give a crude material, which was purified by flash column chromatography (hexanes-EtOAc = 3:1) to afford aldol product **11d** (193 mg, 0.713 mmol, 36%) as a white solid. R_f = 0.21 (hexanes-EtOAc = 3:1); $[\alpha]_D^{28}$ −60 (*c* 0.76, CH_2Cl_2); IR (ATR, cm^{-1}): 3506, 2963, 1769, 1692, 1384, 1202, 710, 629; ^1H NMR (400 MHz, $CDCl_3$): δ 4.45 (ddd, *J* = 7.2, 3.6, 3.6 Hz, 1H), 4.28 (dd, *J* = 9.2, 7.2 Hz, 1H), 4.22 (dd, *J* = 9.2, 3.6 Hz, 1H), 4.13 (qd, *J* = 7.2, 6.4 Hz, 1H), 3.44 (ddd, *J* = 10.0, 6.4, 6.4 Hz, 1H), 2.76 (d, *J* = 10.0 H, 1H), 2.46−2.34 (m, 1H), 1.76−1.62 (m, 1H), 1.56−1.46 (m, 1H), 1.21 (d, *J* = 7.2 Hz, 3H), 1.28−1.12 (m, 1H), 0.97−0.88 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.6, 154.2, 79.5, 63.2, 58.8, 39.6, 38.0, 28.5, 23.1, 17.9, 16.0, 15.2, 14.6, 11.5; LRMS (EI) *m*/*z*: 272 [M + H^+]; HRMS (ESI) *m*/*z*: calcd for $C_{14}H_{25}NO_4Na$ 294.1676 [M + Na^+], found 294.1678.

The Structure of 11d Was Confirmed by the Following Procedure. A screw cap test tube was charged with **11d** (4.5 mg, 17 μmol), dry CH_2Cl_2 (55 μL) and 2,6-lutidine (5.5 μL, 47.6 μmol). To the solution was added TBSOTf (5.8 μL, 0.442 mmol) at −42 °C. After stirring for 14 h at room temperature, the reaction mixture was quenched with H_2O. The resulting mixture was extracted with CH_2Cl_2 three times. The combined organic extracts were washed with saturated aqueous $NaHCO_3$, brine, dried over Na_2SO_4, filtered, and concentrated under reduced. The residue was purified by preparative TLC (hexanes-EtOAc = 5:1) to afford silyl ether **S2** as a pale yellow oil (3.1 mg, 11 μmol, 65%). R_f = 0.53 (hexanes-EtOAc = 3:1). $[\alpha]_D^{26}$ −12.9 (*c* 1.34, $CHCl_3$); IR (neat, cm^{-1}): 2960, 2928, 2880, 2855, 1782, 1699, 1387, 1254, 1202, 1057, 837; ^1H NMR (400 MHz, $CDCl_3$): δ 4.46−4.38 (m, 1H), 4.30−4.15 (m, 2H), 4.10−4.00 (m, 1H), 2.44−2.30 (m, 1H), 1.63−1.44 (m, 3H), 1.22−1.10 (m, 1H), 1.12 (d, *J* = 6.4 Hz, 3H), 0.94−0.89 (m, 12H), 0.89−0.84 (m, 9H), 0.09 (s, 3H), 0.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.3, 153.7, 62.6, 58.8, 43.3, 38.9, 28.3, 28.2, 26.1, 24.4, 18.3, 18.2, 16.3, 14.2, 13.7, 12.4, −4.2, −4.7 (two signals are missing due to overlap); HRMS (ESI^+) *m*/*z*: calcd for $C_{20}H_{39}NO_4SiNa$ 408.2541 [M + Na^+], found 408.2534. A screw cap test tube was charged with silyl ether **S2** (3.1 mg, 11 μmol), dry MeOH (2.2 μL, 55 μmol), and dry THF (55 μL). To the solution was added $LiBH_4$ (1.2 mg, 55 μmol) at 0 °C. After stirring for 10 h at room temperature, 1 M aqueous NaOH was added at 0 °C. then warmed to room temperature. The resulting mixture was extracted with CH_2Cl_2 three times. The combined organic extracts were washed with brine, dried over $NaSO_4$, filtered, and concentrated under reduced pressure to give a crude material, which was purified by silica gel column chromatography (hexanes-EtOAc = 5:1) to afford alcohol **S3** (0.8 mg, 11 μmol, 28%) as a pale yellow oil. R_f = 0.63 (hexanes-ethyl acetate = 3:1); $[\alpha]_D^{26}$ +6.3 (*c* 0.52, $CHCl_3$); IR (neat, cm^{-1}): 3483, 2959, 2930, 2857, 1787, 1706, 1464, 1387, 1254, 1053, 1026, 836; ^1H NMR (400 MHz, $CDCl_3$): δ 3.70−3.62 (m, 1H), 3.62−3.50 (m, 2H), 2.74 (br s, 1H), 1.92−1.80 (m, 1H), 1.62−1.44 (m, 2H), 1.22−1.04 (m, 1H), 0.98 (d, *J* = 7.2 Hz, 3H), 0.95−0.85 (m, 15H), 0.11 (s, 3H), 0.09 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 81.7, 66.4, 41.0, 36.4, 26.0, 25.3, 18.2, 16.7, 14.8, 12.3, −4.23 (three signals are missing due to overlap). Spectral data matched the reported data of **S3**.[29]

(−)-(2R,3S,4S)-β-Hydroxy Ester ***8a***.[10] A screw cap test tube was charged with aldol product **11a** (15 mg, 55 μmol) and anhydrous MeOH (120 μL) at 0 °C. To the solution was added sodium methoxide (3.5 mg, 64 μmol). After stirring for 90 min at 0 °C, the reaction was quenched with aqueous NH_4Cl. The mixture was extracted with EtOAc three times. The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated under reduced pressure to give a crude material, which was purified by flash column chromatography (hexanes-EtOAc = 5:1) to afford β-hydroxy ester **8a** (8.8 mg, 51 μmol, 91%) as a colorless oil. R_f = 0.38 (hexanes-EtOAc = 3:1); $[\alpha]_D^{24}$ −4.1 (*c* 0.60, CH_2Cl_2); IR (neat, cm^{-1}): 3507, 2964, 1735, 1720, 1458, 1202, 1056, 996, 968; ^1H NMR (400 MHz, $CDCl_3$): δ 3.71 (s, 3H), 3.67 (ddd, *J* = 8.0, 4.0, 3.2 Hz, 1H), 2.68 (qd, *J* = 7.2, 3.2 Hz, 1H), 2.48 (d, *J* = 4.0 Hz, 1H), 1.77 (dqd, *J* = 15.2, 7.6, 2.8 Hz, 1H), 1.51−1.41 (m, 1H), 1.17 (d, *J* = 7.2 Hz, 3H), 1.24−1.12 (m, 1H), 0.91 (t, *J* = 7.6 Hz, 3H), 0.83 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.1, 75.1, 51.7, 41.4, 36.9, 24.8, 14.9, 10.9, 9.6; LRMS (EI) *m*/*z*: 175 [M + H^+]; HRMS (ESI) *m*/*z*: calcd for $C_9H_{18}O_3Na$ 197.1148 [M + Na^+], found 197.1143.

(−)-(2S,3R,4S)-β-Hydroxy Ester ***8b***.[10] A screw cap test tube was charged with aldol product **11b** (10 mg, 37 μmol) and anhydrous MeOH (80 μL) at 0 °C. To the solution was added sodium methoxide (2.0 mg, 43 μmol). After stirring for 20 min at 0 °C, the reaction was quenched with aqueous NH_4Cl. The mixture was extracted with EtOAc three times. The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated under reduced pressure to give a crude material, which was purified by flash column chromatography (hexanes-EtOAc = 5:1) to afford β-hydroxy ester **8b** (5.2 mg, 30 μmol, 81%) as a colorless oil. R_f = 0.36 (hexanes-EtOAc = 3:1); $[\alpha]_D^{24}$ −1.2 (*c* 0.53, CH_2Cl_2); IR (neat, cm^{-1}): 3504, 2964, 1737, 1720, 1459, 1261, 1200, 1169; ^1H NMR (400 MHz, $CDCl_3$): δ 3.72−3.65 (m, 1H), 3.70 (s, 3H), 2.68 (qd, *J* = 7.2, 5.2 Hz, 1H), 2.15 (d, *J* = 4.8 Hz, 1H), 1.52−1.34 (m, 2H), 1.22−1.10 (m, 1H), 1.21 (d, *J* = 7.2 Hz, 3H), 0.96 (d, *J* = 6.8 Hz, 3H), 0.90 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.6, 75.1, 51.7, 42.2, 37.1, 25.9, 13.9, 11.5, 11.1; LRMS (EI) *m*/*z*: 174 [M^+]; HRMS (ESI) *m*/*z*: calcd for $C_9H_{18}O_3Na$ 197.1148 [M + Na^+], found 197.1149. Spectral data matched the reported data.[7]

(−)-(2R,3R,4S)-β-Hydroxy Ester ***8c***.[10] A screw cap test tube was charged with aldol product **11c** (10 mg, 37 μmol) and anhydrous MeOH (80 μL) at 0 °C. To the solution was added sodium methoxide (2.0 mg, 43 μmol). After stirring for 20 min at 0 °C, the reaction was quenched with aqueous NH_4Cl, and the mixture was extracted with EtOAc three times. The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated under reduced pressure to give a crude material, which was purified by flash column chromatography (hexanes-EtOAc = 3:1) to afford β-hydroxy ester **8c** (5.3 mg, 30 μmol, 82%) as a colorless oil. R_f = 0.33 (hexanes-EtOAc = 3:1); $[\alpha]_D^{26}$ −9.3 (*c* 0.45, CH_2Cl_2); IR (neat, cm^{-1}): 3523, 2963, 1738, 1721, 1458, 1260, 1198, 1172, 992, 774; ^1H NMR (400 MHz, $CDCl_3$): δ 3.72 (s, 3H), 3.62 (ddd, *J* = 8.0, 6.4, 3.6 Hz, 1H), 2.65 (dq, *J* = 8.0, 7.2 Hz, 1H), 2.37 (d, *J* = 6.4 Hz, 1H), 1.54−1.40 (m, 2H), 1.36−1.23 (m, 1H), 1.16 (d, *J* = 7.2 Hz, 3H), 0.92 (t, *J* = 7.6 Hz, 3H), 0.88 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.0, 75.7, 51.8, 43.0, 36.8, 26.6, 14.4, 12.4, 11.7; LRMS (EI) *m*/*z*: 175 [M + H^+]; HRMS (ESI) *m*/*z*: calcd for $C_9H_{18}O_3Na$ 197.1148 [M + Na^+], found 197.1139. Spectral data matched the reported data.[11]

(+)-(2R,3S,4S)-β-Hydroxy Ester ***8d***.[10] A screw cap test tube was charged with aldol product **11d** (10 mg, 37 μmol) and anhydrous MeOH (80 μL) at 0 °C. To the solution was added sodium methoxide (2.0 mg, 43 μmol). After stirring for 20 min at 0 °C, the reaction was quenched with aqueous NH_4Cl, and the mixture was extracted with EtOAc three times. The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated under reduced pressure to give a crude material, which was purified by flash column chromatography (hexanes-EtOAc = 3:1) to afford β-hydroxy ester **8d** (4.1 mg, 24 μmol, 64%) as a colorless oil. R_f = 0.33 (hexanes-EtOAc = 3:1); $[\alpha]_D^{25}$ +4.8 (*c* 0.51, CH_2Cl_2); IR (neat, cm^{-1}): 3522, 2963, 1734, 1719, 1458, 1260, 1199, 1172, 1044, 997; ^1H NMR (400 MHz, $CDCl_3$): δ 3.71 (s, 3H), 3.38 (ddd, *J* = 8.4, 6.4, 5.6 Hz, 1H), 2.73 (qd, *J* = 7.2, 5.6 Hz, 1H), 2.56 (d, *J* = 8.4 Hz, 1H), 1.69−1.58 (m, 1H), 1.53−1.41 (m, 1H), 1.24 (d, *J* = 7.2 Hz, 3H), 1.22−1.12 (m, 1H), 0.92 (d, *J* = 6.8 Hz, 3H), 0.90 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.9, 77.9, 51.7, 41.9, 38.2, 23.6, 15.8, 15.1, 11.4; LRMS (EI) *m*/*z*: 175 [M + H^+];

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HRMS (ESI) m/z: calcd for $C_9H_{18}O_3Na$ 197.1148 [M + Na^+], found 197.1147.

*(−)-(2R,3S,4S)-THP-Protected Aldol Product (−)-**12**.* A screw cap test tube was charged with aldol product (−)-**11a** (250 mg, 0.921 mmol) and dry CH_2Cl_2 (3.0 mL). To the solution were added DHP (168 μL, 1.84 mmol) and $TsOH·H_2O$ (1.8 mg, 9.2 μmol). After stirring for 3 h at room temperature, the reaction was quenched with H_2O. The aqueous layer was extracted with CH_2Cl_2 two times. The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated under reduced pressure to give a crude material, which was purified by flash column chromatography (hexanes-EtOAc = 3:1) to afford THP-protected β-hydroxy ester (−)-**12** (295 mg, 0.830 mmol, 90%) as a pale yellow oil. R_f = 0.26 (hexanes-EtOAc = 3:1). The physical data of diastereomeric mixture (−)-**12**: $[\alpha]_D^{26}$ −70.7 (*c* 1.04, $CHCl_3$); IR (neat, cm^{-1}): 2962, 1780, 1700, 1384, 1227, 1202, 903, 753; ^1H NMR (400 MHz, $CDCl_3$): δ 4.57−4.52 (m, 0.5H), 4.45−4.40 (m, 0.5H), 4.40−4.30 (m, 1H), 4.28−4.20 (m, 1H), 4.22−4.18 (m, 1H), 4.10−4.00 (m, 0.5H), 4.01−3.89 (m, 0.5H), 3.88−3.81 (m, 1H), 3.81−3.76 (m, 1H), 3.48−3.34 (m, 1H), 2.52−2.34 (m, 1H), 1.85−1.66 (m, 2H), 1.63−1.40 (m, 6H), 1.21 (dd, *J* = 6.8, 3.2 Hz, 3H), 1.13−1.01 (m, 1H) 0.97 (d, *J* = 7.2 Hz, 3H), 0.95−0.85 (m, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.4, 175.0, 154.1, 153.5, 101.3, 100.3, 82.0, 81.9, 64.3, 63.34, 63.31, 63.2, 59.3, 58.9, 40.7, 40.0, 39.2, 38.3, 30.90, 30.85, 28.4, 25.4, 25.3, 25.0, 24.8, 20.8, 20.2, 18.1, 18.0, 15.2, 14.8, 14.6, 13.1, 12.0, 11.7, 11.1 (two signals are missing due to overlap); HRMS (ESI) m/z: calcd for $C_{19}H_{33}NO_5Na$ 378.2251 [M + Na^+], found 378.2253.

*(−)-(2R,3S,4S)-THP-Protected β-Hydroxy Carboxylic Acid (−)-**13**.* A screw cap test tube was charged with (−)-**12** (9.1 mg, 26 μmol), dry THF (75 μL), and H_2O (22 μL). To the solution were added H_2O_2 (34% w/w solution in H_2O, 20 μL, 0.18 mmol) and $LiOH·H_2O$ (1.6 mg, 38 μmol) at 0 °C. The reaction mixture was warmed to at room temperature and stirred for 24 h. The reaction was quenched with saturated aqueous $Na_2S_2O_3$ and 0.1 M HCl aq. The aqueous layer was extracted with EtOAc 10 times. The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give a crude material, which was purified by flash column chromatography (hexanes-EtOAc = 5:1) to afford THP-protected β-hydroxy carboxylic acid (−)-**13** (5.1 mg, 21 μmol, 82%) as a pale yellow oil. R_f = 0.13 (hexanes-EtOAc = 3:1). The physical data of diastereomeric mixture (−)-**13**: $[\alpha]_D^{28}$ −19 (*c* 0.80, $CHCl_3$); IR (neat, cm^{-1}): 2942, 1708, 1457, 1131, 1077, 1034, 813, 669; ^1H NMR (400 MHz, $CDCl_3$): δ 4.62−4.58 (m, 0.5H), 4.56−4.51 (m, 0.5H), 3.97−3.84 (m, 1.5H), 3.78 (dd, *J* = 6.0, 4.4 Hz, 0.5H), 3.52−3.41 (m, 1H), 2.86−2.77 (m, 0.5H), 2.76−2.68 (m, 0.5H), 1.85−1.70 (m, 2H), 1.70−1.45 (m, 6H), 1.21 (d, *J* = 7.2 Hz, 1.5H), 1.16 (d, *J* = 6.8 Hz, 1.5H), 1.20−1.15 (m, 1H), 0.95 (d, *J* = 7.2 Hz, 1.5H), 0.91 (d, *J* = 6.8 Hz, 1.5H), 0.89 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 181.5, 179.8, 101.7, 100.0, 84.0, 82.1, 63.9, 63.4, 41.8, 41.3, 38.5, 37.3, 31.03, 31.00, 25.4, 25.1, 25.0, 24.5, 20.7, 20.2, 15.6, 15.4, 11.7, 11.5, 11.2 (one signal is missing due to overlap); HRMS (ESI) m/z: calcd for $C_{13}H_{24}O_4Na$ 267.1567 [M + Na^+], found 267.1560.

*(+)-(2S,3R,4R)-Aldol Product **11e**.*[7] A flame-dried 20 mL two-necked flask was charged with oxazolidinone (+)-**9** (200 mg, 1.08 mmol) and dry CH_2Cl_2 (1.9 mL) under Ar. To the solution was added *n*-Bu_2BOTf (1.2 mL, 1.00 M in CH_2Cl_2, 1.19 mmol) at −78 °C. After stirring for 10 min, Et_3N (210 μL, 1.51 mmol) was added dropwise. The solution was stirred for 1 h at −78 °C and for 1 h at 0 °C, then recooled to −78 °C. To the resulting mixture was slowly added a solution of (*R*)-2-methylbutanal ((−)-**10**)[9] (110 mg, 1.28 mmol) in dry CH_2Cl_2 (868 μL). After stirring for 30 min at −78 °C and for 2 h at 0 °C, the reaction was quenched with pH 6.86 phosphate buffer (868 μL) and MeOH (868 μL), followed by 34% H_2O_2 (34% w/w solution in H_2O, 520 μL). The mixture was vigorously stirred at 0 °C for 1.5 h. The aqueous layer was extracted with CH_2Cl_2 three times. The combined organic extracts were washed with brine and dried over $MgSO_4$, filtered, and concentrated under reduced pressure to give a crude material, which was purified by flash column chromatography (hexanes-EtOAc = 3:1) to afford aldol product **11e** (154 mg, 0.567 mmol, 53%) as a white solid. R_f = 0.19 (hexanes-EtOAc = 3:1); $[\alpha]_D^{26}$ +61 (*c* 0.80, CH_2Cl_2); IR (ATR, cm^{-1}): 3464, 2963, 1765, 1685, 1387, 1372, 1238, 1205, 704, 640; ^1H NMR (400 MHz, $CDCl_3$): δ 4.47 (ddd, *J* = 9.2, 8.4, 3.2 Hz, 1H), 4.29 (dd, *J* = 9.2, 8.4 Hz, 1H), 4.22 (dd, *J* = 9.2, 3.2 Hz, 1H), 3.97 (qd, *J* = 7.2, 2.4 Hz, 1H), 3.61 (ddd, *J* = 9.2, 2.8, 2.4 Hz, 1H), 3.10 (d, *J* = 2.8 Hz, 1H), 2.40−2.30 (m, 1H), 1.86−1.74 (m, 1H), 1.55−1.40 (m, 1H), 1.23 (d, *J* = 7.2 Hz, 3H), 1.27−1.24 (m, 1H), 0.93 (d, *J* = 7.6 Hz, 3H), 0.91 (t, *J* = 7.2 Hz, 3H), 0.89 (d, *J* = 6.8 Hz, 3H), 0.85 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.4, 153.4, 74.5, 63.3, 58.2, 39.3, 36.7, 28.3, 25.2, 17.9, 14.70, 14.67, 10.8, 10.0; HRMS (ESI) m/z: calcd for $C_{14}H_{25}NO_4Na$ 294.1676 [M + Na^+], found 294.1688. Spectral data matched the reported data.[13]

*(+)-(2S,3R,4R)-THP-Protected Aldol Product (+)-**12**.* A screw cap test tube was charged with aldol product **11e** (30 mg, 0.11 mmol) and dry CH_2Cl_2 (349 μL). To the solution were added DHP (20 μL, 0.22 mmol) and $TsOH·H_2O$ (0.21 mg, 1.1 μmol). After stirring for 2 h at room temperature, the reaction was quenched with H_2O. The aqueous layer was extracted with CH_2Cl_2 five times. The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give a crude material, which was purified by flash column chromatography (hexanes-EtOAc = 5:1) to afford (+)-**12** (29.8 mg, 83.8 μmol, 76%) as a pale yellow oil. R_f = 0.35 (hexanes-EtOAc = 3:1). The physical data of diastereomeric mixture (+)-**12** is following: $[\alpha]_D^{28}$ +68 (*c* 0.52, $CHCl_3$); IR (neat, cm^{-1}): 2962, 1780, 1700, 1385, 1228, 1202, 1130, 1032; ^1H NMR (400 MHz, $CDCl_3$): δ 4.57−4.52 (m, 0.5H), 4.45−4.40 (m, 0.5H), 4.40−4.30 (m, 1H), 4.28−4.20 (m, 1H), 4.22−4.18 (m, 1H), 4.10−4.00 (m, 0.5H), 4.00−3.88 (m, 0.5H), 3.86−3.76 (m, 2H), 3.48−3.32 (m, 1H), 2.52−2.32 (m, 1H), 1.86−1.76 (m, 2H), 1.65−1.38 (m, 6H), 1.21 (dd, *J* = 6.8, 3.6 Hz, 3H), 1.13−1.00 (m, 1H), 0.98−0.95 (m, 3H), 0.94−0.83 (m, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.5, 175.0, 154.1, 153.6, 101.3, 100.3, 82.1, 81.9, 64.3, 63.35, 63.31, 63.2, 59.3, 58.9, 40.7, 40.0, 39.3, 38.3, 30.91, 30.87, 28.4, 25.4, 25.3, 25.0, 24.8, 20.8, 20.2, 18.1, 18.0, 15.2, 14.8, 14.6, 13.2, 12.0, 11.7, 11.1 (two signals are missing due to overlap); HRMS (ESI) m/z: calcd for $C_{19}H_{33}NO_5Na$ 378.2251 [M + Na^+], found 378.2253.

*(+)-(2S,3R,4R)-THP-Protected β-Hydroxy Carboxylic Acid (+)-**13**.* A screw cap test tube was charged with THP-protected aldol product (+)-**12** (30 mg, 0.084 mmol), dry THF (250 μL) and H_2O (72 μL). To the solution were added H_2O_2 (34% w/w solution in H_2O, 60 μL, 0.59 mmol) and $LiOH·H_2O$ (5.3 mg, 0.13 mmol) at 0 °C. The reaction mixture was warmed to room temperature and stirred for 24 h. The reaction was quenched with saturated aqueous $Na_2S_2O_3$ and 0.1 M HCl aq. The aqueous layer was extracted with EtOAc six times. The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give a crude material, which was purified by flash column chromatography (hexanes-EtOAc = 3:1) to afford THP-protected β-hydroxy carboxylic acid (+)-**13** (17.3 mg, 70.8 mmol, 84%) as a pale yellow oil. R_f = 0.22 (hexanes-EtOAc = 3:1). The physical data of diastereomeric mixture (+)-**13** is following: $[\alpha]_D^{28}$ +20 (*c* 0.59, $CHCl_3$); IR (neat, cm^{-1}): 2941, 1707, 1456, 1201, 1131, 1077, 1026; ^1H NMR (400 MHz, $CDCl_3$): δ 4.65−4.60 (m, 0.5H), 4.60−4.54 (m, 0.5H), 4.00−3.85 (m, 1.5H), 3.77−3.72 (m, 0.5H), 3.54−3.44 (m, 1H), 2.94−2.84 (m, 0.5H), 2.80−2.70 (m, 0.5H), 1.87−1.77 (m, 2H), 1.64−1.60 (m, 6H), 1.21(d, *J* = 7.2 Hz, 1.5H), 1.18 (d, *J* = 7.2 Hz, 1.5H), 1.18−1.10 (m, 1H), 0.98−0.85 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 181.6, 180.0, 101.6, 100.0, 84.0, 82.1, 63.8, 63.4, 41.8, 41.3, 38.6, 37.4, 31.03, 31.00, 25.4, 25.1, 25.0, 24.5, 20.7, 20.2, 15.5, 15.4, 11.7, 11.5, 11.2 (one signal is missing due to overlap); HRMS (ESI) m/z: calcd for $C_{13}H_{24}O_4Na$ 267.1567 [M + Na^+], found 267.1563.

*(−)-Deacetylaranotin (**5**).*[14] A screw cap test tube was charged with acetylaranotin (−)-**1** (2.0 mg, 40 μmol) and dry CH_2Cl_2 (100 μL). To the solution was added 36% HCl aq. (2.5 mL) in MeOH (98 μL). The reaction mixture was stirred at room temperature for 16.5 h. The reaction mixture was diluted with EtOAc, water, and saturated aqueous $NaHCO_3$. The resulting mixture was extracted with EtOAc three times. The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give a crude material, which was purified by preparative TLC (CH_2Cl_2-acetone = 20:1) to afford

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(−)-deacetylaranotin (**5**) (1.2 mg, 2.9 μmol, 72%) as a white solid. R_f = 0.27 (CH_2Cl_2-acetone = 10:1); $[\alpha]_D^{26}$ −546 (*c* 0.210, $CHCl_3$); IR (KBr, cm^{-1}): 3339, 1693, 1666, 1655, 1445, 1431, 1387, 1283, 1144, 1036; ^1H NMR (600 MHz, $CDCl_3$): δ 6.60 (s, 2H), 6.27 (dd, *J* = 8.9, 2.4 Hz, 2H), 5.88 (s, 2H), 4.81 (dd, *J* = 8.4, 2.4 Hz, 2H), 4.78 (d, *J* = 7.2 Hz, 2H), 4.62 (d, *J* = 7.2 Hz, 2H), 3.88 (dt, *J* = 16.8, 1.8 Hz, 2H), 2.92 (d, *J* = 16.8 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 165.4, 139.0, 138.9, 109.7, 107.6, 75.4, 70.7, 68.0, 36.2; HRMS (ESI^+) *m*/*z*: calcd for $C_{18}H_{16}N_2O_6S_2Na$ 443.0347 [M + Na^+], found 443.0358.

(−)-Diester ***14***. A screw cap test tube was charged with (−)-deacetylaranotin (**5**) (2.30 mg, 5.47 μmol), THP-protected β-hydroxy carboxylic acid (−)-**13** (5.1 mg, 20.9 μmol), and dry CH_2Cl_2 (100 μL). To the solution were added DMAP (2.00 mg, 16.4 μmol) and WSCD·HCl (5.24 mg, 27.4 μmol). The reaction mixture was stirred for 5 h at room temperature. The reaction mixture was diluted with hexane and EtOAc, and SiO_2 was added. The resulting suspension was passed through a pad of Celite. The organic solvents were removed under reduced pressure to give a crude material, which was purified by preparative TLC (hexanes-EtOAc = 3:2) to afford diester **14** (2.01 mg, 2.30 μmol, 42%). R_f = 0.69 (hexanes-EtOAc = 1:1). The physical data of diastereomeric mixture **14** is following: $[\alpha]_D^{29}$ −308 (*c* 0.201, $CHCl_3$); IR (neat, cm^{-1}): 2942, 2876, 1732, 1713, 1652, 1456, 1358, 1200, 1133, 1026, 998, 757; ^1H NMR (600 MHz, $CDCl_3$): δ 6.60 (dd, *J* = 11.4, 1.8 Hz, 2H), 6.31 (dt, *J* = 8.4, 2.4 Hz, 1H), 6.27 (dt, *J* = 8.4, 2.4 Hz, 1H), 5.74−5.62 (m, 2H), 5.09−5.04 (m, 2H), 4.89 (dd, *J* = 7.8, 1.8 Hz, 1H), 4.63−4.54 (m, 3H), 4.13−4.03 (m, 2H), 3.94−3.77 (m, 4H), 3.52−3.30 (m, 3H), 3.02−2.84 (m, 1.5H), 2.77−2.56 (m, 1.5H), 1.84−1.70 (m, 2H), 1.70−1.44 (m, 14H), 1.20−1.10 (m, 2H), 1.15 (d, *J* = 7.2 Hz, 3H,), 1.09 (d, *J* = 6.6 Hz, 3H), 0.97−0.85 (m, 12H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 175.0, 174.0, 162.4, 141.2, 140.63, 140.62, 140.59, 139.2, 139.0, 105.73, 105.70, 105.2, 100.3, 99.0, 83.8, 81.1, 75.8, 69.7, 63.2, 63.15, 63.12, 63.02, 62.99, 62.4, 41.3, 41.1, 38.4, 38.2, 34.1, 34.0, 31.0, 30.9, 25.5, 25.10, 25.08, 20.1, 19.6, 15.6, 15.3, 11.8, 11.6, 10.7, 9.9, 0.0; HRMS (ESI) *m*/*z*: calcd for $C_{44}H_{60}N_2O_{12}S_2Na$ 895.3480 [M + Na^+], found 895.3437.

(−)-Bis-β-hydroxy Ester ***15***. A screw cap test tube was charged with diester **14** (2.01 mg, 2.30 μmol), MeOH (50 μL), and CH_2Cl_2 (50 μL). To the solution was added PPTS (2.31 mg, 9.20 μmol), and the reaction mixture was stirred at room temperature for 5 h. The reaction mixture was purified by preparative TLC (hexanes-EtOAc = 3:2) to afford bis-β-hydroxy ester **15** (1.07 mg, 1.52 μmol, 66%). R_f = 0.32 (hexanes-EtOAc = 1:1); $[\alpha]_D^{25}$ −254 (*c* 0.107, $CHCl_3$); IR (neat, cm^{-1}): 3253, 2963, 2934, 2877, 1709, 1653, 1362, 1140, 968, 755; ^1H NMR (600 MHz, $CDCl_3$): δ 6.61 (d, *J* = 1.9 Hz, 2H), 6.29 (dd, *J* = 8.2, 2.1 Hz, 2H), 5.62 (d, *J* = 8.6 Hz, 2H), 5.12 (dd, *J* = 8.6, 1.2 Hz, 2H), 4.54 (dd, *J* = 8.2, 1.2 Hz, 2H), 4.08 (d, *J* = 18.2 Hz, 2H), 3.65 (dd, *J* = 9.1, 2.4 Hz, 2H), 2.93 (d, *J* = 18.2 Hz, 2H), 2.63 (qd, *J* = 7.2, 2.4 Hz, 2H), 1.77 (dqd, *J* = 15.1, 7.4, 2.9 Hz, 2H), 1.48−1.40 (m, 2H), 1.20−1.14 (m, 2H), 1.12 (d, *J* = 7.2 Hz, 6H), 0.90 (t, *J* = 7.4 Hz, 6H), 0.81 (d, *J* = 6.7 Hz, 6H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 175.4, 162.6, 141.3, 139.5, 113.3, 105.3, 75.7, 74.7, 70.3, 62.7, 41.9, 37.1, 34.0, 25.1, 15.0, 10.9, 9.1; HRMS (ESI) *m*/*z*: calcd for $C_{34}H_{44}N_2O_{10}S_2Na$ 727.2330 [M + Na^+], found 727.2299.

(−)-Diester ***16***. A screw cap test tube was charged with (−)-deacetylaranotin (**5**) (2.06 mg, 4.90 μmol), THP-protected β-hydroxy carboxylic acid (+)-**13** (5.01 mg, 20.5 μmol), and dry CH_2Cl_2 (100 μL). To the solution were added DMAP (1.85 mg, 15.1 μmol) and WSCD·HCl (3.87 mg, 20.2 μmol). The reaction mixture was stirred at room temperature for 10 h. The reaction mixture was diluted with hexane and EtOAc, and SiO_2 was added. The resulting suspension was passed through a pad of Celite. The organic solvents were removed under reduced pressure to give a crude material, which was purified by preparative TLC (hexanes-EtOAc = 1:1) to afford diester **16** (1.63 mg, 1.87 μmol, 38%). R_f = 0.61 (hexanes-EtOAc = 1:1). The physical data of diastereomeric mixture (−)-**16** is following: $[\alpha]_D^{24}$ −165 (*c* 0.0815, $CHCl_3$); IR (neat, cm^{-1}): 2939, 1731, 1715, 1354, 1141, 1026, 669; ^1H NMR (600 MHz, $CDCl_3$): δ 6.68−6.58 (m, 2H), 6.35−6.25 (m, 2H), 5.60 (d, *J* = 8.4 Hz, 1H), 5.55 (d, *J* = 9.0 Hz, 1H), 5.17−5.05 (m, 2H), 4.72 (d, *J* = 7.8 Hz, 1H,), 4.61−4.59 (m, 1H), 4.55 (d, *J* = 7.8 Hz, 1H), 4.54−4.49 (m, 1H), 4.10 (d, *J* = 18.0 Hz, 2H), 3.98−3.80 (m, 4H), 3.50−3.34 (m, 2.5H), 2.92 (d, *J* = 18.0 Hz, 2H), 2.72−2.56 (m, 1.5H), 1.86−1.75 (m, 2H), 1.75−1.42 (m, 14H), 1.32−1.20 (m, 2H), 1.20−1.14 (m, 6H), 0.98−0.82 (m, 12H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 175.1, 170.2, 162.5, 162.4, 141.2, 140.8, 139.4, 139.2, 113.7, 105.7, 105.3, 104.9, 102.5, 101.2, 100.2, 82.7, 81.2, 75.7, 71.4, 70.3, 70.0, 63.5, 63.0, 62.7, 41.61, 41.55, 38.9, 37.6, 34.4, 34.0, 31.2, 31.1, 29.0, 25.5, 25.4, 25.1, 25.0, 20.8, 20.4, 15.7, 11.9, 11.8, 11.6, 11.0; HRMS (ESI) *m*/*z*: calcd for $C_{44}H_{60}N_2O_{12}S_2Na$ 895.3480 [M + Na^+], found 895.3450.

*(−)-SCH 64874 (****17****).* A screw cap test tube was charged with diester **16** (1.63 mg, 1.87 μmol), MeOH (50 μL), and CH_2Cl_2 (50 μL). To the solution was added PPTS (1.88 mg, 7.47 μmol), and the reaction mixture was stirred at 40 °C for 5 h. The reaction mixture was purified by preparative TLC (hexanes-EtOAc = 3:2) to afford **17** (1.14 mg, 1.62 μmol, 86%). R_f = 0.48 (hexanes-EtOAc = 1:1); $[\alpha]_D^{29}$ −169 (*c* 0.141, $CHCl_3$); IR (neat, cm^{-1}): 3518, 2963, 2917, 1715, 1651, 1456, 1362, 1179, 1142, 969, 755; ^1H NMR (600 MHz, $CDCl_3$): δ 6.61 (d, *J* = 1.9 Hz, 2H), 6.30 (dd, *J* = 8.2, 2.1 Hz, 2H), 5.68 (ddd, *J* = 8.6, 2.1, 2.1 Hz, 2H), 5.09 (dd, *J* = 8.6, 1.9 Hz, 2H), 4.53 (dd, *J* = 8.2, 2.1 Hz, 2H), 4.08 (d, *J* = 18.2 Hz, 2H), 3.68 (d, *J* = 9.5 Hz, 2H), 2.92 (2H, dt, *J* = 18.2, 1.9 Hz), 2.63 (2H, qd, *J* = 7.2, 1.7 Hz), 1.81 (dqd, *J* = 15.3, 7.4, 3.1 Hz, 2H), 1.49−1.43 (m, 2H), 1.20−1.10 (m, 2H), 1.14 (d, *J* = 7.8 Hz, 6H), 0.90 (t, *J* = 7.4 Hz, 6H), 0.79 (d, *J* = 6.7 Hz, 6H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 175.5, 162.7, 141.4, 139.6, 113.1, 105.1, 75.7, 73.7, 69.9, 62.9, 41.6, 36.5, 33.9, 25.5, 14.9, 10.9, 8.8; HRMS (ESI) *m*/*z*: calcd for $C_{34}H_{44}N_2O_{10}S_2Na$ 727.2330 [M + Na^+], found 727.2297.

(4S,6S)-β-Keto Ester ***19***. A screw cap test tube was charged with oxazolidinone **24**[18] (20 mg, 66 μmol), dry MeOH (26 μL, 0.66 μmol), and dry THF (330 μL). To the solution was added $LiBH_4$ (14 mg, 0.66 mmol) at 0 °C. The reaction mixture was warmed at room temperature and was stirred for 1 h. The reaction was quenched with 1 M NaOH aq. at 0 °C. The reaction mixture was diluted with water and extracted with EtOAc three times. The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure at 0 °C to give a crude material, which was purified by flash column chromatography (hexanes-EtOAc = 3:1) to afford alcohol **25** as a hexanes-EtOAc solution. All the solvent was not removed due to the volatility of the product. R_f = 0.22 (hexanes-EtOAc = 5:1). A screw cap test tube was charged with the hexanes-EtOAc solution of **25**, Et_3N (46 μL, 0.33 mmol), dry DMSO (110 μL), and dry CH_2Cl_2 (220 μL). To the solution was added SO_3·Py (52 mg, 0.33 mmol) at 0 °C. The resulting solution was stirred at 0 °C for 30 min. The reaction was quenched with water at 0 °C and then warmed to room temperature. The reaction mixture was extracted with CH_2Cl_2 three times. The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure at 0 °C to give a crude material as a CH_2Cl_2 solution, which was purified by flash column chromatography (hexanes-EtOAc = 5:1) to afford aldehyde **26** as a hexanes-EtOAc solution. All the solvent was not removed due to the volatility of the product. R_f = 0.42 (hexanes-EtOAc = 5:1). A screw-top test tube was charged with $SnCl_2$ (13 mg, 66 μmol) and dry CH_2Cl_2 (100 μL). To the solution was added diazo ester **27** (17 mg, 0.13 mmol) and a hexanes-EtOAc solution of **26**. After stirring at room temperature for 1.5 h, the reaction mixture was diluted with water and extracted with CH_2Cl_2 three times. The combined organic extracts were washed with water three times, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give a crude material, which was purified by flash column chromatography (hexanes-EtOAc = 5:1) to afford β-keto ester **19a** and **19b** (3.6 mg, 16 μmol, 24% over 3 steps from **24**) as a colorless oil. R_f = 0.48 (hexanes-EtOAc = 5:1). The physical data of a 1:1 mixture of **19a** and **19b**: IR (neat, cm^{-1}): 2963, 2930, 2876, 2855, 1747, 1738, 1732, 1715, 1462, 1456, 1377, 1246, 1194, 1121, 997; ^1H NMR (400 MHz, $CDCl_3$): δ 4.22−4.10 (m, 2H), 3.68 (q, *J* = 7.2 Hz, 0.5H), 3.63 (q, *J* = 7.2 Hz, 0.5H), 2.92−2.81 (m, 1H), 1.79 (ddd, *J* = 13.6, 8.4, 5.6 Hz, 0.5H), 1.68 (ddd, *J* = 13.6, 7.6, 6.0 Hz, 0.5H), 1.39−1.23 (m, 2.5H), 1.33 (d, *J* = 6.8 Hz, 1.5H), 1.32 (d, *J* = 7.2 Hz, 1.5H), 1.261 (dd, *J* = 7.2, 7.2 Hz, 1.5H), 1.257 (dd, *J* = 7.2, 6.8 Hz, 1.5H), 1.16−1.00 (m, 2H), 1.10 (d, *J* = 6.8 Hz, 1.5H), 1.09

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(d, J = 6.8 Hz, 1.5H), 0.91−0.82 (m, 6.5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 209.6, 170.5, 61.3, 61.2, 51.9, 51.3, 43.4, 43.3, 40.5, 39.7, 32.1, 32.0, 29.4, 29.2, 19.4, 19.3, 17.6, 17.1, 14.07, 14.05, 13.1, 12.9, 11.1, 11.0 (two signals are missing due to overlap); LRMS (EI) 228; HRMS (EI) m/z: calcd for $C_{13}H_{25}O_3$ 229.1804 [M + H$^+$], found 229.1802.

(−)-(2S,4R)-Oxazolidinone ***29***. A flame-dried 50 mL two-necked round-bottomed flask was charged with dry THF (10 mL) and then NaHMDS (1.9 M in THF, 3.7 mL, 7.0 mmol) at −78 °C. To the solution was added oxazolidinone **28**[19] (1.45 g, 5.00 mmol) in THF (5 mL) via cannula at −78 °C over 5 min. The resulting solution was stirred for 1 h. To the solution was added MeI (1.56 mL, 25.0 mmol) dropwise at −78 °C over 3 min. After stirring at −78 °C for 1 h, the reaction was quenched with AcOH at −78 °C and then warmed to room temperature. The reaction mixture was diluted with water and extracted with EtOAc three times. The combined organic extracts were washed with water and brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give a crude material, which was purified by flash column chromatography (hexanes-EtOAc = 5:1) to afford oxazolidinone **29** (1.07 g, 3.53 mmol, 71%) as a colorless oil. R_f = 0.22 (hexanes-EtOAc = 5:1); $[\alpha]_D^{25}$ −55 (c 0.97, $CHCl_3$); IR (neat, cm^{-1}): 2962, 2929, 2874, 1782, 1698, 1455, 1386, 1350, 1238, 1208, 1099, 1015, 971, 760, 743, 702; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.33 (dd, J = 7.8, 7.2 Hz, 2H), 7.29−7.26 (m, 1H), 7.22 (d, J = 7.8 Hz, 2H), 4.67 (ddt, J = 9.6, 7.8, 2.4 Hz, 1H), 4.19 (dd, J = 8.4, 7.8 Hz, 1H), 4.17 (dd, J = 9.0, 3.0 Hz, 1H), 3.82 (dt, J = 9.0, 7.2 Hz, 1H), 3.27 (dd, J = 13.8, 2.4 Hz, 1H), 2.77 (dd, J = 13.2, 9.6 Hz, 1H), 1.58−1.51 (m, 1H), 1.45−1.29 (m, 3H), 1.23−1.13 (m, 1H), 1.20 (d, J = 6.6 Hz, 3H), 0.88 (d, J = 6.0 Hz, 3H), 0.87 (dd, J = 7.8, 6.6 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 177.7, 153.0, 135.3, 129.4, 128.9, 127.3, 66.0, 55.4, 40.1, 37.9, 35.4, 32.0, 29.8, 18.8, 17.2, 11.3; LRMS (EI) m/z: 303 [M$^+$]; HRMS (EI) m/z: calcd for $C_{18}H_{25}NO_3$ 303.1834 [M$^+$], found 303.1819.

(4R,6S)-β-Keto Ester ***20a*** *and* ***20b***. A screw cap test tube was charged with oxazolidinone **29** (20 mg, 66 μmol), dry MeOH (26 μL, 0.66 mmol), and dry THF (330 μL). To the solution was added $LiBH_4$ (14 mg, 0.66 mmol) at 0 °C. After stirring at room temperature for 1 h, the reaction was quenched with 1 M NaOH aq. at 0 °C then warmed to room temperature. The mixture was diluted with water and extracted with EtOAc three times. The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure at 0 °C to give a crude material, which was purified by flash column chromatography (hexanes-EtOAc = 3:1) to afford alcohol **30** as a hexanes-EtOAc solution. All the solvent was not removed due to the volatility of the product. R_f = 0.22 (hexanes-EtOAc = 5:1). A screw cap test tube was charged with the hexanes-EtOAc solution of **30**, Et_3N (46 μL, 0.33 mmol), dry DMSO (110 μL), and dry CH_2Cl_2 (220 μL). To the solution was added SO_3·Py (52 mg, 0.33 mmol) at 0 °C. After stirring at 0 °C for 30 min, the reaction was quenched with water at 0 °C and then warmed to room temperature. The reaction mixture was extracted with CH_2Cl_2 three times. The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure at 0 °C to give a crude material in CH_2Cl_2, which was purified by flash column chromatography (hexanes-EtOAc = 5:1) to afford a crude aldehyde in hexanes-EtOAc solution. All the solvent was not removed due to the volatility of the product. R_f = 0.42 (hexanes-EtOAc = 5:1). A screw cap test tube was charged with $SnCl_2$ (13 mg, 66 μmol) and dry CH_2Cl_2 (100 μL), to which was added diazo ester **27** (17 mg, 0.13 mmol) and the crude aldehyde as a hexanes-EtOAc solution. After stirring at room temperature for 1.5 h, the reaction mixture was diluted with water and extracted with CH_2Cl_2 three times. The combined organic extracts were washed with water three times, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give a crude material, which was purified by flash column chromatography (hexanes-EtOAc = 5:1) to afford a mixture of β-keto ester **20a** and **20b** (3.0 mg, 13 μmol, 20% over 3 steps from **29**) as a colorless oil. R_f = 0.48 (hexanes-EtOAc = 5:1). The physical data of a 1:1 mixture of **20a** and **20b**: IR (neat, cm^{-1}): 2964, 2936, 2876, 1747, 1715, 1462, 1456, 1377, 1244, 1194, 1120; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.18 (q, J = 7.2 Hz, 1H), 4.17 (q, J = 7.2 Hz, 1H), 3.67 (q, J = 3.2 Hz, 0.5H), 3.65 (q, J = 7.2 Hz, 0.5H), 2.82 (dq, J = 12.8, 6.8 Hz, 1H), 1.53−1.43 (m, 0.5H), 1.43−1.24 (m, 2.5H), 1.33 (d, J = 7.2 Hz, 1.5H), 1.32 (d, J = 7.2 Hz, 1.5H), 1.26 (dd, J = 7.2, 7.2 Hz, 3H), 1.16 (dq, J = 14.4, 6.8 Hz, 0.5H), 1.12−1.05 (m, 1H), 1.07 (d, J = 6.8 Hz, 1.5H), 1.07 (d, J = 7.2 Hz, 1.5H), 0.91−0.82 (m, 6.5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 209.9, 209.8, 170.6, 170.5, 61.3, 51.5, 51.3, 43.3, 43.2, 39.9, 39.2, 32.0, 31.8, 30.0, 29.8, 18.9, 18.8, 16.5, 15.9, 14.1, 13.1, 13.0, 11.31, 11.27 (two signals are missing due to overlap); LRMS (EI) 228; HRMS (EI) m/z: calcd for $C_{13}H_{25}O_3$ 229.1804 [M + H$^+$], found 229.1801.

*(+)-(2S,3R,4S,6S)-Oxazolidinone (***32***).* A flame-dried 20 mL two-necked round-bottomed flask was charged with (3*S*)-3-propionyl-4-benzyloxazolidin-2-one (296 mg, 1.27 mmol) and dry CH_2Cl_2 (1.2 mL). To the solution was added *n*-Bu_2BOTf (411 mg, 1.50 mmol) at 0 °C, and the resulting solution was stirred at 0 °C for 2 min. To the solution was added Et_3N (209 μL, 1.50 mmol) at 0 °C, and the solution was stirred at 0 °C for 10 min. To the solution was added a hexanes-EtOAc solution of aldehyde **26** dropwise at −78 °C, and the solution was stirred at −78 °C for 1 h and then at 0 °C for 1 h. The reaction was quenched with pH 7.0 phosphorus buffer (1 mL) and MeOH (4.1 mL), then MeOH-34% H_2O_2 aq. (2:1, 4.1 mL) at 0 °C. The resulting solution was stirred at 0 °C for 1 h, then warmed to room temperature. The reaction mixture was diluted with water and extracted with Et_2O three times. The combined organic extracts were washed with 5% $NaHCO_3$ and brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure at 0 °C to give a crude material, which was purified by flash column chromatography (hexanes-EtOAc = 5:1) to afford aldol product **32** (166 mg, 679 μmol) as a white solid. In addition, the remaining alcohol **25** gave product **32** (380 mg, 994 μmol). In total 546 mg (65%) of **32** was obtained from **24** over 3 steps. R_f = 0.18 (hexanes-EtOAc = 5:1); m.p.: 61−62 °C (hexanes, white prism); $[\alpha]_D^{26}$ +32.3 (c 1.57, $CHCl_3$); IR (neat, cm^{-1}): 3503, 2961, 2926, 2876, 1782, 1697, 1454, 1385, 1352, 1209, 1103, 970, 762, 748, 702; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.34 (t, J = 7.2 Hz, 2H), 7.28 (t, J = 7.2 Hz, 1H), 7.21 (d, J = 7.2 Hz, 2H), 4.72−4.67 (m, 1H), 4.23 (dd, J = 9.0, 7.2 Hz, 1H), 4.19 (dd, J = 9.0, 3.0 Hz, 1H), 3.99 (ddd, J = 14.4, 7.2, 4.8 Hz, 1H), 3.67 (dd, J = 6.0, 4.2 Hz, 1H), 3.26 (dd, J = 13.2, 3.0 Hz, 1H), 2.79 (dd, J = 13.2, 3.0 Hz, 1H), 2.46 (br s, 1H), 1.70−1.63 (m, 1H), 1.51−1.46 (m, 1H), 1.45−1.38 (m, 1H), 1.32 (ddd, J = 13.2, 7.2, 4.8 Hz, 1H), 1.28 (d, J = 7.8 Hz, 3H), 1.06 (dq, J = 15.6, 7.8 Hz, 1H), 0.98−0.92 (m, 1H), 0.96 (d, J = 6.0 Hz, 3H), 0.88 (d, J = 6.0 Hz, 3H), 0.88−0.86 (m, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 177.4, 152.9, 135.0, 129.4, 128.9, 127.4, 75.2, 66.1, 55.1, 40.4, 40.0, 37.7, 33.1, 31.4, 28.3, 20.0, 15.4, 11.7, 11.0; LRMS (EI) 361.2 [M$^+$]; HRMS (EI) m/z: calcd for $C_{21}H_{31}NO_4$ 361.2253 [M$^+$], found 361.2243.

(−)-(2S,3R,4S,6S)-β-Hydroxy Carboxylic Acid ***33***. A screw cap test tube was charged with H_2O_2 (34% w/w solution in H_2O, 39 μL, 0.39 mmol), LiOH·H_2O (3.5 mg, 83 μmol), and H_2O (45 μL). To the solution was added aldol product **32** (20.0 mg, 55.3 μmol) in THF (164 μL) dropwise at 0 °C. After stirring at room temperature for 15 min, the reaction was quenched with saturated aqueous $Na_2S_2O_3$ and 1 M aqueous HCl. The aqueous layer was extracted with EtOAc three times. The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give a crude material, which was purified by preparative TLC (CH_2Cl_2-EtOAc = 20:1) to afford β-hydroxy carboxylic acid **33** (10.0 mg, 47.5 μmol, 86%) as a colorless oil. R_f = 0.32 (hexanes-EtOAc = 1:1); $[\alpha]_D^{27}$ −16.8 (c 1.24, $CHCl_3$); IR (neat, cm^{-1}): 3403, 2962, 2921, 2877, 2852, 1710, 1460, 1380, 1204, 982; ^{1}H NMR (600 MHz, $CDCl_3$): δ 3.69 (dd, J = 5.4, 5.4 Hz, 1H), 2.73 (dq, J = 7.2, 5.4 Hz, 1H), 1.73−1.65 (m, 1H), 1.50−1.43 (m, 1H), 1.43−1.35 (m, 1H), 1.32−1.23 (m, 1H), 1.25 (d, J = 7.8 Hz, 3H), 1.10−1.01 (m, 1H), 0.99 (m, 1H), 0.95 (d, J = 6.0 Hz, 3H), 0.89−0.84 (m, 6H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 181.5, 75.3, 42.4, 40.6, 33.0, 31.2, 28.5, 19.8, 14.7, 11.7, 11.0; LRMS (FAB$^+$) 203; HRMS (FAB$^+$) m/z: calcd for $C_{11}H_{23}O_3$ 203.1669 [M + H$^+$], found 203.1658.

(−)-(2S,3R,4S,6S)-Ethyl Ester ***34***. A screw cap test tube was charged with β-hydroxy carboxylic acid **33** (5.0 mg, 25 μmol) and acetone (411 μL). To the solution was added EtI (25.0 μL, 247 μmol) and K_2CO_3

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(17.0 mg, 124 μmol) at room temperature. After stirring at 50 °C for 3 h, the reaction mixture was diluted with $CHCl_3$ and filtered through a pad of Celite. The filter cake was washed with $CHCl_3$. The filtrate was concentrated under reduced pressure to give a crude material, which was purified by preparative TLC (EtOAc) to afford ethyl ester **34** (5.0 mg, 22 μmol, 89%) as a colorless oil. R_f = 0.73 (hexanes-EtOAc = 1:1); $[\alpha]_D^{27}$ −12 (*c* 0.90, $CHCl_3$); IR (neat, cm^{-1}): 3507, 2963, 2930, 2877, 2855, 1733, 1715, 1462, 1376, 1336, 1254, 1181, 1162, 1114, 1095, 1046, 985; ^1H NMR (600 MHz, $CDCl_3$): δ 4.19−4.10 (m, 2H), 3.62 (br s, 1H), 2.65 (dq, *J* = 6.6, 6.6 Hz, 1H), 2.09 (br s, 1H), 1.61 (dq, *J* = 12.6, 6.6 Hz, 1H), 1.49−1.34 (m, 2H), 1.31−1.22 (m, 1H), 1.27 (dd, *J* = 8.4, 6.0 Hz, 3H), 1.21 (d, *J* = 6.6 Hz, 3H), 1.10−1.00 (m, 1H), 0.98−0.88 (m, 1H), 0.93 (d, *J* = 6.6 Hz, 3H), 0.88−0.80 (m, 6H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 176.1, 75.3, 60.5, 42.6, 40.7, 32.9, 31.2, 28.5, 19.8, 14.5, 14.2, 12.2, 11.0; LRMS (FAB^+) 231; HRMS (FAB^+) *m*/*z*: calcd for $C_{13}H_{27}O_3$ 231.1960 [M + H^+], found 231.1963.

(−)-(2S,3R,4S,6S)-THP-Protected β-Hydroxy Carboxylic Acid ***41***. A flame-dried 50 mL two-necked round-bottomed flask was charged with oxazolidinone **32** (180 mg, 498 μmol), DHP (70.0 μL, 767 μmol), and dry CH_2Cl_2 (3.3 mL). To the solution was added PPTS (12.5 mg, 48.9 μmol). After stirring at room temperature for 20 min, additional DHP (70.0 μL, 767 mmol) and PPTS (12.5 mg, 48.9 μmol) were added. After stirring for additional 15 min, PPTS (12.5 mg, 48.9 μmol) was added, and the stirring was continued for more 3 h. The reaction mixture was diluted with CH_2Cl_2. The separated organic layer was washed twice with 13.2% aqueous sodium chloride, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give a crude material as a colorless oil, which was used for the next reaction without further purification. R_f = 0.47 (hexanes-EtOAc = 3:1). A 50 mL two-necked round-bottomed flask was charged with the crude material, THF (6.75 mL), and H_2O (2.25 mL). To the mixture was added LiOH·H_2O (41 mg, 1.0 mmol) and H_2O_2 (34% w/w solution in H_2O, 0.29 mL, 2.9 mmol) at 0 °C and warmed at room temperature for 1 h. Additional LiOH·H_2O (41 mg, 1.0 mmol) and H_2O_2 (34% w/w solution in H_2O, 291 μL, 2.91 mmol) were added at 0 °C. After stirring at room temperature for 6 h, the reaction was quenched with saturated aqueous $Na_2S_2O_3$ and 1 M aqueous HCl. The separated aqueous layer was extracted with EtOAc three times. The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give a crude material, which was purified by flash column chromatography (hexanes-EtOAc = 3:1) to afford THP-protected β-hydroxy carboxylic acid **41** (127 mg, 443 μmol, 89%) as a colorless oil. R_f = 0.12 (hexanes-EtOAc = 3:1); $[\alpha]_D^{27}$ +12.3 (*c* 3.04, $CHCl_3$); IR (neat, cm^{-1}): 2957, 2876, 2853, 1711, 1705, 1462, 1456, 1132, 1034, 1026, 997; ^1H NMR (600 MHz, $CDCl_3$): δ 4.63 (dd, *J* = 7.2, 3.0 Hz, 0.5H), 4.55 (dd, *J* = 4.8, 2.4 Hz, 0.5H), 4.00−3.93 (m, 1H), 3.82 (dd, *J* = 6.0, 3.6 Hz, 0.5H), 3.74 (dd, *J* = 5.4, 3.6 Hz, 0.5H), 3.53−3.48 (m, 1H), 2.93 (dq, *J* = 13.2, 6.6 Hz, 0.5H), 2.76 (dq, *J* = 13.2, 6.6 Hz, 0.5H), 1.87−1.71 (m, 3H), 1.62−1.45 (m, 7.5H), 1.40−1.31 (m, 1.5H), 1.20 (d, *J* = 7.2 Hz, 1.5H), 1.19 (d, *J* = 7.8 Hz, 1.5H), 1.15−1.05 (m, 0.5H), 1.02−0.94 (m, 0.5H), 0.94 (d, *J* = 6.6 Hz, 1.5H), 0.89−0.84 (m, 7.5H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 181.5, 180.1, 101.8, 100.4, 82.9, 81.7, 64.2, 63.4, 42.7, 42.4, 41.1, 40.9, 33.9, 33.2, 31.5, 31.4, 31.1, 30.9, 29.1, 28.7, 25.3, 25.1, 20.8, 20.2, 19.8, 19.4, 15.4, 15.1, 13.1, 12.6, 11.1, 11.0; LRMS (FAB^+) 287; HRMS (FAB^+) *m*/*z*: calcd for $C_{16}H_{30}O_4$ 287.2222 [M + H^+], found 287.2218.

(−)-Diol ***35***. A screw cap test tube was charged with diacetate **36** (12.0 mg, 22.4 μmol) and MeOH (224 μL). To the solution was added K_2CO_3 (15.0 mg, 112 μmol). After stirring at room temperature for 0.5 h, the reaction mixture was diluted with water and extracted with EtOAc three times. The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give a crude material, which was purified by preparative TLC (CH_2Cl_2-acetone =20:1) to afford diol **35** (10.1 mg, 22.4 μmol, quant.) as a white solid. R_f = 0.36 (CH_2Cl_2-acetone = 10:1); $[\alpha]_D^{27}$ −274 (*c* 0.305, $CHCl_3$); IR (neat, cm^{-1}): 3393, 2918, 1691, 1661, 1651, 1404, 1339, 1196, 1130, 910, 731; ^1H NMR (600 MHz, $CDCl_3$): δ 6.55 (s, 2H), 6.23 (dd, *J* = 7.8, 1.8 Hz, 2H), 4.92 (dd, *J* = 7.8, 1.8 Hz, 2H), 4.88−4.84 (m, 2H), 4.68 (d, *J* = 7.8 Hz, 2H), 4.59 (br s, 2H), 3.04 (s, 4H), 2.28 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 166.5, 138.1, 137.9, 110.8, 107.6, 72.6, 69.3, 64.1, 39.5, 14.8; HRMS (ESI^+) *m*/*z*: calcd for $C_{20}H_{22}N_2O_6S_2Na$ 473.0817 [M + Na^+], found 473.0796.

THP-Protected β-Hydroxy Ester ***42***. A screw cap test tube was charged with core skeleton **35** (8.7 mg, 19 μmol), carboxylic acid **41** (5.5 mg, 19 μmol), and CH_2Cl_2 (100 μL). To the solution was added DMAP (2.3 mg, 19 μmol) and WSCD·HCl (7.4 mg, 39 μmol) at 0 °C. After stirring at reflux for 2 h, the reaction was quenched with 1 M HCl aq. The resulting mixture was extracted with CH_2Cl_2 three times. The combined organic extracts were washed with H_2O and brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by preparative TLC (CH_2Cl_2-acetone = 20:1) to afford THP-protected β-hydroxy ester **42** (5.0 mg, 7.0 μmol, 36%) as a colorless oil with recovery of the core skeleton **35** (2.6 mg, 5.8 μmol, 30%). R_f = 0.47 (CH_2Cl_2-acetone = 10:1); $[\alpha]_D^{27}$ −224 (*c* 0.640, $CHCl_3$); IR (neat, cm^{-1}): 3420, 2957, 2928, 1732, 1693, 1681, 1666, 1651, 1633, 1392, 1128, 1026, 756; ^1H NMR (500 MHz, $CDCl_3$): δ 6.60−6.55 (m, 1H), 6.52 (d, *J* = 1.5 Hz, 1H), 6.32−6.25 (m, 1H), 6.23−6.19 (m, 1H), 5.78 (ddd, *J* = 8.0, 2.0, 2.0 Hz 0.4H), 5.75 (ddd, *J* = 8.0, 2.0, 2.0 Hz, 0.6H), 5.23−5.13 (m, 1H), 4.95−4.91 (m, 1H), 4.89 (d, *J* = 7.5 Hz, 1H), 4.70−4.55 (m, 2H), 4.51−4.40 (m, 1H), 3.96−3.83 (m, 2H), 3.50−3.42 (m, 0.6H), 3.43−3.36 (m, 0.4H), 3.14−2.93 (m, 4H), 2.71−2.60 (m, 1H), 2.30−2.27 (m, 6H), 1.85−1.75 (m, 1H), 1.75−1.65 (m, 1H), 1.67−1.60 (m, 1H), 1.60−1.42 (m, 5H), 1.42−1.33 (m, 1H), 1.31 (d, *J* = 7.0 Hz, 1.2H), 1.25 (d, *J* = 7.5 Hz, 1.8H), 1.15 (dd, *J* = 7.0, 4.0 Hz, 1H), 1.13−0.90 (m, 2H), 0.95 (d, *J* = 6.0 Hz, 1.8H), 0.92 (d, *J* = 9.0 Hz, 1.2H), 0.89−0.80 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 174.6, 174.3, 166.9, 164.10, 164.5, 139.6, 139.3, 137.94, 137.92, 137.8, 137.6, 110.8, 109.7, 109.6, 107.9, 107.8, 106.1, 105.8, 102.0, 100.5, 83.2, 81.7, 72.60, 72.57, 72.1, 71.8, 70.57, 70.54, 69.30, 69.26, 64.17, 64.15, 63.5, 60.6, 60.5, 60.3, 43.2, 42.6, 41.2, 41.1, 40.6, 40.5, 40.3, 40.2, 34.3, 34.1, 31.48, 31.47, 31.3, 31.1, 29.1, 28.8, 28.3, 25.4, 25.3, 21.1, 20.5, 20.2, 19.9, 19.8, 1.6, 15.5, 14.9, 14.83, 14.81, 14.79, 14.6, 12.7, 12.1, 11.2, 11.1, 11.0; HRMS (ESI^+) *m*/*z*: calcd for $C_{36}H_{50}N_2O_9S_2Na$ 741.2855 [M + Na^+], found 741.2820.

β-Hydroxy Ester ***43***. A screw cap test tube was charged with **42** (11.0 mg, 15.3 μmol), MeOH (76 μL), and CH_2Cl_2 (76 μL). To the solution was added PPTS (7.7 mg, 31 μmol). After stirring at 40 °C for 1.5 h, the reaction mixture was diluted with CH_2Cl_2. The organic layer was washed twice with 13.2% aqueous sodium chloride, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give a crude material, which was purified by preparative TLC (CH_2Cl_2-acetone = 20:1) to afford the desired β-hydroxy ester **43** (7.6 mg, 12 μmol, 78%) as a pale yellow solid. R_f = 0.49 (CH_2Cl_2-acetone =10:1); $[\alpha]_D^{21}$ −243 (*c* 0.760, $CHCl_3$); IR (neat, cm^{-1}): 3479, 2961, 2924, 2874, 1728, 1693, 1666, 1659, 1393, 1339, 1194, 1126, 756; ^1H NMR (500 MHz, $CDCl_3$): δ 6.61 (dd, *J* = 2.5, 2.0 Hz, 1H), 6.51 (s, 1H), 6.32 (dd, *J* = 8.5, 2.0 Hz, 1H), 6.21 (dd, *J* = 8.5, 2.5 Hz, 1H), 5.88 (ddd, *J* = 8.0, 2.0, 2.0 Hz, 1H), 5.16 (d, *J* = 7.5 Hz, 1H), 4.93 (dd, *J* = 8.0, 2.0 Hz, 1H), 4.91−4.87 (m, 1H), 4.71−4.66 (m, 1H), 4.62, (dd, *J* = 8.5, 2.0 Hz, 1H), 4.43 (br s, 1 H), 3.77 (dd, *J* = 8.0, 2.5 Hz, 1H), 3.14−2.95 (m, 4H), 2.72 (dq, *J* = 7.5, 3.0 Hz, 1H), 2.31 (s, 3H), 2.30 (s, 3H), 1.67−1.59 (m, 1H), 1.55−1.40 (m, 3H), 1.22 (d, *J* = 7.0 Hz, 3H), 1.21−1.15 (m, 1H), 1.04−0.97 (m, 1H), 0.99 (d, *J* = 6.0 Hz, 3H), 0.94−0.82 (m, 7H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 175.1, 166.8, 164.8, 139.9, 138.1, 138.0, 137.6, 110.8, 109.4, 107.8, 105.6, 74.7, 72.5, 71.8, 70.3, 69.6, 64.2, 60.8, 42.3, 40.6, 40.5, 40.4, 33.1, 31.3, 27.7, 20.3, 15.9, 14.9, 14.8, 10.9, 9.8; HRMS (ESI^+) *m*/*z*: calcd for $C_{31}H_{42}N_2O_8S_2Na$ 657.2280 [M + Na^+], found 657.2269.

(−)-(2R,4R)-Oxazolidinone ***45***. A flame-dried 50 mL two-necked round-bottomed flask was charged with dry THF (7 mL). To the solution was added NaHMDS (1.9 M in THF, 2.6 mL, 4.9 mmol) at −78 °C and then oxazolidinone **44** (1.02 g, 3.52 mmol) in THF (5 mL) via cannula at −78 °C over 5 min. After stirring stirred at −78 °C for 0.5 h, MeI (1.09 mL, 17.6 mmol) was added dropwise at −78 °C over 3 min. After stirring at −78 °C for 2 h, the reaction was quenched with AcOH at −78 °C and allowed to warm to room temperature. The reaction mixture was diluted with water and extracted with EtOAc three times. The combined organic extracts were washed with water and brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give a crude material, which was purified by flash

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column chromatography (hexanes-EtOAc = 5:1) to afford oxazolidinone **45** (909 mg, 2.99 mmol, 85%) as a colorless oil. R_f = 0.28 (hexanes-EtOAc = 5:1); $[\alpha]_D^{27}$ −68.6 (*c* 4.13, $CHCl_3$); IR (neat, cm^{-1}): 2962, 2929, 2874, 1781, 1698, 1456, 1387, 1350, 1289, 1241, 1209, 1099, 1016, 973, 742, 702; ^1H NMR (600 MHz, $CDCl_3$): δ 7.34 (t, *J* = 7.8 Hz, 2H), 7.29−7.24 (m, 1H), 7.22 (d, *J* = 7.8 Hz, 2H), 4.69 (ddt, *J* = 9.6, 7.2, 3.0 Hz, 1H), 4.20 (dd, *J* = 9.0, 7.8 Hz, 1H), 4.17 (dd, *J* = 9.0, 3.0 Hz, 1H), 3.90−3.84 (m, 1H), 3.26 (dd, *J* = 13.2, 3.0 Hz, 1H), 2.77 (dd, *J* = 13.8, 9.6 Hz, 1H), 1.85 (ddd, *J* = 13.8, 9.0, 5.4 Hz, 1H), 1.42−1.29 (m, 2H), 1.22 (d, *J* = 7.2 Hz, 3H), 1.19−1.09 (m, 2H), 0.88 (dd, *J* = 7.8, 6.6 Hz, 3H), 0.86 (d, *J* = 6.0 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 177.3, 152.9, 135.2, 129.4, 128.8, 127.2, 65.9, 55.2, 40.4, 37.8, 35.3, 32.2, 29.3, 19.3, 18.3, 11.2; LRMS (EI) *m*/*z*: 303 [M^+]; HRMS (EI) *m*/*z*: calcd for $C_{18}H_{25}NO_3$ 303.1834 [M^+], found 303.1822. Spectral data matched the reported data.[27]

*(2R,3S,4R,6R)-Oxazolidinone **49**.* A flame-dried 30 mL two-necked round-bottomed flask was charged with oxazolidinone **45** (400 mg, 1.32 mmol), dry MeOH (266 μL, 6.59 mmol), and dry THF (6.6 mL). To the solution was added $LiBH_4$ (143 mg, 6.59 mmol) at 0 °C. After stirring at room temperature for 5 h, the reaction was quenched with 1 M NaOH aq. at 0 °C then warmed to room temperature. The reaction mixture was diluted with water and extracted with EtOAc three times. The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure at 0 °C to give a crude material, which was purified by flash column chromatography (hexanes-EtOAc = 3:1) to afford alcohol **46** as a hexanes-EtOAc solution. All the solvent was not removed due to the volatility of the product. R_f = 0.22 (hexanes-EtOAc = 5:1). A flame-dried 20 mL two-necked round-bottomed flask was charged with a hexanes-EtOAc solution **46**, Et_3N (918 μL, 6.59 mmol), dry DMSO (1.3 mL), and dry CH_2Cl_2 (2.6 mL). To the solution was added SO_3·Py (1.05 g, 6.59 mmol) at 0 °C. After stirring at 0 °C for 15 min, the reaction was quenched with water at 0 °C. The reaction mixture was extracted with CH_2Cl_2 three times. The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure at 0 °C to give a crude material, which was purified by flash column chromatography (hexanes-EtOAc = 3:1) to afford aldehyde **47** as a hexanes-EtOAc solution. All the solvent was not removed due to the volatility of the product. R_f = 0.42 (hexanes-EtOAc = 5:1). A flame-dried 20 mL two-necked round-bottomed flask was charged with (3*R*)-3-propionyl-4-benzyloxazolidin-2-one (338 mg, 1.45 mmol) and dry CH_2Cl_2 (1.3 mL). To the solution was added *n*-Bu_2BOTf (469 mg, 1.71 mmol) at 0 °C. After stirring at 0 °C for 10 min, Et_3N (239 μL, 1.71 mmol) was added at 0 °C. Then, after stirring at 0 °C for 10 min, a hexanes-EtOAc solution of **48** was added dropwise at −78 °C. The resulting solution was stirred at −78 °C for 1 h and then warmed to 0 °C over 35 min. The reaction was quenched with pH 7.0 phosphorus buffer (1.5 mL) and MeOH (4 mL), then MeOH-34% H_2O_2 aq. (2:1, 6 mL) at 0 °C. The resulting solution was stirred at 0 °C for 1 h and then warmed to room temperature. The reaction mixture was diluted with water and extracted with Et_2O three times. The combined organic extracts were washed with 5% $NaHCO_3$ and brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure at 0 °C to give a crude material, which was purified by flash column chromatography (hexanes-EtOAc = 5:1) to afford oxazolidinone **49** (213 mg, 593 μmol, 45% over 3 steps from **45**) as a white solid. R_f = 0.18 (hexanes-EtOAc = 5:1); m.p.: 62−63 °C (hexanes, white prism); $[\alpha]_D^{27}$ −34.5 (*c* 1.54, $CHCl_3$). Spectral data matched the compound **32**.

*(−)-(2R,3S,4R,6R)-Carboxylic Acid **50**.* A flame-dried 20 mL two-necked round-bottomed flask was charged with oxazolidinone **49** (190 mg, 526 μmol), DHP (144 μL, 1.58 mmol), and dry CH_2Cl_2 (3.5 mL). To the solution was added PPTS (53 mg, 0.21 mmol). After stirring at room temperature for 1 h, additional DHP (48.0 μL, 526 μmol) and PPTS (13.3 mg, 52.6 μmol) were added. After stirring at room temperature for 0.5 h, the reaction mixture was diluted with CH_2Cl_2. The separated organic layer was washed twice with 13.2% aqueous sodium chloride, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give a crude material as a colorless oil, which was used to the next reaction without further purification. R_f = 0.47 (hexanes-EtOAc = 3:1). A 20 mL two-necked round-bottomed flask was charged the crude material, THF (2 mL), and H_2O (0.6 mL). To the solution was added H_2O_2 (34% w/w solution in H_2O, 268 μL, 2.63 mmol) and LiOH·H_2O (44 mg, 1.1 mmol) at 0 °C. After stirring at room temperature for 10 h, the reaction was quenched with saturated aqueous $Na_2S_2O_3$ and 1 M HCl aq. The separated aqueous layer was extracted with EtOAc three times. The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give a crude material, which was purified by flash column chromatography (hexanes-EtOAc = 3:1) to afford carboxylic acid **50** (98.1 mg, 341 μmol, 65% over 2 steps from **49**) as a as a colorless oil. R_f = 0.12 (hexanes-EtOAc = 3:1); $[\alpha]_D^{27}$ −12.7 (*c* 3.35, $CHCl_3$). Spectral data matched the compound **41**.

*(−)-(2R,3S,4S,6S)-Oxazolidinone **54** (for Preparation of β-Hydroxy Carboxylic Acid **54**).* A flame-dried 30 mL two-necked round-bottomed flask was charged with oxazolidinone **24** (400 mg, 1.32 mmol), dry MeOH (266 μL, 6.59 mmol), and dry THF (6.6 mL). To the solution was added $LiBH_4$ (143 mg, 6.59 μmol) at 0 °C. After stirring at room temperature for 5 h, the reaction was quenched with 1 M NaOH at 0 °C. The reaction mixture was diluted with water and extracted with EtOAc three times. The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure at 0 °C to give a crude material, which was purified by flash column chromatography (hexanes-EtOAc = 3:1) to afford alcohol **25** as a hexanes-EtOAc solution. All the solvent was not removed due to the volatility of the product. R_f = 0.22 (hexanes-EtOAc = 5:1). A flame-dried 20 mL two-necked round-bottomed flask was charged with a hexanes-EtOAc solution of **25**, Et_3N (918 μL, 6.59 mmol), dry DMSO (1.3 mL), and dry CH_2Cl_2 (2.6 mL). To the solution was added SO_3·Py (1.05 g, 6.59 mmol) at 0 °C. After stirring at 0 °C for 10 min, the reaction was quenched with water at 0 °C. The reaction mixture was extracted with CH_2Cl_2 three times. The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure at 0 °C to give a crude material, which was purified by flash column chromatography (hexanes-EtOAc = 3:1) to afford aldehyde **26** as a hexanes-EtOAc solution. All the solvent was not removed due to the volatility of the product. R_f = 0.42 (hexanes-EtOAc = 5:1). A flame-dried 20 mL two-necked round-bottomed flask was charged with (3*R*)-3-propionyl-4-benzyloxazolidin-2-one (338 mg, 1.45 mmol) and dry CH_2Cl_2 (1.3 mL). To the solution was added *n*-Bu_2BOTf (469 mg, 1.71 mmol) at 0 °C. After stirring at 0 °C for 10 min, Et_3N (239 μL,1.71 mmol) was added at 0 °C, and the resulting solution was stirred at 0 °C for 10 min. Then, a hexanes-EtOAc solution **26** was added dropwise at −78 °C, and the resulting solution was stirred at −78 °C for 1 h and then 0 °C for 0.5 h. The reaction was quenched with pH 7.0 phosphorus buffer (1.5 mL) and MeOH (4 mL), then MeOH-34% H_2O_2 aq. (2:1, 6 mL) at 0 °C. The resulting solution was stirred at 0 °C for 1 h and then warmed to room temperature. The reaction mixture was diluted with water and extracted with Et_2O three times. The combined organic extracts were washed with 5% $NaHCO_3$ and brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure at 0 °C to give a crude material, which was purified by flash column chromatography (CH_2Cl_2) to afford **S4** (390 mg, 1.08 mmol, 82% over 3 steps from **24**) as a white solid. R_f = 0.15 (hexanes-EtOAc = 5:1); $[\alpha]_D^{27}$ −56.1 (*c* 2.04, $CHCl_3$); m.p.: 86−87 °C (hexanes, white prism); IR (neat, cm^{-1}): 3524, 2961, 2930, 2874, 1782, 1697, 1454, 1385, 1350, 1236, 1209, 1107, 982, 970, 762, 702; ^1H NMR (600 MHz, $CDCl_3$): δ 7.36−7.32 (m, 2H), 7.30−7.25 (m, 1H), 7.22−7.19 (m, 2H), 4.69 (ddt, *J* = 9.6, 7.8, 3.6 Hz, 1H), 4.21 (dd, *J* = 9.0, 7.8 Hz, 1H), 4.19 (dd, *J* = 9.0, 3.0 Hz, 1H), 3.97 (dq, *J* = 7.2, 3.0 Hz, 1H), 3.59 (dd, *J* = 8.4, 3.0 Hz, 1H), 3.26 (dd, *J* = 13.2, 3.6 Hz, 1H), 2.97 (dd, *J* = 13.2, 9.6 Hz, 1H), 2.72 (br s, 1H), 1.68−1.60 (m, 2H), 1.49−1.40 (m, 2H), 1.25 (d, *J* = 6.6 Hz, 3H), 1.06−0.98 (m, 1H), 0.96−0.91 (m, 1H), 0.90−0.85 (m, 9H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 177.8, 152.8, 135.0, 129.4, 129.0, 127.4, 76.1, 66.1, 55.2, 40.2, 39.7, 37.8, 33.5, 31.8, 27.9, 20.4, 16.0, 11.1, 10.3; LRMS (EI) 361; HRMS (EI) *m*/*z*: calcd for $C_{21}H_{31}NO_4$ 361.2253 [M^+], found 361.2235.

*(−)-(2R,3S,4S,6S)-THP-Protected β-Hydroxy Carboxylic Acid **54**.* A flame-dried 20 mL two-necked round-bottomed flask was charged with the above oxazolidinone **S4** (190 mg, 526 μmol), DHP (144 μL, 1.58 mmol), and dry CH_2Cl_2 (3.5 mL). To the solution was added PPTS

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(53 mg, 0.21 mmol). After stirring at room temperature for 1.5 h, the reaction was diluted with CH_2Cl_2. The separated organic layer was washed twice with 13.2% aqueous sodium chloride, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give a crude material as a colorless oil, which was used to the next reaction without further purification. R_f = 0.33 (hexanes-EtOAc = 5:1). A 20 mL two-necked round-bottomed flask was charged with the crude material, THF (2.0 mL), and H_2O (0.6 mL). To the solution was added H_2O_2 (34% w/w solution in H_2O, 0.27 mL, 2.6 mmol) and $LiOH{\cdot}H_2O$ (44 mg, 1.1 mmol) at 0 °C. After stirring at room temperature for 9 h, the reaction was quenched with saturated aqueous $Na_2S_2O_3$ and 1 M aqueous HCl. The separated aqueous layer was extracted with EtOAc three times. The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give a crude material, which was purified by flash column chromatography (hexanes-EtOAc = 3:1) to afford THP-protected β-hydroxy carboxylic acid **54** (83.0 mg, 289 mmol, 55% over 2 steps from the oxazolidinone **S4**) as a colorless oil. R_f = 0.19 (hexanes-EtOAc = 3:1); $[\alpha]_D^{27}$ −24.3 (*c* 2.35, $CHCl_3$); IR (neat, cm^{-1}): 2957, 2875, 2854, 1737, 1708, 1462, 1381, 1282, 1234, 1201, 1167, 1131, 1077, 1084, 998, 962, 905, 869, 813; ^1H NMR (500 MHz, $CDCl_3$): δ 4.63 (dd, *J* = 5.0, 3.0 Hz, 0.5H), 4.56 (dd, *J* = 6.0, 2.0 Hz, 0.5H), 3.95−3.89 (m, 1H), 3.85 (dd, *J* = 5.0, 5.0 Hz, 0.5H), 3.74 (dd, *J* = 5.0, 5.0 Hz, 0.5H), 3.52−3.43 (m, 1H), 2.82 (dq, *J* = 7.0, 4.5 Hz, 0.5H), 2.71 (dq, *J* = 7.0, 4.5 Hz, 0.5H), 1.89−1.69 (m, 3H), 1.61−1.33 (m, 7.5H), 1.22 (d, *J* = 7.5 Hz, 1.5H), 1.19 (d, *J* = 7.0 Hz, 1.5H), 1.07−0.65 (m, 1.5H), 0.97 (d, *J* = 7.0 Hz, 1.5H), 0.91 (d, *J* = 7.0 Hz, 1.5H), 0.89−0.83 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 181.9, 180.6, 101.0, 100.2, 83.7, 82.1, 63.6, 63.1, 41.7, 41.3, 39.7, 39.5, 34.9, 33.5, 31.7, 31.6, 31.0, 30.9, 28.4, 28.0, 25.4, 25.2, 20.5, 20.2, 19.98, 19.97, 16.6, 16.5, 12.5, 11.6, 11.0, 10.8; LRMS (FAB^+) 287; HRMS (FAB^+) *m*/*z*: calcd for $C_{16}H_{31}O_4$ 287.2222 [M + H^+], found 287.2216.

THP-Protected β-Hydroxy Ester ***S5***. A screw cap test tube was charged with the core skeleton **35** (11 mg, 24 μmol), THP-protected β-hydroxy carboxylic acid **54** (6.4 mg, 24 μmol), and CH_2Cl_2 (120 μL). To the solution was added DMAP (3.0 mg, 24 μmol) and WSCD·HCl (9.3 mg, 49 μmol) at 0 °C. After stirring at reflux for 2 h, the reaction was quenched with 1 M aqueous HCl. The resulting mixture was extracted with CH_2Cl_2 three times. The combined organic extracts were washed with H_2O and brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give a residue, which was purified by preparative TLC (CH_2Cl_2-acetone = 40:1) to afford THP-protected β-hydroxy ester **S5** (5.4 mg, 7.6 μmol, 31%) as a pale yellow solid with recovery of the core skeleton **35** (3.5 mg, 7.8 μmol, 32%). R_f = 0.45 (CH_2Cl_2-acetone =10:1); $[\alpha]_D^{27}$ −235 (*c* 0.215, $CHCl_3$); IR (neat, cm^{-1}): 3435, 2961, 2926, 2876, 1732, 1695, 1676, 1674, 1666, 1659, 1385, 1198, 1128, 1026, 756; ^1H NMR (600 MHz, $CDCl_3$): δ 6.58 (s, 1H), 6.52 (s, 1H), 6.33−6.27 (m, 1H), 6.23−6.19 (m, 1H), 5.96−5.93 (m, 0.4H), 5.92−5.87 (m, 0.6H), 5.14−5.09 (m, 1H), 4.93 (dd, *J* = 8.4, 1.8 Hz, 1H), 4.90 (d, *J* = 8.4 Hz, 1H), 4.71 (dd, *J* = 7.8, 1.8 Hz, 1H), 4.67 (br s, 1H), 4.61 (ddd, *J* = 13.8, 7.2, 4.8 Hz, 1H), 4.45−4.39 (m, 1H), 3.96−3.87 (m, 0.6H), 3.87−3.80 (m, 0.4H), 3.50−3.43 (m, 0.6H), 3.41−3.35 (m, 0.4H), 3.13−2.94 (m, 4H), 2.71−2.66 (m, 1H), 2.29 (s, 3.6H), 2.28 (s, 2.4H), 1.83−1.74 (m, 1H), 1.72−1.65 (m, 1H), 1.60−1.38 (m, 8H), 1.30−1.16 (m, 1H), 1.22 (d, *J* = 7.2 Hz, 1.2H), 1.15 (d, *J* = 7.2 Hz, 1.8H), 1.08−1.00 (m, 1H), 1.00−0.82 (m, 10H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 175.3, 174.2, 167.0, 166.9, 164.2, 164.1, 139.7, 139.3, 138.0, 137.90, 137.86, 137.6, 137.5, 110.9, 109.6, 109.4, 108.0, 107.9, 106.0, 105.6, 99.8, 99.0, 83.4, 81.2, 72.61, 72.56, 71.4, 71.0, 70.5, 69.4, 69.3, 64.1, 63.0, 62.5, 60.9, 60.6, 41.0, 40.55, 40.51, 40.48, 40.2, 40.10, 40.05, 34.8, 34.2, 31.9, 31.7, 30.9, 28.4, 28.0, 25.5, 25.4, 20.4, 20.1, 20.0, 19.7, 16.8, 16.5, 14.91, 14.86, 14.72, 14.70, 11.6, 11.1, 11.0, 10.6 (six signals are missing due to overlap); HRMS (ESI^+) *m*/*z*: calcd for $C_{36}H_{50}N_2O_9S_2Na$ 741.2855 [M + Na^+], found 741.2832.

β-Hydroxy Ester ***51***. A screw cap test tube was charged with THP-protected β-hydroxy ester **S5** (2.7 mg, 3.9 μmol), MeOH (25 μL), and CH_2Cl_2 (25 μL). To the solution was added PPTS (2.0 mg, 7.8 μmol). After stirring at 50 °C for 1.5 h, the reaction mixture was diluted with CH_2Cl_2. The separated organic layer was washed twice with 13.2% aqueous sodium chloride, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give a crude material, which was purified by preparative TLC (CH_2Cl_2-acetone = 20:1) to afford β-hydroxy ester **51** (1.7 mg, 8.3 μmol, 72%) as a white solid. R_f = 0.14 (CH_2Cl_2-acetone = 20:1); $[\alpha]_D^{25}$ −330 (*c* 0.151, $CHCl_3$); IR (neat, cm^{-1}): 3468, 2961, 2926, 2874, 1732, 1693, 1680, 1676, 1666, 1651, 1393, 1385, 1339, 1192, 1126, 754; ^1H NMR (500 MHz, $CDCl_3$): δ 6.62−6.58 (m, 1H), 6.54−6.51 (m, 1H), 6.31 (dd, *J* = 8.5, 2.5 Hz, 1H), 6.22 (dd, *J* = 8.0, 2.5 Hz. 1H), 5.80 (ddd, *J* = 8.5, 2.0, 2.0 Hz, 1H), 5.22−5.17 (m, 1H), 4.93 (dd, *J* = 8.0, 2.5 Hz, 1H), 4.93−4.87 (m, 1H), 4.72−4.64 (m, 1H), 4.66 (dd, *J* = 8.5, 2.0 Hz, 1H), 4.43 (br s, 1 H), 3.67 (dd, *J* = 8.5, 2.5 Hz, 1H), 3.13−2.95 (m, 4H), 2.69 (dq, *J* = 7.5, 3.0 Hz, 1H), 2.53 (br s, 1H), 2.299 (s, 3H), 2.297 (s, 3H), 1.69 (ddd, *J* = 13.0, 9.0, 3.0 Hz, 1H), 1.65−1.39 (m, 3H), 1.20 (d, *J* = 7.0 Hz, 3H), 1.07−0.99 (m, 1H), 0.97−0.90 (m, 1H), 0.89 (d, *J* = 6.5 Hz, 3H), 0.86 (dd, *J* = 7.5, 7.5 Hz, 3H), 0.83 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 175.5, 166.8, 164.4, 139.8, 138.05, 137.95, 137.6, 110.9, 109.5, 107.8, 105.7, 75.9, 72.6, 72.2, 70.4, 69.4, 64.1, 60.4, 42.0, 40.5, 40.4, 40.3, 33.6, 31.8, 27.9, 20.5, 16.1, 14.9, 14.8, 11.0, 9.6; HRMS (ESI^+) *m*/*z*: calcd for $C_{31}H_{42}N_2O_8S_2Na$ 657.2280 [M + Na^+], found 657.2273.

β-Keto Ester ***37***. A screw cap test tube was charged with the β-hydroxy ester **43** (2.9 mg, 4.6 μmol) and dry CH_2Cl_2 (76 μL). To the solution was added Dess−Martin periodinane (2.3 mg, 9.1 μmol) at 0 °C. After stirring at 0 °C for 1.5 h, the separated organic layer was washed with saturated aqueous $NaHCO_3$ and brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give a crude material, which was purified by preparative TLC (CH_2Cl_2-acetone = 20:1) to afford a 2:3 mixture of β-keto ester **37** and its C2′ epimer, **38** (1.0 mg, 1.6 μmol, 34%) as a pale yellow solid with recovery of the diol (1.2 mg, 1.9 μmol, 41%). R_f = 0.43 (CH_2Cl_2-acetone = 10:1). The physical data of a 2:3 mixture of **37** and **38**: IR (neat, cm^{-1}): 3410, 2963, 2925, 2874, 2853, 1744, 1693, 1680, 1674, 1666, 1658, 1651, 1385, 1339, 1192, 1128, 1005, 754; ^1H NMR (600 MHz, $CDCl_3$): δ 6.62−6.58 (m, 1H), 6.53 (s, 1H), 6.33−6.27 (m, 1H), 6.21 (d, *J* = 7.8, 1H), 5.95−5.90 (m, 0.6H), 5.75−5.71 (m, 0.4H), 5.25 (d, *J* = 7.2 Hz, 0.4H), 5.11 (d, *J* = 8.4 Hz, 0.6H), 4.95−4.92 (m, 1H), 4.92−4.88 (m, 1H), 4.73−4.70 (m, 0.4H), 4.68 (dd, *J* = 9.0, 8.4 Hz, 1H), 4.63−4.60 (m, 0.6H), 4.45 (m, 0.4H), 4.39 (m, 0.6H), 3.70 (q, *J* = 7.2 Hz, 0.6H), 3.65 (q, *J* = 7.2 Hz, 0.4H), 3.13−2.87 (m, 5H), 2.32−2.26 (m, 6H), 1.80−1.70 (m, 1H), 1.41 (d, *J* = 6.6 Hz, 1.2H), 1.41−1.25 (m, 2H), 1.32 (d, *J* = 7.2 Hz, 1.8H), 1.17 (d, *J* = 7.2 Hz, 1.8H), 1.16−1.04 (m, 2H), 1.08 (d, *J* = 7.2 Hz, 1.2H), 0.91−0.84 (m, 6H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 210.5, 210.0, 169.7, 169.4, 166.80, 166.78, 164.3, 164.2, 139.9, 139.6, 138.1, 138.0, 137.7, 110.9, 110.8, 109.4, 109.3, 107.9, 107.8, 105.4, 105.0, 73.0, 72.6, 72.5, 71.9, 70.5, 70.3, 69.6, 69.3, 64.1, 60.7, 60.3, 51.7, 50.9, 43.9, 43.1, 40.6, 40.3, 40.2, 40.0, 39.9, 32.2, 32.0, 29.4, 29.3, 19.5, 19.4, 17.4, 17.3, 14.94, 14.88, 14.78, 14.6, 12.7, 11.2, 11.1 (Six signals are missing due to overlap.); HRMS (ESI^+) *m*/*z*: calcd for $C_{31}H_{40}N_2O_8S_2Na$ 655.2124 [M + Na^+], found 655.2148.

β-Keto Ester ***38***. A screw cap test tube was charged with β-hydroxy ester **51** (1.5 mg, 2.4 μmol) and dry CH_2Cl_2 (40 μL). To the solution was added Dess−Martin periodinane (1.2 mg, 4.7 μmol) at 0 °C. After stirring at 0 °C for 45 min, additional Dess−Martin periodinane (1.2 mg, 4.7 μmol) was added at 0 °C, and the resulting mixture was stirred at 0 °C for 15 min. The reaction mixture was diluted with CH_2Cl_2. The organic layer was washed with saturated aqueous $NaHCO_3$ and brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give a crude material, which was purified by preparative TLC (CH_2Cl_2-acetone = 20:1) to afford a 5:1 mixture of **38** and its C2′ epimer, **37** (1.0 mg, 1.6 μmol, 67%) as a white solid with recovery of β-hydroxy ester **51** (0.50 mg, 0.65 μmol, 27%). R_f = 0.45 (CH_2Cl_2-acetone =10:1); $[\alpha]_D^{27}$ −220 (*c* 0.090, $CHCl_3$); IR (neat, cm^{-1}): 3410, 2963, 2925, 2874, 2853, 1746, 1693, 1678, 1674, 1666, 1645, 1385, 1339, 1192, 1128, 1005, 752; ^1H NMR (600 MHz, $CDCl_3$): δ 6.61−6.58 (m, 1H), 6.53 (s, 1H), 6.30 (dd, *J* = 7.8, 2.4 Hz, 1H), 6.22 (dd, *J* = 8.4, 2.4 Hz, 1H), 5.92 (ddd, *J* = 8.4, 2.4, 2.4 Hz, 1H), 5.11 (d, *J* = 9.0 Hz, 1H), 4.93 (dd, *J* = 8.4, 2.4 Hz, 1H), 4.92−4.88 (m, 1H), 4.67 (d, *J* = 7.8 Hz, 1H), 4.62 (dd, *J* = 7.8, 1.8 Hz, 1H), 4.39 (br s, 1H), 3.70 (q,

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J = 7.2 Hz, 1H), 3.13−2.99 (m, 4H), 2.99−2.89 (m, 1H), 2.31 (s, 3H), 2.29 (s, 3H), 1.74 (ddd, J = 13.8, 7.8, 5.4 Hz, 1H), 1.43−1.24 (m, 2H), 1.32 (d, J = 7.2 Hz, 3H), 1.17 (d, J = 7.2 Hz, 3H), 1.16−1.04 (m, 2H), 0.91−0.80 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 210.5, 169.3, 166.8, 164.3, 139.9, 138.1, 138.0, 137.7, 110.8, 109.3, 107.9, 105.0, 72.5, 71.9, 70.3, 69.6, 64.1, 60.7, 50.9, 43.8, 40.6, 40.2, 40.0, 32.2, 29.3, 19.3, 17.3, 14.9, 14.5, 12.8, 11.1; HRMS (ESI$^+$) m/z: calcd for $C_{31}H_{40}N_2O_8S_2Na$ 655.2124 [M + Na^+], found 655. 2105.

(+)-(2S,3R,4R,6R)-Oxazolidinone ***S6***. A flame-dried 30 mL two-necked round-bottomed flask was charged with oxazolidinone **45** (400 mg,1.32 mmol), dry MeOH (266 μL, 6.59 mmol), and dry THF (6.6 mL). To the solution was added $LiBH_4$ (143 mg, 6.59 mmol) at 0 °C. After stirring at 0 °C for 11.5 h, the reaction was quenched with 1 M NaOH aq. at 0 °C. The reaction mixture was diluted with water and extracted with EtOAc three times. The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure at 0 °C to give a crude material, which was purified by flash column chromatography (hexanes-EtOAc = 3:1) to afford alcohol **46** as a hexanes-EtOAc solution. All the solvent was not removed due to the volatility of the product. R_f = 0.22 (hexanes-EtOAc = 5:1). A flame-dried 20 mL two-necked round-bottomed flask was charged with a hexanes-EtOAc solution of **46**, Et_3N (918 μL, 6.59 mmol), dry DMSO (1.3 mL), and dry CH_2Cl_2 (2.6 mL). To the solution was added SO_3·Py (1.05 g, 6.59 mmol) at 0 °C. After stirring at 0 °C for 15 min, the reaction was quenched with water at 0 °C. The reaction mixture was extracted with CH_2Cl_2 three times. The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure at 0 °C to give a crude material, which was purified by flash column chromatography (hexanes-EtOAc = 3:1) to afford aldehyde **47** in hexanes-EtOAc solution. All the solvent was not removed due to the volatility of the product. R_f = 0.42 (hexanes-EtOAc = 5:1). A flame-dried 20 mL two-necked round-bottomed flask was charged with (3S)-3-propionyl-4-benzyloxazolidin-2-one (338 mg, 1.45 mmol) and dry CH_2Cl_2 (1.3 mL). To the solution was added n-Bu_2BOTf (469 mg, 1.71 mmol) at 0 °C. After stirring at 0 °C for 10 min, Et_3N (239 μL, 1.71 mmol) was added at 0 °C. Then, after stirring at 0 °C for 10 min, a CH_2Cl_2 solution of aldehyde **47** was added dropwise at −78 °C and stirring was continued at −78 °C for 1 h and at 0 °C for 0.5 h. The reaction was quenched with pH 7.0 phosphorus buffer (1.5 mL) and MeOH (4 mL), then MeOH-34% H_2O_2 aq. (2:1, 6 mL) at 0 °C. After stirring at 0 °C for 1 h, the reaction mixture was diluted with water and extracted with Et_2O three times. The combined organic extracts were washed with 5% $NaHCO_3$ brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure at 0 °C to give a crude material, which was purified by flash column chromatography (CH_2Cl_2 only) to afford the corresponding aldol product **S6** (174 mg, 482 μmol, 33% over 3 steps from **45**) as a colorless solid. R_f = 0.15 (hexanes-EtOAc = 5:1); m.p.: 88.9−89.4 °C (hexanes, white prism); $[\alpha]_D^{27}$ +57.1 (c 1.26, $CHCl_3$). Spectral data matched the compound **S4**.

(+)-(2S,3R,4R,6R)-THP-Protected β-Hydroxy Carboxylic Acid ***S7***. A flame-dried 20 mL two-necked round-bottomed flask was charged with the above aldol product **S6** (174 mg, 482 mmol), DHP (132 μL,1.45 mmol), and dry CH_2Cl_2 (2.5 mL). To the solution was added PPTS (48 mg, 0.19 mmol). After stirring at room temperature for 1.5 h, the reaction mixture was diluted with CH_2Cl_2. The separated organic layer was washed twice with 13.2% aqueous sodium chloride, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give a crude material as a colorless oil, which was used to the next reaction without further purification. R_f = 0.33 (hexanes-EtOAc = 5:1). A 20 mL two-necked round-bottomed flask was charged with the crude material, dry THF (1.8 mL), and H_2O (0.6 mL). To the solution was added H_2O_2 (34% w/w solution in H_2O, 0.24 mL, 2.4 mmol) and LiOH·H_2O (40 mg, 0.96 mmol) at 0 °C. After stirring at room temperature for 10.5 h, the reaction was quenched with saturated aqueous $Na_2S_2O_3$ and 1 M aqueous HCl. The aqueous layer was extracted with EtOAc three times. The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give a crude material, which was purified by flash column chromatography (hexanes-EtOAc = 3:1) to afford the THP-protected β-hydroxy carboxylic acid **S7** (94.2 mg, 328 mmol, 68% over 2 steps from **S6**) as a colorless oil. R_f = 0.15 (hexanes-EtOAc = 5:1); $[\alpha]_D^{27}$ +21.0 (c 4.40, $CHCl_3$). Spectral data matched the compound **54**.

THP-Protected β-Hydroxy Ester ***S8***. A screw cap test tube was charged with the core skeleton **35** (11 mg, 24 μmol), the above THP-protected β-hydroxy carboxylic acid **S7** (6.4 mg, 24 μmol), and CH_2Cl_2 (120 μL). The solution was cooled to 0 °C. To the solution was added DMAP (3.0 mg, 24 μmol) and WSCD·HCl (9.3 mg, 49 μmol) at 0 °C. After stirring the resulting mixture at reflux for 3 h, the reaction was quenched with 1 M aqueous HCl. The resulting mixture was extracted with CH_2Cl_2 three times. The combined organic extracts were washed with H_2O and brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give a residue, which was purified by preparative TLC (CH_2Cl_2-EtOAc = 40:1) to afford THP-protected β-hydroxy ester **S8** (6.4 mg, 8.9 μmol, 37%) as a colorless oil with recovery of the core skeleton **35** (3.5 mg, 7.8 μmol, 32%). R_f = 0.47 (CH_2Cl_2-acetone = 10:1); $[\alpha]_D^{27}$ −196 (c 0.300, $CHCl_3$); IR (neat, cm^{-1}): 3420, 2961, 2926, 2876, 1732, 1691, 1676, 1668, 1662, 1654, 1385, 1198, 1126, 1026, 756; ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.60−6.56 (m, 1H), 6.52 (s, 1H), 6.32−6.25 (m, 1H), 6.24−6.19 (m, 1H), 5.83 (ddd, J = 7.5, 2.0, 2.0 Hz, 0.4H), 5.76 (ddd, J = 8.0, 2.0, 2.0 Hz, 0.6H), 5.23−5.08 (m, 1H), 4.95−4.86 (m, 1.6H), 4.84 (dd, J = 8.0, 2.0 Hz, 0.4H), 4.70−4.59 (m, 2H), 4.52−4.40 (m, 1H), 3.97−3.82 (m, 2H), 3.51−3.43 (m, 0.6H), 3.41−3.35 (m, 0.4H), 3.12−2.95 (m, 4H), 2.69−2.59 (m, 1H), 2.30−2.26 (m, 6H), 1.85−1.75 (m, 1H), 1.75−1.65 (m, 1H), 1.60−1.35 (m, 8H), 1.28 (d, J = 7.0 Hz, 1.2H), 1.25−1.15 (m, 1H), 1.24 (d, J = 7.0 Hz, 1.8H), 1.08−0.78 (m, 11H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 174.8, 174.1, 166.94, 166.87, 164.2, 164.1, 139.6, 139.2, 137.93, 137.86, 137.6, 110.84, 110.81, 109.6, 109.4, 107.9, 107.8, 106.2, 105.7, 101.6, 100.1, 84.1, 81.8, 72.6, 72.1, 71.7, 70.5, 70.4, 69.4, 64.1, 63.9, 63.2, 60.7, 60.4, 41.73, 41.70, 40.5, 40.43, 40.35, 40.32, 40.0, 34.9, 33.8, 31.79, 31.76, 31.3, 31.1, 28.3, 28.0, 25.5, 25.3, 20.9, 20.4, 20.19, 20.16, 16.60, 16.58, 14.86, 14.81, 14.7, 11.7, 11.1, 10.9, 10.3, 9.0 (Seven signals are missing due to overlap.); HRMS (ESI$^+$) m/z: calcd for $C_{36}H_{50}N_2O_9S_2K$ 757.2595 [M + K^+], found 757.2612.

β-Hydroxy Ester ***52***. A screw cap test tube was charged with the above THP-protected β-hydroxy ester **S8** (6.0 mg, 8.4 μmol), MeOH (50 μL), and CH_2Cl_2 (50 μL). To the solution was added PPTS (4.2 mg, 17 μmol). After stirring at 50 °C for 2.5 h, the reaction mixture was diluted with CH_2Cl_2. The separated organic layer was washed twice with 13.2% aqueous sodium chloride, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give a crude material, which was purified by preparative TLC (CH_2Cl_2-acetone = 20:1) to afford β-hydroxy ester **52** (3.0 mg, 4.7 μmol, 56%) as a white solid. R_f = 0.39 (CH_2Cl_2-acetone = 10:1); $[\alpha]_D^{25}$ −277 (c 0.125, $CHCl_3$); IR (neat, cm^{-1}): 3501, 2961, 2924, 2874, 1728, 1691, 1666, 1651, 1393, 1385, 1194, 1126, 978, 756; ^{1}H NMR (600 MHz, $CDCl_3$): δ 6.61 (s, 1H), 6.51 (s, 1H), 6.33 (dd, J = 9.4, 2.4 Hz, 1H), 6.21 (dd, J = 8.4, 2.4 Hz, 1H), 5.89 (ddd, J = 7.8, 1.8, 1.8 Hz, 1H), 5.15 (d, J = 8.4 Hz, 1H), 4.93 (dd, J = 8.4, 2.4 Hz, 1H), 4.89 (d, J = 7.2 Hz, 1H), 4.68 (d, J = 7.2 Hz, 1H), 4.62 (dd, J = 8.4, 2.4 Hz, 1H), 4.43 (br s, 1H), 3.77 (dd, J = 9.0, 1.2 Hz, 1H), 3.12−2.96 (m, 5H), 2.69 (dq, J = 7.2, 1.2 Hz, 1H), 2.32 (s, 3H), 2.31 (s, 3H), 1.76 (ddd, J = 13.8, 9.6, 3.6 Hz, 1H), 1.62−1.41 (m, 3H), 1.21 (d, J = 6.6 Hz, 3H), 1.03 (dq, J = 13.2, 7.2 Hz, 1H), 0.92 (ddd, J = 13.8, 9.6, 4.2 Hz, 1H), 0.89 (d, J = 7.2 Hz, 3H), 0.86 (d, J = 7.2 Hz, 3H), 0.80 (d, J = 6.0 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 175.4, 166.8, 164.9, 139.9, 138.2, 137.6, 110.8, 109.3, 107.8, 105.6, 75.0, 72.5, 71.8, 70.2, 69.6, 64.2, 60.8, 42.1, 41.0, 40.7, 40.3, 33.2, 31.8, 28.0, 20.5, 15.9, 14.9, 14.8, 11.1, 9.0: HRMS (ESI$^+$) m/z: calcd for $C_{31}H_{42}N_2O_8S_2Na$ 657.2280 [M + Na^+], found 657.2252.

β-Keto Ester ***39***. A screw cap test tube was charged with β-hydroxy ester **52** (2.5 mg, 3.9 μmol) and dry CH_2Cl_2 (40 μL). To the solution was added Dess−Martin periodinane (2.0 mg, 7.9 μmol) at 0 °C. After stirring at 0 °C for 1 h, additional Dess−Martin periodinane (1.0 mg, 3.9 μmol) was added, and the resulting mixture was stirred at 0 °C for 1 h. The reaction mixture was diluted with CH_2Cl_2. The separated organic layer was washed with saturated aqueous $NaHCO_3$ and brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give a crude material, which was purified by preparative TLC

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(CH_2Cl_2-acetone = 20:1) to afford a 3:2 mixture of **39** and its C2′ epimer **40** (1.2 mg, 1.9 μmol, 48%) as a pale yellow solid with recovery of β-hydroxy ester **52** (0.90 mg, 1.4 μmol, 36%). R_f = 0.45 (CH_2Cl_2-acetone = 10:1). The physical data of 3:2 mixture of **39** and **40**: IR (neat, cm^{-1}): 3400, 2963, 2924, 2874, 2853, 1738, 1712, 1693, 1680, 1674, 1666, 1658, 1645, 1385, 1339, 1194, 1126, 1003, 752; ^1H NMR (600 MHz, $CDCl_3$): δ 6.62−6.58 (m, 1H), 6.53 (s, 1H), 6.32 (dd, *J* = 8.4, 2.4 Hz, 0.6H), 6.29 (dd, *J* = 8.4, 2.4 Hz, 0.4H), 6.22 (dd, *J* = 8.4, 2.4 Hz, 1H), 5.92 (ddd, *J* = 8.4, 2.4, 2.4 Hz, 0.4H), 5.74 (ddd, *J* = 7.8, 2.4, 2.4 Hz, 0.6H), 5.27−5.22 (m, 0.6H), 5.12−5.08 (m, 0.4H), 4.95−4.92 (m, 1H), 4.92−4.88 (m, 1H), 4.72 (dd, *J* = 8.4, 1.8 Hz, 0.6H), 4.71−4.65 (m, 1H), 4.60 (dd, *J* = 8.4, 1.8 Hz, 0.4H), 4.49−4.44 (m, 0.6H), 4.42−4.37 (m, 0.4H), 3.72 (q, *J* = 7.2 Hz, 0.4H), 3.64 (q, *J* = 7.2 Hz, 0.6H), 3.13−2.98 (m, 4.4H), 2.90 (dq, *J* = 13.8, 6.6 Hz, 0.6H), 2.33−2.31 (m, 3H), 2.30 (s, 1.8H), 2.29 (s, 1.2H), 1.82 (ddd, *J* = 13.8, 8.4, 5.4 Hz, 0.4H), 1.67 (ddd, *J* = 13.2, 7.8, 6.0 Hz, 0.6H), 1.40 (d, *J* = 7.2 Hz, 1.8H), 1.40−1.24 (m, 3H), 1.33 (d, *J* = 7.2 Hz, 1.2H), 1.13 (d, *J* = 7.2 Hz, 1.8H), 1.12 (d, *J* = 7.2 Hz, 1.2H), 1.11−1.03 (m, 1H), 0.92−0.84 (m, 6H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 210.20, 210.17, 169.6, 169.3, 166.82, 166.79, 164.3, 164.2, 139.9, 139.6, 138.1, 138.0, 137.7, 110.8, 109.4, 109.3, 107.9, 107.8, 105.3, 105.0, 73.0, 72.62, 72.57, 71.9, 70.44, 70.38, 69.5, 69.4, 64.2, 64.1, 60.7, 60.4, 52.0, 50.4, 44.0, 43.3, 40.5, 40.4, 40.3, 40.2, 39.7, 32.1, 29.7, 29.5, 20.2, 19.52, 19.49, 17.3, 17.0, 14.91, 14.88, 14.77, 14.6, 13.0, 12.9, 11.2, 11.1 (five signals are missing due to overlap); HRMS (ESI^+) *m*/*z*: calcd for $C_{31}H_{40}N_2O_8S_2Na$ 655.2124 [M + Na^+], found 655.2120.

THP-Protected β-Hydroxy Ester ***S9***. A screw cap test tube was charged with **35** (14 mg, 31 μmol), **50** (8.9 mg, 31 μmol), and CH_2Cl_2 (80 μL). To the solution was added DMAP (3.8 mg, 31 μmol) and WSCD·HCl (11.9 mg, 62.1 μmol) at 0 °C. After stirring at reflux for 2 h, the reaction was quenched with 1 M aqueous HCl. The resulting mixture was extracted with CH_2Cl_2 three times. The combined organic extracts were washed with H_2O and brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by preparative TLC (CH_2Cl_2-acetone = 20:1) to afford the desired THP-protected β-hydroxy ester **S9** (8.0 mg, 11 μmol, 36%) as a pale yellow solid with recovery of **35** (7.0 mg, 16 μmol, 50%). R_f = 0.41 (CH_2Cl_2-acetone = 10:1); $[\alpha]_D^{27}$ −229 (*c*, 0.515, $CHCl_3$); IR (neat, cm^{-1}): 3400, 2957, 2928, 2874, 1732, 1693, 1681, 1666, 1658, 1651, 1385, 1198, 1128, 1026, 754, 667; ^1H NMR (500 MHz, $CDCl_3$): δ 6.61−6.57 (m, 1H), 6.54−6.49 (m, 1H), 6.33−6.25 (m, 1H), 6.22−6.18 (m, 1H), 5.90 (ddd, *J* = 8.0, 2.5, 2.5 Hz, 0.4H), 5.88 (ddd, *J* = 8.0, 2.5, 2.5 Hz, 0.6H), 5.23−5.10 (m, 1H), 4.93 (dd, *J* = 8.0, 2.0 Hz, 0.6H), 4.92−4.85 (m, 1H), 4.83 (dd, *J* = 8.0, 2.0 Hz, 0.4H), 4.70−4.63 (m, 1.2H), 4.62−4.57 (m, 0.8H), 4.42 (br s, 1H), 3.95−3.84 (m, 1H), 3.84−3.80 (m, 1H), 3.48−3.42 (m, 0.5H), 3.42−3.36 (m, 0.5H), 3.14−2.95 (m, 4H), 2.75−2.65 (m, 1H), 2.30−2.26 (m, 6H), 1.85−1.75 (m, 1H), 1.75−1.65 (m, 3H), 1.65−1.42 (m, 6H), 1.42−1.33 (m, 1H), 1.23 (d, *J* = 7.0 Hz, 1.2H), 1.17 (d, *J* = 7.0 Hz, 1.8H), 1.10−0.93 (m, 2H), 0.96 (d, *J* = 7.0 Hz, 1.8H), 0.94 (d, *J* = 7.0 Hz, 1.2H), 0.90−0.78 (m, 7H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 175.0, 174.4, 167.0, 166.9, 164.10, 164.07, 139.8, 139.4, 137.95, 137.86, 137.82, 137.61, 137.57, 110.8, 109.6, 109.5, 108.0, 107.9, 105.9, 105.6, 100.5, 99.4, 83.1, 81.1, 72.6, 71.5, 71.2, 70.51, 70.48, 64.12, 64.10, 63.2, 63.0, 60.7, 60.5, 41.8, 41.4, 41.1, 41.0, 40.6, 40., 40.4, 40.2, 34.4, 34.0, 31.7, 31.5, 30.95, 30.93, 28.9, 28.4, 25.44, 25.40, 20.2, 20.1, 20.0, 19.6, 15.8, 15.7, 14.86, 14.83, 14.7, 12.4, 11.8, 11.1, 11.0 (six signals are missing due to overlap); HRMS (ESI^+) *m*/*z*: calcd for $C_{36}H_{50}N_2O_9S_2Na$ 741.2855 [M + Na^+], found 741.2835.

β-Hydroxy Ester ***53***. A screw cap test tube was charged with the THP-protected β-hydroxy ester **S9** (4.0 mg, 5.6 μmol), MeOH (28 μL), and CH_2Cl_2 (28 μL). To the solution was added PPTS (2.8 mg, 11 μmol). After stirring at 50 °C for 1.5 h, the reaction mixture was diluted with CH_2Cl_2. The separated organic layer was washed twice with 13.2% aqueous sodium chloride, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give a crude material, which was purified by preparative TLC (CH_2Cl_2-acetone = 20:1) to afford β-hydroxy ester **53** (2.7 mg, 4.3 μmol, 76%) as a pale yellow solid. R_f = 0.34 (CH_2Cl_2-acetone = 10:1); $[\alpha]_D^{22}$ −253 (*c* 0.530, $CHCl_3$); IR (neat, cm^{-1}): 3468, 2962, 2924, 2876, 1732, 1693, 1680, 1666, 1651, 1393, 1384, 1337, 1192, 1128, 756; ^1H NMR (500 MHz, $CDCl_3$): δ 6.61−6.57 (m, 1H), 6.54−6.51 (m, 1H), 6.31 (dd, *J* = 8.5, 2.5 Hz, 1H), 6.22 (dd, *J* = 8.0, 2.5 Hz, 1H), 5.79 (ddd, *J* = 8.0, 2.0, 2.0 Hz, 1H), 5.19 (d, *J* = 8.5 Hz, 1H), 4.93 (dd, *J* = 8.5, 2.0 Hz, 1H), 4.89 (d, *J* = 7.5 Hz, 1H), 4.71−4.66 (m, 1H), 4.64 (dd, *J* = 8.0, 2.0 Hz, 1H), 4.42 (d, *J* = 6.0 Hz, 1H), 3.67 (dd, *J* = 7.0, 6.0 Hz, 1H), 3.14−2.95 (m, 4H), 2.69 (ddd, *J* = 14.0, 7.5, 4.5 Hz, 1H), 2.30 (s, 3H), 2.29 (s, 3H), 1.68−1.59 (m, 1H), 1.50−1.37 (m, 2H), 1.27−1.19 (m, 1H), 1.22 (d, *J* = 7.0 Hz, 3H), 1.06−0.92 (m, 2H), 0.98 (d, *J* = 6.5 Hz, 3H), 0.88−0.83 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 175.3, 166.8 164.3, 139.8, 138.00, 137.95, 137.6, 110.9, 109.6, 107.8, 105.6, 75.5, 72.6, 72.1, 70.4, 69.4, 64.1, 60.4, 42.3, 40.6, 40.4, 40.2, 33.3, 31.3, 28.1, 20.0, 15.1, 14.84, 14.80, 11.0, 10.9; HRMS (ESI^+) *m*/*z*: calcd for $C_{31}H_{42}N_2O_8S_2Na$ 657.2280 [M + Na^+], found 657.2268.

β-Keto Ester ***40***. A screw cap test tube was charged with the β-hydroxy ester **53** (2.7 mg, 4.3 μmol) and dry CH_2Cl_2 (70 μL). To the solution was added Dess−Martin periodinane (2.1 mg, 8.5 μmol) at 0 °C. After stirring at 0 °C for 1.5 h, the reaction mixture was diluted with CH_2Cl_2. The separated organic layer was washed with saturated aqueous $NaHCO_3$ and brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give a crude material, which was purified by preparative TLC (CH_2Cl_2-acetone = 10:1) to afford a 5:1 mixture of β-keto ester **40** and its C2′ epimer, **39** (1.0 mg, 1.6 μmol, 37%) as a pale yellow solid with recovery of the β-hydroxy ester **53** (1.2 mg, 1.9 μmol, 44%). The physical data of a 5:1 mixture of **39** and **40**: R_f = 0.43 (CH_2Cl_2-acetone = 10:1); $[\alpha]_D^{27}$ −246 (*c* 0.210, $CHCl_3$); IR (neat, cm^{-1}): 3400, 2963, 2926, 2876, 1747, 1713, 1693, 1682, 1666, 1651, 1634, 1396, 1385, 1194, 1124, 1003, 754; ^1H NMR (600 MHz, $CDCl_3$): δ 6.60 (s, 1H), 6.53 (s, 1H), 6.29 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.22 (dd, *J* = 8.4, 2.4 Hz, 1H), 5.96−5.92 (m, 1H), 5.14−5.09 (m, 1H,), 4.94 (dd, *J* = 8.4, 1.2 Hz, 1H), 4.93−4.87 (d, *J* = 7.8 Hz, 1H), 4.71−4.65 (m, 1H), 4.61 (dd, *J* = 8.4, 1.8 Hz, 1H), 4.39 (br s, 1H), 3.72 (q, *J* = 7.2 Hz, 1H), 3.14−2.98 (m, 5H), 2.31 (s, 3H), 2.29 (s, 3H), 1.87−1.79 (m, 1H), 1.43−1.25 (m, 2H), 1.33 (d, *J* = 7.2 Hz, 3H), 1.19−1.03 (m, 5H), 0.96−0.84 (m, 6H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 210.2, 169.3, 166.8, 164.3, 139.9, 138.1, 138.0, 137.6, 110.8, 109.4, 107.9, 105.0, 72.6, 71.9, 70.4, 69.5, 64.1, 60.7, 50.4, 44.0, 40.5, 40.2, 39.7, 32.1, 29.5, 19.5, 17.3, 14.9, 14.6, 13.0, 11.2; HRMS (ESI^+) *m*/*z*: calcd for $C_{31}H_{40}N_2O_8S_2Na$ 655.2124 [M + Na^+], found 655.2123.

THP-Protected β-Hydroxy Ester ***55***. A screw cap test tube was charged with (−)-deacetylaranotin (**5**) (4.3 mg, 10 μmol), THP-protected β-hydroxy carboxylic acid **54** (2.3 mg, 8.2 μmol), and CH_2Cl_2 (200 μL). To the solution was added DMAP (1.2 mg, 10 μmol) and WSCD·HCl (3.9 mg, 20 μmol) at 0 °C. After stirring at reflux for 2.5 h, the reaction was quenched with 1 M aqueous HCl. The resulting mixture was extracted with CH_2Cl_2 three times. The combined organic extracts were washed with water and brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by preparative TLC (CH_2Cl_2-acetone = 10:1) to afford THP-protected β-hydroxy ester **55** (1.5 mg, 2.1 μmol, 21%, d.r. = 5:1) as a white solid with recovery of (−)-deacetylaranotin (**5**) (1.9 mg, 4.4 mmol, 44%). R_f = 0.59 (CH_2Cl_2-acetone = 10:1); $[\alpha]_D^{27}$ −460 (*c* 0.044, $CHCl_3$); IR (neat, cm^{-1}): 3360, 2953, 2930, 2874, 2853, 1732, 1715, 1693, 1456, 1441, 1362, 1281, 1200, 1140, 1078, 1026, 997, 752. The ^1H and ^{13}C NMR data of major diastereomer: ^1H NMR (500 MHz, $CDCl_3$): δ 6.66−6.62 (m, 1H), 6.58−6.53 (m, 1H), 6.31 (dd, *J* = 8.0, 2.0 Hz, 1H), 6.26 (dd, *J* = 8.5, 2.0 Hz, 1H), 5.92−5.89 (m, 1H), 5.71 (dt, *J* = 9.0, 2.0 Hz, 1H), 5.10−5.05 (m, 1H), 4.90−4.86 (m, 0.5H), 4.79 (dd, *J* = 8.5, 2.0 Hz, 1H), 4.78−4.73 (m, 1.5H), 4.62−4.58 (m, 2H), 4.08−4.04 (m, 1H), 3.95−3.81 (m, 2H), 3.47−3.43 (m, 1H), 3.08 (d, *J* = 18.5 Hz, 1H), 2.74 (d, *J* = 17.5 Hz, 1H), 2.68−2.62 (m, 1H), 1.82−1.75 (m, 2H), 1.72−1.63 (m, 1H), 1.60−1.38 (m, 6H), 1.20−1.12 (m, 1H), 1.11 (d, *J* = 7.0 Hz, 3H), 1.07−0.95 (m, 2H), 0.95 (d, *J* = 7.0 Hz, 3H), 0.92−0.84 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 175.1, 165.4, 141.2, 139.5, 138.80, 138.76, 112.7, 109.7, 108.2, 105.2, 99.1, 81.4, 74.7, 70.7, 69.6, 67.9, 62.92, 62.88, 40.9, 39.9, 35.7, 34.8, 34.6, 31.9, 30.9, 29.7, 28.4, 25.5, 20.5, 20.2, 19.9, 16.7, 111.7, 11.1; HRMS (ESI^+) *m*/*z*: calcd for $C_{34}H_{44}N_2O_9S_2Na$ 711.2386 [M + Na^+], found 711.2377.

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β-Hydroxy Ester ***56***. A screw cap test tube was charged with THP-protected β-hydroxy ester **55** (2.7 mg, 3.9 μmol), MeOH (25 μL), and CH_2Cl_2 (25 μL). To the solution was added PPTS (2.0 mg, 7.8 μmol) at room temperature. After stirring at 50 °C for 1.5 h, the reaction mixture was diluted with CH_2Cl_2. The organic layer was washed twice with 13.2% aqueous sodium chloride, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give a crude material, which was used to the next reaction without further purification. The physical data of the purified β-hydroxy ester **56**: R_f = 0.41 (CH_2Cl_2-acetone = 10:1); $[\alpha]_D^{27}$ −380 (*c* 0.065, $CHCl_3$); IR (neat, cm^{-1}): 3508, 3350, 2959, 2928, 2874, 2853, 1715, 1693, 1682, 1454, 1371, 1281, 1184, 1140, 756; ^1H NMR (600 MHz, $CDCl_3$): δ 6.65 (d, *J* = 1.8 Hz, 1H), 6.57 (s, 1H), 6.32 (dd, *J* = 8.4, 3.0 Hz, 1H), 6.26 (dd, *J* = 8.4, 2.4 Hz, 1H), 5.87 (d, *J* = 1.8 Hz, 1H), 5.68 (dt, *J* = 8.4, 1.8 Hz, 1H), 5.16−5.12 (m, 1H), 4.81−4.78 (m, 1H), 4.78−4.75 (m, 1H), 4.63−4.59 (m, 1H), 4.59−4.55 (m, 1H), 4.10−4.04 (m, 1H), 3.93 (dt, *J* = 17.4, 1.8 Hz, 1H), 3.66−3.63 (m, 1H), 3.09 (d, *J* = 18.6 Hz, 1H), 2.77 (d, *J* = 17.4 Hz, 1H), 2.66 (ddd, *J* = 14.4, 7.8, 3.0 Hz, 1H), 2.37 (d, *J* = 4.8 Hz, 1H), 1.67−1.42 (m, 3H), 1.23−1.20 (m, 1H), 1.15 (d, *J* = 9.6 Hz, 3H), 1.08−0.99 (m, 1H), 0.95 (ddd, *J* = 13.2, 9.0, 4.2 Hz, 1H), 0.90 (d, *J* = 6.6 Hz, 3H), 0.87 (dd, *J* = 7.8, 6.6 Hz, 3H), 0.84 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ175.2, 165.3, 144.4, 141.5, 139.7, 139.0, 117.6, 109.7, 105.2, 96.7, 93.8, 75.9, 74.8, 70.6, 70.2, 67.9, 62.6, 42.0, 41.2, 40.4, 35.7, 34.6, 33.8, 31.8, 28.0, 20.5, 16.2, 11.1, 9.5; HRMS (ESI^+) *m*/*z*: calcd for $C_{29}H_{36}N_2O_8S_2Na$ 627.1811 [M + Na^+], found 627.1807.

*Hirsutellomycin (****57****).* A screw cap test tube was charged with the crude β-hydroxy ester **56** and dry CH_2Cl_2 (50 μL). To the solution was added Dess−Martin periodinane (1.4 mg, 5.6 μmol) at 0 °C. After stirring at 0 °C for 1.5 h, the reaction mixture was diluted with CH_2Cl_2. The organic layer was washed with saturated aqueous $NaHCO_3$ and brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give a crude material, which was purified by preparative TLC (CH_2Cl_2-acetone = 20:1) to afford **57** (0.80 mg, 1.3 μmol) as a colorless oil with recovery of β-hydroxy ester **56** (0.80 mg, 1.3 μmol), which was placed in a flame-dried screw cap test tube and dissolved in dry CH_2Cl_2 (50 μL). To the solution was added Dess−Martin periodinane (0.70 mg, 2.6 μmol) at 0 °C. After stirring at 0 °C for 1.5 h, the reaction mixture was diluted with CH_2Cl_2. The organic layer was washed with saturated aqueous $NaHCO_3$, followed by brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give a crude material, which was purified by preparative TLC (CH_2Cl_2-acetone = 20:1) to afford **57** (0.56 mg, 0.91 μmol) as a pale yellow solid with recovery of **56** (0.18 mg, 0.030 μmol). The combined yield of hirsutellomycin (**57**) was 1.26 mg (58%, over 3 steps from **55**). Synthetic hirsutellomycin (**57**) existed as a 10:1 mixture of **57** and its C2′ epimer **57**. R_f = 0.57 (CH_2Cl_2-acetone = 10:1); $[\alpha]_D^{27}$ −410 (*c* 0.095, $CHCl_3$); IR (neat, cm^{-1}): 3342, 2961, 2930, 2874, 2851, 1747, 1715, 1693, 1682, 1454, 1371, 1188, 1140, 754; ^1H NMR (500 MHz, $CDCl_3$): δ 6.64 (d, *J* = 2.0 Hz, 1H), 6.58 (s, 1H), 6.31 (dd, *J* = 8.5, 2.5 Hz, 1H), 6.26 (dd, *J* = 8.5, 2.5 Hz, 1H), 5.92−5.85 (m, 1H), 5.78−5.74 (m, 1H), 5.07 (dd, *J* = 8.5, 1.5 Hz, 1H), 4.79 (dd, *J* = 8.5, 2.0 Hz, 1H), 4.79−4.74 (m, 1H), 4.64−4.58 (m, 1H), 4.55 (dd, *J* = 8.5, 2.0 Hz, 1H), 4.05 (d, *J* = 17.5 Hz, 1H), 3.92 (d, *J* = 17.0 Hz, 1H), 3.66 (q, *J* = 7.0 Hz, 1H), 3.08 (d, *J* = 18.5 Hz, 1H), 2.92 (q, *J* = 7.0 Hz, 1H), 2.79 (d, *J* = 17.0 Hz, 1H,), 1.73 (ddd, *J* = 13.5, 7.5, 6.0 Hz, 1H), 1.42−1.15 (m, 2H), 1.28 (d, *J* = 7.0 Hz, 3H), 1.20−1.03 (m, 2H), 1.15 (d, *J* = 6.5 Hz, 3H), 0.89 (d, *J* = 6.5 Hz, 3H), 0.87 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 210.4, 169.2, 165.3, 162.5, 141.4, 139.6, 138.8, 112.6, 109.7, 108.1, 104.8, 76.4, 74.8, 70.7, 69.9, 67.9, 62.9, 51.0, 43.7, 40.0, 35.8, 34.6, 32.2, 29.3, 19.4, 17.2, 12.8, 11.1 (one signal is missing due to overlap); HRMS (ESI^+) *m*/*z*: calcd for $C_{29}H_{34}N_2O_8S_2Na$ 625.1654 [M + Na^+], found 625.1661.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b02452.

Copies of ^1H and ^{13}C NMR spectra. (PDF)

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Notes

The authors declare no competing financial interest.

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