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Structural determination of (–)-SCH 64874 and hirsutellomycin by semi-synthesis

Hidetoshi Tokuyama^{a,*}, Kaori Yamada^a, Hideto Fujiwara^a, Juri Sakata^a, Kentaro Okano^a, Malipan Sappan^b, Masahiko Isaka^{b,*}

^aGraduate School of Pharmaceutical Sciences, Tohoku, University, Aramaki, Aoba-ku, Sendai 980-8578, Japan

^bNational Center for Genetic Engineering and Biotechnology (BIOTEC), 113 Thailand Science Park, Phaholyothin Road, Klong Luang, Pathumthani 12120, Thailand



ABSTRACT: The structure of a C_2 -symmetric epidithiodiketopiperazine alkaloid, SCH 64874, was determined by semi-synthesis. 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 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 (ETPs) 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 (Fig. 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 posses potent anti-tuberculosis 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 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 semi-synthesis of **4** and **6**, aiming at the elucidation of the structure of these compounds.



Fig. 1 Epidithiodiketopiperazines (ETPs)

Structural determination of SCH 64874

We designed a strategy for the semi-synthesis 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 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 semi-synthesize (-)-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.

Scheme 1. Strategy for structural determination of SCH 64874 (4).



Esters **8a** and **8b** were synthesized using the Evans aldol reaction (Scheme 2).⁷ Treatment of (–)-**9** with *n*-Bu₂BOTf⁸/Et₃N, 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*-Bu₂BOTf/*i*-Pr₂NEt, followed by addition of (+)-10 in the presence of SnCl₄, 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 ester 8a and 8b.



Reagents and conditions: a) n-Bu₂BOTf, Et₃N, CH₂Cl₂, -78 to 0 °C then (+)-**10**, -78 to 0 °C, 63% (single diastereomer); b) NaOMe, MeOH, 0 °C, 91%; c) n-Bu₂BOTf, Et₃N, CH₂Cl₂, -78 to 0 °C; (+)-**10**, -78 to 0 °C, 83% (single diastereomer); d) NaOMe, MeOH, 0 °C, 81%.

Scheme 3. Synthesis of ester 8c and 8d.



Reagents and conditions: a) n-Bu₂BOTf, i-Pr₂NEt, CH₂Cl₂, -78 to 0 °C; (+)-**10**, SnCl₄, -78 to 0 °C, dr = 4:1; separation, 47%; b) NaOMe, MeOH, 0 °C, 82%; c) n-Bu₂BOTf, i-Pr₂NEt, CH₂Cl₂, -78 to 0 °C; (+)-**10**, SnCl₄, -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 ¹³C-NMR chemical shifts between the side chains of **4** and each of the diastereomers **8a–d** were calculated (Fig. 2). Differences between the ¹³C-NMR spectra of **4** and those of **8a**, **8b** and **8c** were smaller than those of **8d**. Next, we compared their ¹H-NMR spectra to that of **4** (Fig. 3). It was observed that the ¹H-NMR spectrum of **8a** was very close to that of **4**, whereas that of **8b**, **8c**, and **8d** 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

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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·HCl/DMAP to give diester 14 in moderate yield. Finally, the THP groups were removed by a careful treatment with PPTS¹⁵ to obtain **15**. In addition, 17 was also derived from (-)-5 and two (+)-13 fragments by the same protocol.





3' 5' 8b

Fig. 2 Comparative study of ¹³C-NMR data (100 MHz, CDCl₃)



Fig. 3 Comparative study of ¹H-NMR data (400 MHz, CDCl₃)

The difference between the chemical shifts in the ¹³C- and ¹H-NMR spectra of **4** and synthetic compounds **15** and **17**. (Fig. 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** ($[\alpha]_D^{29} = -169^\circ$ (c = 0.141, CHCl₃), lit. $[\alpha]_D^{29} = -301.1^\circ$ (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 acid (-)-13 and (+)-13.



Reagents and conditions: a) DHP, TsOH·H₂O, CH₂Cl₂, rt, 90%; b) LiOH H₂O, H₂O₂, THF-H₂O (7:2), 0 °C to rt, 82%; c) DHP, TsOH·H₂O, CH₂Cl₂, rt, 76%; d) LiOH·H₂O, H₂O₂, THF-H₂O (7:2), 0 °C to rt, 84%.

Scheme 5. Synthesis of two candidates of SCH 64874 (4)



Reagents and conditions: a) 0.9% aq. HCl in MeOH, rt, 72%; b) (-)-13 WSCD·HCl, DMAP, CH₂Cl₂, rt, 42%; c) PPTS, MeOH-CH₂Cl₂, rt, 66%; d) (+)-13 WSCD·HCl, DMAP, CH₂Cl₂, rt, 38%; e) PPTS, MeOH-CH₂Cl₂, rt to 40 °C, 86%.

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Structural determination of hirsutellomycin

The focus of our investigation then moved onto the structural determination of hirsutellomycin (6) by semi-synthesis. 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 (¹H-NMR, ¹³C-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 $\mathbf{6}$ shares the same relative configuration of it's deacetylaranotin core. Unfortunately, due to a lack of data regarding its optical rotation, it was impossible to determine the absolute stereochemistry of 6. However, the fact that all of the analogous fungal epipolythiodiketopiperazines, including 1, 2, 3, 17, aranotin, and apoaranotin, contain (-)-deacetylaranotinlike (dihydrooxepine-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 semi-synthesis strategy similar to the one used for SCH 64874 using a (–)-deacetylaranotin (5).

We planned an efficient strategy for the semi-synthesis 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 concept¹⁷ 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

Scheme 6. Strategy for structural determination of hirsutellomycin (6)



Determination of relative stereochemistry of the whole molecule by condensation of 23 or ent-23 with (–)-5

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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 deacetylaranotin core, respectively, which could be used to determine the relative stereochemistry of **6**.

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 oxazolidinone with LiBH₄ provided alcohol 25, which was then subjected to Parikh–Doering oxidation²⁰ to give aldehyde 26. Treatment of aldehyde 26 with diazoester 27 afforded 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.

Scheme 7. Synthesis of β -keto esters 19 and 20.



Reagents and conditions: a) LiBH₄, THF-MeOH, 0 °C to rt; b) SO₃·Py, Et₃N, CH₂Cl₂-DMSO, 0 °C to rt; c) **27**, SnCl₂, CH₂Cl₂, rt, 24% (3 steps, **19a:19b** = 1:1); d) NaHMDS, THF,– 78 °C; MeI, 71% (single diastereomer); e) LiBH₄, THF-MeOH; f) SO₃·Py, Et₃N, CH₂Cl₂-DMSO, 0 °C to rt; g) **27**, SnCl₂, CH₂Cl₂, rt, 20% (3 steps, **20a:20b** = 1:1).

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* (Fig. 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, 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 stereo-

chemistry 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 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 periodinane²⁴ gave a 1:1 mixture of **19a** and **19b**.



Fig. 5 Comparative study of 1 H-NMR spectrum (400 MHz, CDCl₃)

Scheme 8. Trial for the synthesis of β -keto ester 19a.



Reagents and conditions: a) **31**, -78 to 0 °C; separation, 65% (3 steps from **24**); b) LiOH·H₂O, H₂O₂, THF, 0 °C to rt, 86%; c) K₂CO₃, EtI, acetone, 50 °C, 89%; d) Dess-Martin periodinane, CH₂Cl₂, 0 °C, 90% (**19a:19b** = 1:1).

The revised strategy is depicted in Scheme 9. We considered that the stereochemistry on the side chain of C2' was strongly affected by the core skeleton, and so a thermodynamically more stable compound should exist. With this hypothesis, we planed 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 (–)-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 9. Strategy for determination of relative configuration



Scheme 10 illustrates one example of introduction of side chain fragments onto the core skeleton **35**. The aldol product **32** was converted into a carboxylic acid **41** *via* protection of hydroxyl group and hydrolysis of chiral auxiliary. Treatment of diacetate **36** with K₂CO₃ in MeOH produced alcohol **35**, which was condensed with carboxylic acid **41** to give the ester **42** in moderate yield. Acidic deprotection of THP group¹⁵ gave β -hydroxy ester **43**.

Scheme 10. Introduction of the side chain fragments



Reagents and conditions: a) DHP, PPTS, rt; b) $LiOH \cdot H_2O$, H_2O_2 , THF, 0 °C to rt, 89% (2 steps); c) K_2CO_3 , MeOH, rt, quant.; d) **41**, WSCD · HCl, DMAP, CH₂Cl₂, reflux, 36%; e) PPTS, MeOH-CH₂Cl₂, 40 °C, 78%.

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 oxidation²⁰ (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 group¹⁵ 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 configura-

tional stability of the C2' position of the resultant esters was then carefully inspected (Scheme 12).

Scheme 11. Synthesis of carboxylic acid 50.



Reagents and conditions: a) NaHMDS, THF, -78 °C; MeI, 85% (single diastereomer); b) LiBH₄, THF-MeOH, 0 °C to rt; c) SO₃·Py, Et₃N, CH₂Cl₂-DMSO, 0 °C to rt; d) **48**, -78 to 0 °C, 45% (3 steps); e) DHP, PPTS, CH₂Cl₂, rt; f) LiOH·H₂O, H₂O₂, THF, 0 °C to rt, 65% (2 steps).

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 12. Thermal stability of 2' configuration



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 ¹³C-NMR spectra of **6** and the model compounds **38** and **40** (Fig. 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**.



Fig. 6 Comparative study of ¹³C-NMR data (150 MHz, CDCl₃)

At this stage, we were ready to determine the relative configuration of hirsutellomycin (6) through the semi-synthesis 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 deprotection of the THP group using PPTS¹⁵ 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 ¹³C-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.

Scheme 13. Synthesis of β -keto ester 57.



Reagents and conditions: a) WSCD·HCl, DMAP, CH₂Cl₂, reflux, 21%; b) PPTS, MeOH-CH₂Cl₂, 50 °C, 66%; c) DMP, CH₂Cl₂, 0 °C, 58 % (3 steps, dr 2'*R*:2'*S* = 10:1, This reaction was carried out once again by using recovered SM).

Conclusion

In conclusion, we accomplished to semi-synthesize (-)-SCH 64874 (4) and hirsutellomycin (6) from (-)-deacetylaranotin (5). Based on these semi-syntheses, 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, Et₃N, 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 ¹³C-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 structure of compounds S1-S9 were indicated in supporting information.

Search for acetylaranotin-producing fungal strains. To find acetylaranotin producing fungal strains, ten 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 (CDCl₃). Four strains produced acetylaranotion (1) and bisdethiodi(methylthio) acetylaranotin (36). In all cases the efficacy of the proruction of 1 were 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, NaNO₃ 3.0 g/L, K₂HPO₄ 1.0 g/L, MgSO₄·7H₂O 0.5 g/L, KCl 0.5 g/L, FeSO₄·7H₂O 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 \times 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. H₂O (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-CH₂Cl₂) and preparative HPLC using a reversed-phase column

(MeOH/H₂O = 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.

(+)-(4R)-Oxazolidinone (+)-9. A flame-dried 100-mL twonecked flask was charged with (4R)-(-)-4-isopropyl-2oxazolidinone (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 nhexane, 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 NH₄Cl was added. The resulting mixture was extracted with CH₂Cl₂ eight times. The combined organic extracts were washed with brine, dried over MgSO4, 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, CHCl₃); IR (neat, cm⁻¹): 2966, 1785, 1700, 1389, 1375, 1248, 1205, 1073, 1026, 758, 700; ¹H NMR (400 MHz, CDCl₃): 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); ¹³C NMR (100 MHz, CDCl₃): 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 C₁₀H₁₇NO₃Na 222.1101 [M+Na⁺], found 222.1095.

(-)-(4S)-Oxazolidinone (-)-9. A flame-dried 50-mL twonecked flask was charged with (4S)-(-)-4-isopropyl-2oxazolidinone (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 nhexane, 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 NH₄Cl was added to the reaction mixture. The resulting mixture was extracted with CH₂Cl₂ eight times. The combined organic extracts were dried over MgSO₄, 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, CHCl₃); IR (neat, cm⁻¹): 2966, 1784, 1703, 1389, 1375, 1248, 1208, 1072, 1026, 773, 700; ¹H NMR (400 MHz, CDCl₃): 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); ¹³C NMR (100 MHz, CDCl₃): 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 C₉H₁₅NO₃Na 208.0917 [M+Na⁺], found 208.0915.

(-)-(2*R*,3*S*,4*S*)-Aldol product 11a.⁷ A flame-dried 50-mL twonecked flask was charged with oxazolidinone (-)-9 (300 mg, 1.62 mmol) and dry CH₂Cl₂ (4.4 mL) under Ar. To the solution was added *n*-Bu₂BOTf (4.0 mL, 0.75 M in CH₂Cl₂, 3.0 mmol) at -78 °C. After stirring for 10 min, Et₃N (553 μ L, 3.97 mmol) was added dropwise. The solution was stirred for 1 h at -78 °C and for 100 min at 0 °C, then re-cooled to -78 °C. To the resulting mixture was slowly added a solution of (*S*)-2methylbutanal ((+)-10) (1.17 mL, 16.2 mmol) in dry CH₂Cl₂ (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% H₂O₂ (2.4 mL). The mixture was vigorously stirred at 0 °C for 30 min. The aqueous layer was extracted with CH₂Cl₂ three times. The combined organic extracts were washed with NaHCO₃, dried over MgSO₄, 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.: $98-101^{\circ}$ C (hexanes-CHCl₃, white needle); $[\alpha]_D^{24} - 70$ (*c* 0.80, CH₂Cl₂); IR (ATR, cm⁻¹): 3463, 2963, 1764, 1684, 1387, 1372, 1238, 1206, 777, 705, 640; ¹H NMR (400 MHz, CDCl₃): 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); ¹³C NMR (100 MHz, CDCl₃): 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 C₁₄H₂₅NO₄Na 294.1676 [M+Na⁺], found 294.1679.

The structure of 11a was confirmed by following procedure

A screw cap test tube was charged with 11a (60 mg, 0.22 mmol) and dry Et₂O (0.8 mL). To the solution was added LiBH₄ (10 mg, 0.442 mmol) at -42 °C. After stirring for 14 h at room temperature, aqueous NH₄Cl was added at 0 °C. The resulting mixture was extracted with CH₂Cl₂ three times. The combined organic extracts were washed with brine, dried over NaSO₄, 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, CHCl₃); IR (neat, cm⁻¹): 3353, 2964, 2933, 2877, 1748, 1463, 1384, 1144, 1074, 1032, 973; ¹H NMR (400 MHz, CDCl₃): 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); ¹³C NMR (150 MHz, CDCl₃): 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 twonecked flask was charged with oxazolidinone (+)-9 (300 mg, 1.62 mmol) and dry CH₂Cl₂ (4.4 mL) under Ar. To the solution was added n-Bu₂BOTf (4.0 mL, 0.75 M in CH₂Cl₂, 3.0 mmol) at -78 °C. After stirring for 10 min, Et₃N (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, re-cooled 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 CH₂Cl₂ (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% H₂O₂ (2.4 mL). The mixture was vigorously stirred at 0 °C for 30 min. The aqueous layer was extracted with CH₂Cl₂ three times. The combined organic extracts were washed with NaHCO₃, dried over MgSO₄, 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-CHCl₃, white needle); $[\alpha]_D^{23}$ +74 (c 0.80, CH₂Cl₂); IR (ATR, cm⁻¹): 3531, 2963, 1766, 1681, 1381, 1209, 988, 957, 780, 706; ¹H NMR (400 MHz, CDCl₃): δ 4.47

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(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 (gd, 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); ¹³C NMR (100 MHz, CDCl₃): 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 C₁₄H₂₅NO₄Na 294.1676 [M+Na⁺], found 294.1674. Spectral data matched the reported data.'

(+)-(2R,3R,4S)-Aldol product 11c.¹² A flame-dried 30-mL two-necked flask was charged with oxazolidinone (+)-9 (185 12 mg, 1.00 mmol) and dry CH₂Cl₂ (2.0 mL) under Ar. To the 14 solution were added DIPEA (200 µL, 1.15 mmol) and n-Bu₂BOTf (330 mg, 1.20 mmol) at 0 °C. After stirring for 75 min, the solution was cooled to -78 °C. In a separate flame-16 dried 30-mL two-necked flask, (S)-2-methylbutanal ((+)-10) (108 μ L, 1.50 mmol) was placed, to which was added a solu-18 tion of SnCl₄ (88 µL, 0.75 mmol) in 2.0 mL of dry CH₂Cl₂. The 19 resulting mixture was stirred for 5 min and transferred to the enol borate solution via cannula with aid of additional CH₂Cl₂ (1.0 mL). After stirring for 3 h, the reaction was quenched with 22 MeOH-34% H₂O₂ 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 NaHCO₃ and brine, dried over MgSO₄, 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, CH₂Cl₂); IR (ATR, cm⁻¹): 32 3463, 2961, 1757, 1702, 1371, 1221, 1208, 775, 712; ¹H NMR 33 $(400 \text{ MHz}, \text{CDCl}_3)$: 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); ¹³C NMR (100 MHz, CDCl₃): 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 40 (EI) m/z: 271 [M⁺]; HRMS (ESI) m/z: calcd. for C₁₄H₂₅NO₄Na 294.1676 [M+Na⁺], found 294.1681. 42

(-)-(2R,3S,4S)-Oxazolidinone 11d.¹¹ A flame-dried 30-mL two-necked flask was charged with oxazolidinone (-)-9 (370 mg, 2.00 mmol) and dry CH₂Cl₂ (4.0 mL) under Ar. To the colorless solution were added DIPEA (400 µL, 2.30 mmol) and n-Bu₂BOTf (660 mg, 2.40 mmol) at 0 °C. After stirring for 50 min, the solution was cooled to -78 °C. In a separate flamedried 30-mL two-necked flask, (S)-2-methylbutanal ((+)-10) (108 µL, 1.50 mmol) was placed, to which was added solution of SnCl₄ (176 µL, 1.50 mmol) in 4.0 mL of dry CH₂Cl₂. After stirring for 5 min, the solution was transferred to the enol borate solution via cannula with aid of additional CH₂Cl₂ (2.0 mL). After stirring for 6 h, the reaction was quenched with MeOH-34% H₂O₂ aq. (5:1, 12mL). 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 NaHCO3 and brine, dried over MgSO4, filtered, and concentrated under reduced pressure to give a crude material, which was purified by flash column chromatography (hexanesEtOAc = 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); $\left[\alpha\right]_{D_{1}}^{2}$ -60 (c 0.76, CH₂Cl₂); IR (ATR, cm⁻¹): 3506, 2963, 1769, 1692, 1384, 1202, 710, 629; ¹H NMR (400 MHz, CDCl₃): 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);¹³C NMR (100 MHz, CDCl₃): 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 C₁₄H₂₅NO₄Na 294.1676 [M+Na⁺], found 294.1678.

The structure of 11d was confirmed by following procedure

A screw cap test tube equipped charged with 11d (4.5 mg, 17 μ mol), dry CH₂Cl₂ (55 μ L) and 2,6-lutidine (5.5 μ L, 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 H₂O. The resulting mixture was extracted with CH₂Cl₂ three times. The combined organic extracts were washed with saturated aqueous NaHCO₃, brine, dried over Na₂SO₄, filtered, and concentrated under reduced. The residue was purified by preparative TLC (hexanes-EtOAc = 5:1) to afford silvl ether S2 as a pale yellow oil (3.1)mg, 11 μ mol, 65%). R_f = 0.53 (hexanes-EtOAc = 3:1). $[\alpha]_D^{26}$ – 12.9 (c 1.34, CHCl₃); IR (neat, cm⁻¹): 2960, 2928, 2880, 2855, 1782, 1699, 1387, 1254, 1202, 1057, 837; ¹H NMR (400 MHz, CDCl₃): 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); ¹³C NMR (100 MHz, CDCl₃): 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 C₂₀H₃₉NO₄SiNa 408.2541 [M+Na⁺], found 408.2534. A screw cap test tube was charged with silvl ether S2 (3.1 mg, 11 µmol), dry MeOH (2.2 µL, 55 µmol), and dry THF (55 µL). To the solution was added LiBH4 (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 CH₂Cl₂ three times. The combined organic extracts were washed with brine, dried over NaSO₄, 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 μ mol, 28%) as a pale yellow oil. R_f = 0.63 (hexanesethyl acetate = 3:1); $[\alpha]_{\rm D}^{26}$ +6.3 (*c* 0.52, CHCl₃); IR (neat, cm⁻) ¹): 3483, 2959, 2930, 2857, 1787, 1706, 1464, 1387, 1254, 1053, 1026, 836; ¹H NMR (400 MHz, CDCl₃): 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); ¹³C NMR (150 MHz, CDCl₃): 881.7, 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 S3.²⁵

(-)-(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 NH₄Cl. The mixture was extracted with EtOAc three times. The combined organic extracts were dried over MgSO4, 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, CH₂Cl₂); IR (neat, cm⁻¹): 3507, 2964, 1735, 1720, 1458, 1202, 1056, 996, 968; ¹H NMR (400 MHz, CDCl₃): 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); ¹³C NMR (100 MHz, CDCl₃): 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 C₉H₁₈O₃Na 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 NH₄Cl. The mixture was extracted with EtOAc three times. The combined organic extracts were dried over MgSO₄, 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 μ mol, 81%) as a colorless oil. $R_f = 0.36$ (hexanes-EtOAc = 3:1); $[\alpha]_D^{24} - 1.2$ (c 0.53, CH₂Cl₂); IR (neat, cm⁻¹): 3504, 2964, 1737, 1720, 1459, 1261, 1200, 1169; ¹H NMR (400 MHz, CDCl₃): § 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); ¹³C NMR (100 MHz, CDCl₃): 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 C₉H₁₈O₃Na 197.1148 [M+Na⁺], found 197.1149. Spectral data matched the reported data.⁴

(-)-(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 NH₄Cl and the mixture was extracted with EtOAc three times. The combined organic extracts were dried over MgSO4, 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 μ mol, 82%) as a colorless oil. $R_f = 0.33$ (hexanes-EtOAc = 3:1); $[\alpha]_D^{26} - 9.3$ (c 0.45, CH₂Cl₂); IR (neat, cm⁻¹): 3523, 2963, 1738, 1721, 1458, 1260, 1198, 1172, 992, 774; ¹H NMR (400 MHz, CDCl₃): 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); ¹³C NMR (100 MHz, CDCl₃): 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 C₉H₁₈O₃Na 197.1148 [M+Na⁺], found 197.1139.

(+)-(2*R*,3*S*,4*S*)-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 NH₄Cl and the mixture was extracted with EtOAc three times. The combined organic extracts were dried over MgSO₄, 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, CH₂Cl₂); IR (neat, cm⁻¹): 3522, 2963, 1734, 1719, 1458, 1260, 1199, 1172, 1044, 997; ¹H NMR (400 MHz, CDCl₃): 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); ¹³C NMR (100 MHz, CDCl₃): 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⁺]; HRMS (ESI) *m*/*z*: calcd. for C₉H₁₈O₃Na 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 CH₂Cl₂ (3.0 mL). To the solution were added DHP (168 µL, 1.84 mmol) and TsOH·H₂O (1.8 mg, 9.2 µmol). After stirring for 3 h at room temperature, the reaction was quenched with H₂O. The aqueous layer was extracted with CH₂Cl₂ two times. The combined organic extracts were dried over MgSO₄, 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; $\left[\alpha\right]_{D}^{26}$ -70.7 (c 1.04, CHCl₃); IR (neat, cm⁻¹): 2962, 1780, 1700, 1384, 1227, 1202, 903, 753; ¹H NMR (400 MHz, CDCl₃): 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); ¹³C NMR (100 MHz, CDCl₃): 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 C₁₉H₃₃NO₅Na 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 μ mol), dry THF (75 μ L), and H₂O (22 μ L). To the solution were added H₂O₂ (34% w/w solution in H₂O, 20 µL, 0.18 mmol) and LiOH·H₂O (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 Na₂S₂O₃ and 0.1 M HCl aq. The aqueous layer was extracted with EtO-Ac ten times. The combined organic extracts were dried over Na₂SO₄, 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 diastereometric mixture (-)-13; $\left[\alpha\right]_{D}^{28}$ -19 $(c 0.80, CHCl_3)$; IR (neat, cm⁻¹): 2942, 1708, 1457, 1131, 1077, 1034, 813, 669; ¹H NMR (400 MHz, CDCl₃): 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); ¹³C NMR (100 MHz, CDCl₃): 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.);

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HRMS (ESI) m/z: calcd. for C₁₃H₂₄O₄Na 267.1567 [M+Na⁺], found 267.1560.

(+)-(2S,3R,4R)-Aldol product 11e.⁷ A flame-dried 20-mL twonecked flask was charged with oxazolidinone (+)-9 (200 mg, 1.08 mmol) and dry CH₂Cl₂ (1.9 mL) under Ar. To the solution was added n-Bu₂BOTf (1.2 mL, 1.00 M in CH₂Cl₂, 1.19 mmol) at -78 °C. After stirring for 10 min, Et₃N (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, re-cooled 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 μ L), followed by 34% H₂O₂ (34% w/w solution in H₂O, 520 µL). The mixture was vigorously stirred at 0 °C for 1.5 h. The aqueous layer was extracted with CH₂Cl₂ three times. The combined organic extracts were washed with brine and dried over MgSO₄, 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, CH₂Cl₂); IR (ATR, cm⁻¹): 3464, 2963, 1765, 1685, 1387, 1372, 1238, 1205, 704, 640; ¹H NMR (400 MHz, CDCl₃): δ 4.47 (ddd, J = 9.2, 8.4, 3.2Hz, 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); ¹³C NMR (100 MHz, CDCl₃): 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 C₁₄H₂₅NO₄Na 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 CH₂Cl₂ (349 µL). To the solution were added DHP (20 µL, 0.22 mmol) and TsOH·H₂O (0.21 mg, 1.1 µmol). After stirring for 2 h at room temperature, the reaction was quenched with H₂O. The aqueous layer was extracted with CH₂Cl₂ five times. The combined organic extracts were dried over Na₂SO₄, 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 μ mol, 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, CHCl₃); IR (neat, cm⁻¹): 2962, 1780, 1700, 1385, 1228, 1202, 1130, 1032; ¹H NMR (400 MHz, CDCl₃): 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); ¹³C NMR (100 MHz, CDCl₃): 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 C₁₉H₃₃NO₅Na 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 H₂O, 60 µL, 0.59 mmol) and LiOH·H₂O (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 Na₂S₂O₃ and 0.1 M HCl aq. The aqueous layer was extracted with EtOAc six times. The combined organic extracts were dried over Na₂SO₄, 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, CHCl₃); IR (neat, cm⁻¹): 2941, 1707, 1456, 1201, 1131, 1077, 1026; ¹H NMR (400 MHz, CDCl₃): 8 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); ¹³C NMR (100 MHz, CDCl₃): 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 C₁₃H₂₄O₄Na 267.1567 [M+Na⁺], found 267.1563.

(-)-deacetylaranotin (5).¹³ A screw cap test tube was charged with acetylaranotin (-)-1 (2.0 mg, 40 $\mu mol)$ 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 NaHCO₃. The resulting mixture was extracted with EtOAc three times. The organic layer was dried over Na₂SO₄, filtered, and concentrated under reduced pressure to give a crude material, which was purified by preparative TLC (CH₂Cl₂-acetone = 20:1) to afford (-)deacetylaranotin (5) (1.2 mg, 2.9 µmol, 72%) as a white solid. $R_f = 0.27$ (CH₂Cl₂-acetone = 10:1); $[\alpha]_D^{26}$ -546 (c 0.210, CHCl₃); IR (KBr, cm⁻¹): 3339, 1693, 1666, 1655, 1445, 1431, 1387, 1283, 1144, 1036; ¹H NMR (600 MHz, CDCl₃): 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); ¹³C NMR (150 MHz, CDCl₃): 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 βhydroxy carboxylic acid (-)-13 (5.1 mg, 20.9 µmol), and dry CH₂Cl₂ (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 SiO₂ 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 μ mol, 42%). R_f = 0.69 (hexanes-EtOAc = 1:1); The physical data of diastereometric mixture 14 is following; $\left[\alpha\right]_{D}^{2}$ -308 (c 0.201, CHCl₃); IR (neat, cm⁻¹): 2942, 2876, 1732, 1713, 1652, 1456, 1358, 1200, 1133, 1026, 998, 757; ¹H NMR (600 MHz, CDCl₃): 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),

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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); ¹³C NMR (150 MHz, CDCl₃): 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 C₄₄H₆₀N₂O₁₂S₂Na 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 μ mol, 66%). R_f = 0.32 (hexanes-EtOAc = 1:1); $[\alpha]_D^{25}$ -254 (c 0.107, CHCl₃); IR (neat, cm⁻¹): 3253, 2963, 2934, 2877, 1709, 1653, 1362, 1140, 968, 755; ¹H NMR (600 MHz, CDCl₃): δ 6.61 (d, J = 1.9 Hz, 2H), 6.29 (dd, J = 8.2, 2.1Hz, 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); ¹³C NMR (150 MHz, CDCl₃): 8 175.4, 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 βhydroxy 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 SiO₂ 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 μ mol, 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, CHCl₃); IR (neat, cm⁻¹): 2939, 1731, 1715, 1354, 1141, 1026, 669; ¹H NMR (600 MHz, CDCl₃): 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); ¹³C NMR (150 MHz, CDCl₃): 8 175.1, 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 C₄₄H₆₀N₂O₁₂S₂Na 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 μ mol), MeOH (50 μ L), and CH₂Cl₂ (50 μ L). To the solution was added PPTS (1.88 mg, 7.47 μ mol) 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 μ mol, 86%). R_f = 0.48 (hex-

anes-EtOAc = 1:1); $[\alpha]_D^{29} - 169$ (*c* 0.141, CHCl₃); IR (neat, cm⁻¹): 3518, 2963, 2917, 1715, 1651, 1456, 1362, 1179, 1142, 969, 755; ¹H NMR (600 MHz, CDCl₃): 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); ¹³C NMR (150 MHz, CDCl₃): 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 C₃₄H₄₄N₂O₁₀S₂Na 727.2330 [M+Na⁺], found 727.2297.

(4S,6S)-*β*-Keto ester 19. A screw cap test tube was charged with oxazolidinone 24^{15} (20 mg, 66 µmol), dry MeOH (26 µL, 0.66 µmol), and dry THF (330 µL). To the solution was added LiBH₄ (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 Na₂SO₄, 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, Et₃N (46 µL, 0.33 mmol), dry DMSO (110 μ L), and dry CH₂Cl₂ (220 μ L). To the solution was added SO₃·Py (52 mg, 0.33 mmol) at 0 °C. The resulting solution was stirred at 0 °C for 30 min. The reaction was guenched with water at 0 °C and then warmed to room temperature. The reaction mixture was extracted with CH2Cl2 three times. The combined organic extracts were dried over Na₂SO₄, filtered, and concentrated under reduced pressure at 0 °C to give a crude material as a CH₂Cl₂ 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, the reaction mixture was diluted with water and extracted with CH₂Cl₂ three times. The combined organic extracts were washed with water three times, dried over Na₂SO₄, 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, CDCl₃): 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 (d, J = 6.8 Hz, 1.5H), 0.91–0.82 (m, 6.5H); ¹³C NMR (100 MHz, CDCl₃): 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)

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228; HRMS (EI) m/z: calcd. for C₁₃H₂₅O₃ 229.1804 [M+H⁺], found 229.1802.

(-)-(2S,4R)-Oxazolidinone 29. A flame-dried 50-mL twonecked 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**¹⁶ (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 Na2SO4, 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, CHCl₃); IR (neat, cm⁻¹): 2962, 2929, 2874, 1782, 1698, 1455, 1386, 1350, 1238, 1208, 1099, 1015, 971, 760, 743, 702; ¹H NMR (600 MHz, CDCl₃): 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); ¹³C NMR (150 MHz, CDCl₃): 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 C₁₈H₂₅NO₃ 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 LiBH₄ (14 mg, 0.66 mmol) at 0 °C. After stirring at room temperature for 1 h, the reaction was guenched 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 Na₂SO₄, 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, Et₃N (46 µL, 0.33 mmol), dry DMSO (110 μ L) and dry CH₂Cl₂ (220 μ L). To the solution was added SO3 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 CH₂Cl₂ three times. The combined organic extracts were dried over Na₂SO₄, filtered, and concentrated under reduced pressure at 0 °C to give a crude material in CH₂Cl₂, 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 SnCl₂ (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 CH2Cl2 three times. The combined organic extracts were washed with water three times, dried over Na2SO4, filtered, and concentrated ACS Paragon Plus Environment

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 μ mol, 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; ¹H NMR (400 MHz, CDCl₃): 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 = 7.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 = 7.2Hz, 1.5H), 0.91–0.82 (m, 6.5H); ¹³C NMR (100 MHz, CDCl₃): 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 C₁₃H₂₅O₃229.1804 $[M+H^+]$, found 229.1801.

(+)-(2S,3R,4S,6S)-Oxazolidinone (32). A flame-dried 20-mL two-necked round-bottomed flask was charged with (3S)-3propionyl-4-benzyloxazolidin-2-one (296 mg, 1.27 mmol) and dry CH₂Cl₂ (1.2 mL). To the solution was added *n*-Bu₂BOTf (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 Et₃N (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 phosphorous buffer (1 mL) and MeOH (4.1 mL), then MeOH-34% H₂O₂ 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 Et₂O three times. The combined organic extracts were washed with 5% NaHCO₃ and brine, dried over Na₂SO₄, 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); $\left[\alpha\right]_{D}^{26}$ +32.3 (c 1.57, CHCl₃); IR (neat, cm⁻¹): 3503, 2961, 2926, 2876, 1782, 1697, 1454, 1385, 1352, 1209, 1103, 970, 762, 748, 702; ¹H NMR (600 MHz, CDCl₃): 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); ¹³C NMR (150 MHz, CDCl₃): 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 C₂₁H₃₁NO₄ 361.2253 [M⁺], found 361.2243.

(-)-(2*S*,3*R*,4*S*,6*S*)-*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 **s Environment**

saturated aqueous Na₂S₂O₃ and 1 M aqueous HCl. The aqueous layer was extracted with EtOAc three times. The combined organic extracts were dried over Na₂SO₄ 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 μ mol, 86%) as a colorless oil. $R_f = 0.32$ (hexanes-EtOAc = 1:1); $[\alpha]_{D}^{2'}$ -16.8 (c 1.24, CHCl₃); IR (neat, cm⁻¹): 3403, 2962, 2921, 2877, 2852, 1710, 1460, 1380, 1204, 982; ¹H NMR (600 MHz, CDCl₃): 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); ¹³C NMR (150 MHz, CDCl₃): 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 C₁₁H₂₃O₃ 203.1669 [M+H⁺], found 203.1658.

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(-)-(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 K₂CO₃ (17.0 mg, 124 µmol) at room temperature. After stirring at 50 °C for 3 h, the reaction mixture was diluted with CHCl₃ and filtered through a pad of Celite[®]. The filter cake was washed with CHCl₃. 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 μ mol, 89%) as a colorless oil. R_f = 0.73 (hexanes-EtOAc = 1:1); $[\alpha]_{D}^{27}$ -12 (c 0.90, CHCl₃); 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, CDCl₃): 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); ¹³C NMR (150 MHz, CDCl₃): 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 C₁₃H₂₇O₃ 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 μ L, 767 μ mol), and dry CH₂Cl₂ (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 CH2Cl2. The separated organic layer was washed twice with 13.2% aqueous sodium chloride, dried over Na₂SO₄, 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 50-mL two-necked round-bottomed flask was charged with the crude material, THF (6.75 mL), and H₂O (2.25 mL). To the mixture was added LiOH·H₂O (41 mg, 1.0 mmol) and H₂O₂ (34% w/w solution in H₂O, 0.29 mL, 2.9 mmol) at 0 °C and warned at room temperature for 1 h. Additional LiOH·H₂O (41 mg, 1.0 mmol) and H₂O₂ (34% w/w solution in H₂O, 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 Na₂S₂O₃ and 1 M aqueous HCl. The separated aqueous layer was extracted with EtOAc three times. The combined organic extracts were dried over Na₂SO₄, 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, CHCl₃); IR (neat, cm⁻¹): 2957, 2876, 2853, 1711, 1705, 1462, 1456, 1132, 1034, 1026, 997; ¹H NMR (600 MHz, CDCl₃): 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, J = 7.8 Hz, 1.5H), 1.5{Hz}, 1.5{Hz}, 1.5{Hz}, 1.5{Hz}, 1.5{Hz}, 1.5{Hz}, 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); ¹³C NMR (150 MHz, CDCl₃): 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 C₁₆H₃₀O₄ 287.2222 [M+H⁺], found 287.2218.

(-)-Diol 35. A screw cap test tube was charged with diacetate 36 (12.0 mg, 22.4 μ mol) and MeOH (224 μ L). To the solution was added K₂CO₃ (15.0 mg, 112 µmol). After stirred 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 Na₂SO₄ 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 μ mol, quant.) as a white solid. R_f = 0.36 (CH₂Cl₂-acetone = 10:1); $[\alpha]_D^{27}$ –274 (*c* 0.305, CHCl₃); IR (neat, cm⁻¹): 3393, 2918, 1691, 1661, 1651, 1404, 1339, 1196, 1130, 910, 731; ¹H NMR (600 MHz, CDCl₃): 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); ¹³C NMR (150 MHz, CDCl₃): 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 C₂₀H₂₂N₂O₆S₂Na 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 CH₂Cl₂ (100 µL). To the solution was added DMAP (2.3 mg, 19 µmol), 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 CH₂Cl₂ three times. The combined organic extracts were washed with H₂O and brine, dried over Na₂SO₄, 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 μ mol, 36%) as a colorless oil with recovery of the core skeleton 35 (2.6 mg, 5.8 μ mol, 30%). R_f = 0.47 (CH₂Cl₂-acetone = 10:1); $[\alpha]_{D}^{2/}$ -224 (c 0.640, CHCl₃); IR (neat, cm⁻¹): 3420, 2957, 2928, 1732, 1693, 1681, 1666, 1651, 1633, 1392, 1128, 1026, 756; ¹H NMR (500 MHz, CDCl₃): 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 0.4 H), 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-ACS Paragon Plus Environment

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0.80 (m, 6H); 13 C NMR (125 MHz, CDCl₃): 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 C₃₆H₅₀N₂O₉S₂Na 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 CH₂Cl₂ (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 CH₂Cl₂. The organic layer was washed twice with 13.2% aqueous sodium chloride, dried over Na2SO4, 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 μ mol, 78%) as a pale yellow solid. $R_f = 0.49$ (CH₂Cl₂-acetone = 10:1); 1 -243 (c 0.760, CHCl₃); IR (neat, cm⁻¹): 3479, 2961, $[\alpha]_{D}^{2}$ 2924, 2874, 1728, 1693, 1666, 1659, 1393, 1339, 1194, 1126, 756; ¹H NMR (500 MHz, CDCl₃): 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); ¹³C NMR (125 MHz, CDCl₃): 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 C₃₁H₄₂N₂O₈S₂Na 657.2280 [M+Na⁺], found 657.2269.

(-)-(2R,4R)-Oxazolidinone 45. A flame-dried 50-mL twonecked 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 Na₂SO₄, 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 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, CHCl₃); IR (neat, cm⁻¹): 2962, 2929, 2874, 1781, 1698, 1456, 1387, 1350, 1289, 1241, 1209, 1099, 1016, 973, 742, 702; ¹H NMR (600 MHz, CDCl₃): 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); ¹³C NMR (150 MHz, CDCl₃): 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 C₁₈H₂₅NO₃ 303.1834 [M⁺], found 303.1822. Spectral data matched the reported data.²⁵

(2R,3S,4R,6R)-Oxazolidinone 49. A flame-dried 30-mL twonecked 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 LiBH₄ (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 Na₂SO₄, 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, Et₃N (918 µL, 6.59 mmol), dry DMSO (1.3 mL), and dry CH₂Cl₂ (2.6 mL). To the solution was added SO₃·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 CH₂Cl₂ three times. The combined organic extracts were dried over Na₂SO₄, 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 (3R)-3-propionyl-4benzyloxazolidin-2-one (338 mg, 1.45 mmol) and dry CH₂Cl₂ (1.3 mL). To the solution was added n-Bu₂BOTf (469 mg, 1.71 mmol) at 0 °C. After stirring at 0 °C for 10 min, Et₃N (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 phosphorous buffer (1.5 mL) and MeOH (4 mL), then MeOH-34% H₂O₂ 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 Et₂O three times. The combined organic extracts were washed with 5% NaHCO₃ and brine, dried over Na₂SO₄, 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, CHCl₃). 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 CH₂Cl₂ (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 CH₂Cl₂. The separated organic layer was washed twice with 13.2% aqueous sodium chloride, dried over Na₂SO₄, 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-

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bottomed flask was charged the crude material, THF (2 mL), and H₂O (0.6 mL). To the solution was added H₂O₂ (34% w/w solution in H₂O, 268 µL, 2.63 mmol) and LiOH·H₂O (44 mg, 1.1 mmol) at 0 °C. After stirring at room temperature for 10 h, the reaction was quenched with saturated aqueous Na₂S₂O₃ and 1 M HCl aq. The separated aqueous layer was extracted with EtOAc three times. The combined organic extracts were dried over Na₂SO₄, 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, CHCl₃). Spectral data matched the compound **41**.

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(-)-(2R,3S,4S,6S)-Oxazolidinone S4 (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 LiBH₄ (143 mg, 6.59 mmol) 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 Na₂SO₄, 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, Et₃N (918 µL, 6.59 mmol), dry DMSO (1.3 mL), and dry CH₂Cl₂ (2.6 mL). To the solution was added SO₃·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 CH₂Cl₂ three times. The combined organic extracts were dried over Na₂SO₄, 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 twonecked round-bottomed flask was charged with (3R)-3propionyl-4-benzyloxazolidin-2-one (338 mg, 1.45 mmol) and dry CH₂Cl₂ (1.3 mL). To the solution was added *n*-Bu₂BOTf (469 mg, 1.71 mmol) at 0 °C. After stirring at 0 °C for 10 min, Et₃N (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 phosphorous buffer (1.5 mL) and MeOH (4 mL), then MeOH-34% H₂O₂ 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 Et₂O three times. The combined organic extracts were washed with 5% NaHCO₃ and brine, dried over Na₂SO₄, filtered, and concentrated under reduced pressure at 0 °C to give a crude material, which was purified by flash column chromatography (CH₂Cl₂) 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, CHCl₃); 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, CDCl₃): 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); ¹³C NMR (150 MHz, CDCl₃): 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 C₂₁H₃₁NO₄ 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 CH₂Cl₂ (3.5 mL). To the solution was added PPTS (53 mg, 0.21 mmol). After stirring at room temperature for 1.5 h, the reaction was diluted with CH₂Cl₂. The separated organic layer was washed twice with 13.2% aqueous sodium chloride, dried over Na₂SO₄, 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 H₂O (0.6 mL). To the solution was added H₂O₂ (34% w/w solution in H₂O, 0.27 mL, 2.6 mmol) and LiOH·H₂O (44 mg, 1.1 mmol) at 0 °C. After stirring at room temperature for 9 h, the reaction was guenched with saturated aqueous Na₂S₂O₃ and 1 M aqueous HCl. The separated aqueous layer was extracted with EtOAc three times. The combined organic extracts were dried over Na₂SO₄, 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, CHCl₃); 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 $(500 \text{ MHz}, \text{CDCl}_3)$: 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, 5.0Hz, 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); ¹³C NMR (125 MHz, CDCl₃): 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 C₁₆H₃₁O₄ 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 CH₂Cl₂ (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 CH₂Cl₂ three times. The combined organic extracts were washed with H₂O and brine, dried over Na₂SO₄, filtered, and concentrated under reduced pressure to give a residue, which was purified by preparative TLC (CH₂Cl₂-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 (CH₂Cl₂-acetone = 10:1); [α]_D²⁷ -235 (*c* 0.215, CHCl₃); IR (neat, cm⁻¹): 3435, 2961, 2926, 2876, 1732,

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1695, 1676, 1674, 1666, 1659, 1385, 1198, 1128, 1026, 756; ¹H NMR (600 MHz, CDCl₃): 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– 10 1.00 (m, 1H), 1.00–0.82 (m, 10H); ¹³C NMR (150 MHz, 11 CDCl₃): δ 175.3, 174.2, 167.0, 166.9, 164.2, 164.1, 139.7, 12 139.3, 138.0, 137.90, 137.86, 137.6, 137.5, 110.9, 109.6, 109.4, 13 108.0, 107.9, 106.0, 105.6, 99.8, 99.0, 83.4, 81.2, 72.61, 72.56, 14 71.4, 71.0, 70.5, 69.4, 69.3, 64.1, 63.0, 62.5, 60.9, 60.6, 41.0, 15 40.55, 40.51, 40.48, 40.2, 40.10, 40.05, 34.8, 34.2, 31.9, 31.7, 16 30.9, 28.4, 28.0, 25.5, 25.4, 20.4, 20.1, 20.0, 19.7, 16.8, 16.5, 17 14.91, 14.86, 14.72, 14.70, 11.6, 11.1, 11.0, 10.6 (Six signals 18 are missing due to overlap.); HRMS (ESI⁺) m/z: calcd. for 19 C₃₆H₅₀N₂O₉S₂Na 741.2855 [M+Na⁺], found 741.2832. 20

 β -hydroxy ester 51. A screw cap test tube was charged with THP protected β -hydroxy ester S5 (2.7 mg, 3.9 μ mol), MeOH (25 μ L), and CH₂Cl₂ (25 μ L). 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 CH₂Cl₂. The separated organic layer was washed twice with 13.2% aqueous sodium chloride, dried over Na₂SO₄, filtered, and concentrated under reduced pressure to give a crude material, which was purified by preparative TLC (CH₂Cl₂-acetone = 20:1) to afford β -hydroxy ester 51 (1.7 mg, 8.3 μ mol, 72%) as a white solid. R_f = 0.14 $(CH_2Cl_2\text{-acetone} = 20:1); \ [\alpha]_D^{25} -330 \ (c \ 0.151, \ CHCl_3); \ IR$ (neat, cm⁻¹): 3468, 2961, 2926, 2874, 1732, 1693, 1680, 1676, 1666, 1651, 1393, 1385, 1339, 1192, 1126, 754; ¹H NMR (500 MHz, CDCl₃): 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); ¹³C NMR (150 MHz, CDCl₃): 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 C₃₁H₄₂N₂O₈S₂Na 657.2280 [M+Na⁺], found 657.2273.

\beta-Keto ester 37. A screw cap test tube was charged with the β hydroxy ester 43 (2.9 mg, 4.6 $\mu mol)$ and dry CH_2Cl_2 (76 $\mu L).$ 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 NaHCO₃ and brine, dried over Na₂SO₄, 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 umol, 34%) as a pale yellow solid with recovery of the diol (1.2 mg, 1.9 μ mol, 41%). R_f = 0.43 (CH₂Cl₂-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, CDCl₃): 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 = 7.2Hz, 1.8H), 1.16–1.04 (m, 2H), 1.08 (d, J = 7.2 Hz, 1.2H), 0.91– 0.84 (m, 6H); ¹³C NMR (150 MHz, CDCl₃): 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 C₃₁H₄₀N₂O₈S₂Na 655.2124 [M+Na⁺], found 655.2148.

\beta-Keto ester 38. A screw cap test tube was charged with β hydroxy ester 51 (1.5 mg, 2.4 μ mol) and dry CH₂Cl₂ (40 μ L). 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 CH₂Cl₂. The organic layer was washed with saturated aqueous NaHCO3 and brine, dried over Na₂SO₄, filtered, and concentrated under reduced pressure to give a crude material, which was purified by preparative TLC (CH₂Cl₂-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 μ mol, 27%). $R_f = 0.45$ (CH₂Cl₂-acetone = 10:1); $[\alpha]_D^{27}$ -220 (*c* 0.090, CHCl₃); 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, CDCl₃): 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, 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); ¹³C NMR (125 MHz, CDCl₃): 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 LiBH₄ (143 mg, 6.59 mmol) at 0 °C. After stirring at 0 °C for 11.5 h, the reaction was guenched with 1 M NaOH ag. at 0 °C. The reaction mixture was diluted with water and extracted with EtOAc three times. The combined organic extracts were dried over Na₂SO₄, 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 roundbottomed flask was charged with a hexanes-EtOAc solution of 46, Et₃N (918 µL, 6.59 mmol), dry DMSO (1.3 mL), and dry

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 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 CH₂Cl₂ three times. The combined organic extracts were dried over Na2SO4, 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 twonecked round-bottomed flask was charged with (3S)-3propionyl-4-benzyloxazolidin-2-one (338 mg, 1.45 mmol) and dry CH_2Cl_2 (1.3 mL). To the solution was added *n*-Bu₂BOTf (469 mg, 1.71 mmol) at 0 °C. After stirring at 0 °C for 10 min, Et₃N (239 µL, 1.71 mmol) was added at 0 °C. Then, after stirring at 0 °C for 10 min, a CH₂Cl₂ 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 phosphorous buffer (1.5 mL) and MeOH (4 mL), then MeOH-34% H₂O₂ ag. (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 Et₂O three times. The combined organic extracts were washed with 5% NaHCO₃ brine, dried over Na₂SO₄, filtered, and concentrated under reduced pressure at 0 °C to give a crude material, which was purified by flash column chromatography (CH₂Cl₂ 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, CHCl₃). 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 CH₂Cl₂ (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 CH₂Cl₂. The separated organic layer was washed twice with 13.2% aqueous sodium chloride, dried over Na₂SO₄, 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 H₂O (0.6 mL). To the solution was added H₂O₂ (34% w/w solution in H₂O, 0.24 mL, 2.4 mmol) and LiOH·H₂O (40 mg, 0.96 mmol) at 0 °C. After stirring at room temperature for 10.5 h, the reaction was quenched with saturated aqueous Na₂S₂O₃ and 1 M aqueous HCl. The aqueous layer was extracted with EtO-Ac three times. The combined organic extracts were dried over Na₂SO₄, 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); $[\alpha]_{D}^{2/2}$ +21.0 (c 4.40, CHCl₃). 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 CH₂Cl₂ (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 CH₂Cl₂ three times. The combined organic extracts were washed with H₂O and brine, dried over Na₂SO₄, 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 μ mol, 37%) as a colorless oil with recovery of the core skeleton 35 (3.5 mg, 7.8 μ mol, 32%). R_f = 0.47 (CH₂Cl₂-acetone = 10:1); $[\alpha]_{D}^{2/}$ -196 (c 0.300, CHCl₃); IR (neat, cm⁻¹): 3420, 2961, 2926, 2876, 1732, 1691, 1676, 1668, 1662, 1654, 1385, 1198, 1126, 1026, 756; ¹H NMR (500 MHz, CDCl₃): 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, 0.4 H), 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); ¹³C NMR (125 MHz, CDCl₃): 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 CH₂Cl₂ (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 CH₂Cl₂. The separated organic layer was washed twice with 13.2% aqueous sodium chloride, dried over Na₂SO₄, 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 μ mol, 56%) as a white solid. $R_f = 0.39$ (CH₂Cl₂-acetone = 10:1); $[\alpha]_D^{25}$ -277 (c 0.125, CHCl₃); IR (neat, cm⁻¹): 3501, 2961, 2924, 2874, 1728, 1691, 1666, 1651, 1393, 1385, 1194, 1126, 978, 756; ¹H NMR (600 MHz, CDCl₃): 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); ¹³C NMR (150 MHz, CDCl₃): 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 C₃₁H₄₂N₂O₈S₂Na 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 CH₂Cl₂ (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 CH₂Cl₂. The separated organic layer was washed with saturated aqueous NaHCO₃ and brine, dried over

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Na₂SO₄, 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 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 μ mol, 36%). $R_f = 0.45$ (CH₂Cl₂-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, CDCl₃): 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 10 Hz, 1H), 5.92 (ddd, J = 8.4, 2.4, 2.4 Hz, 0.4H), 5.74 (ddd, J =11 7.8, 2.4, 2.4 Hz, 0.6H), 5.27–5.22 (m, 0.6H), 5.12–5.08 (m, 12 0.4H), 4.95–4.92 (m, 1H), 4.92–4.88 (m, 1H), 4.72 (dd, J = 8.4, 13 1.8 Hz, 0.6H), 4.71–4.65 (m, 1H), 4.60 (dd, J = 8.4, 1.8 Hz, 14 0.4H), 4.49–4.44 (m, 0.6H), 4.42–4.37 (m, 0.4H), 3.72 (q, J =15 7.2 Hz, 0.4H), 3.64 (q, J = 7.2 Hz, 0.6H), 3.13–2.98 (m, 4.4H), 16 2.90 (dq, J = 13.8, 6.6 Hz, 0.6H), 2.33–2.31 (m, 3H), 2.30 (s, 17 1.8H), 2.29 (s, 1.2H), 1.82 (ddd, J = 13.8, 8.4, 5.4 Hz, 0.4H), 18 1.67 (ddd, J = 13.2, 7.8, 6.0 Hz, 0.6H), 1.40 (d, J = 7.2 Hz, 19 1.8H), 1.40–1.24 (m, 3H), 1.33 (d, J = 7.2 Hz, 1.2H), 1.13 (d, J 20 = 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); ¹³C NMR (150 MHz, CDCl₃): δ 210.20, 21 210.17, 169.6, 169.3, 166.82, 166.79, 164.3, 164.2, 139.9, 22 23 139.6, 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, 24 64.2, 64.1, 60.7, 60.4, 52.0, 50.4, 44.0, 43.3, 40.5, 40.4, 40.3, 25 40.2, 39.7, 32.1, 29.7, 29.5, 20.2, 19.52, 19.49, 17.3, 17.0, 26 14.91, 14.88, 14.77, 14.6, 13.0, 12.9, 11.2, 11.1 (Five signals 27 are missing due to overlap.); HRMS (ESI⁺) m/z: calcd. for 28 C₃₁H₄₀N₂O₈S₂Na 655.2124 [M+Na⁺], found 655.2120. 29

30 **THP** protected β -hydroxy ester S9. A screw cap test tube was 31 charged with 35 (14 mg, 31 µmol), 50 (8.9 mg, 31 µmol), and CH₂Cl₂ (80 µL). To the solution was added DMAP (3.8 mg, 31 32 µmol) and WSCD·HCl (11.9 mg, 62.1 µmol) at 0 °C. After 33 stirring at reflux for 2 h, the reaction was quenched with 1 M 34 aqueous HCl. The resulting mixture was extracted with CH₂Cl₂ 35 three times. The combined organic extracts were washed with 36 H₂O and brine, dried over Na₂SO₄, filtered, and concentrated 37 under reduced pressure. The residue was purified by prepara-38 tive TLC (CH₂Cl₂-acetone = 20:1) to afford the desired THP 39 protected β -hydroxy ester **S9** (8.0 mg, 11 μ mol, 36%) as a pale 40 yellow solid with recovery of **35** (7.0 mg, 16 μ mol, 50%). R_f = 41 0.41 (CH₂Cl₂-acetone = 10:1); $[\alpha]_D^{27}$ -229 (c, 0.515, CHCl₃); 42 IR (neat, cm⁻¹): 3400, 2957, 2928, 2874, 1732, 1693, 1681, 43 1666, 1658, 1651, 1385, 1198, 1128, 1026, 754, 667; ¹H NMR 44 (500 MHz, CDCl₃): δ 6.61–6.57 (m, 1H), 6.54–6.49 (m, 1H), 45 6.33-6.25 (m, 1H), 6.22-6.18 (m, 1H), 5.90 (ddd, J = 8.0, 2.5, 2.5, 3.546 2.5 Hz, 0.4H), 5.88 (ddd, J = 8.0, 2.5, 2.5 Hz, 0.6H), 5.23–5.10 47 (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), 4.62-48 4.57 (m, 0.8H), 4.42 (br s, 1H), 3.95-3.84 (m, 1H), 3.84-3.80 49 (m, 1H), 3.48-3.42 (m, 0.5H), 3.42-3.36 (m, 0.5H), 3.14-2.95 50 (m, 4H), 2.75–2.65 (m, 1H), 2.30–2.26 (m, 6H), 1.85–1.75 (m, 51 1H), 1.75-1.65 (m, 3H), 1.65-1.42 (m, 6H), 1.42-1.33 (m, 1H), 52 1.23 (d, J = 7.0 Hz, 1.2H), 1.17 (d, J = 7.0 Hz, 1.8H), 1.10– 53 0.93 (m, 2H), 0.96 (d, J = 7.0 Hz, 1.8H), 0.94 (d, J = 7.0 Hz, 54 1.2H), 0.90–0.78 (m, 7H); ¹³C NMR (125 MHz, CDCl₃): δ 55 175.0, 174.4, 167.0, 166.9, 164.10, 164.07, 139.8, 139.4, 56 137.95, 137.86, 137.82, 137.61, 137.57, 110.8, 109.6, 109.5, 57 108.0, 107.9, 105.9, 105.6, 100.5, 99.4, 83.1, 81.1, 72.6, 71.5, 58 71.2, 70.51, 70.48, 64.12, 64.10, 63.2, 63.0, 60.7, 60.5, 41.8, 59 41.4, 41.1, 41.0, 40.6, 40., 40.4, 40.2, 34.4, 34.0, 31.7, 31.5, 60 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 μ mol), MeOH (28 µL), and CH₂Cl₂ (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 CH₂Cl₂. The separated organic layer was washed twice with 13.2% aqueous sodium chloride, dried over Na₂SO₄, filtered, and concentrated under reduced pressure to give a crude material, which was purified by preparative TLC (CH₂Cl₂-acetone = 20:1) to afford β hydroxy ester 53 (2.7 mg, 4.3 µmol, 76%) as a pale yellow solid. $R_f = 0.34$ (CH₂Cl₂-acetone = 10:1); $[\alpha]_D^{22}$ -253 (c 0.530, CHCl₃); IR (neat, cm⁻¹): 3468, 2962, 2924, 2876, 1732, 1693, 1680, 1666, 1651, 1393, 1384, 1337, 1192, 1128, 756; ¹H NMR (500 MHz, CDCl₃): 8 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); ¹³C NMR (125 MHz, CDCl₃): 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 C₃₁H₄₂N₂O₈S₂Na 657.2280 [M+Na⁺], found 657.2268.

\beta-Keto ester 40. A screw cap test tube was charged with the β hydroxy ester 53 (2.7 mg, 4.3 μ mol) and dry CH₂Cl₂ (70 μ L). 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 CH₂Cl₂. The separated organic layer was washed with saturated aqueous NaHCO3 and brine, dried over Na₂SO₄, filtered, and concentrated under reduced pressure to give a crude material, which was purified by preparative TLC (CH₂Cl₂-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**; $R_f = 0.43$ (CH₂Cl₂-acetone = 10:1); $[\alpha]_D^{27}$ -246 (c 0.210, CHCl₃); 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, CDCl₃): 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); ¹³C NMR (150 MHz, CDCl₃): 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 C₃₁H₄₀N₂O₈S₂Na 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 CH₂Cl₂ (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 guenched with 1 M aqueous HCl. The resulting mixture was extracted with CH₂Cl₂ three times. The combined organic extracts were washed with water and brine, dried over Na2SO4, 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%). $R_f = 0.59 (CH_2Cl_2\text{-acetone} = 10:1);$ $[\alpha]_D^{27}$ -460 (c 0.044, CHCl₃); 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 ¹³C NMR data of major diastereomer; ¹H NMR (500 MHz, CDCl₃): 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, 1.5H)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); ¹³C NMR (125 MHz, CDCl₃): 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 C₃₄H₄₄N₂O₉S₂Na 711.2386 [M+Na⁺], found 711.2377. 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 μ L), and CH₂Cl₂ (25 μ L). 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 CH₂Cl₂. The organic layer was washed twice with 13.2% aqueous sodium chloride, dried over Na₂SO₄, 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**; $R_f = 0.41$ (CH₂Cl₂-acetone = 10:1); $[\alpha]_{D}^{27}$ -380 (c 0.065, CHCl₃); IR (neat, cm⁻¹): 3508, 3350, 2959, 2928, 2874, 2853, 1715, 1693, 1682, 1454, 1371, 1281, 1184, 1140, 756; ¹H NMR (600 MHz, CDCl₃): 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); ¹³C NMR (150 MHz, CDCl₃): δ 175.2, 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 CH₂Cl₂ (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 CH₂Cl₂. The organic layer was washed with saturated aqueous NaHCO₃ and brine, dried over Na₂SO₄, 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 umol), which was placed in a flame-dried screw cap test tube and dissolved in dry CH₂Cl₂ (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 CH₂Cl₂. The organic layer was washed with saturated aqueous NaHCO₃ followed by brine, dried over Na₂SO₄, 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 vield 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. $R_f = 0.57$ (CH₂Cl₂-acetone = 10:1); $\left[\alpha\right]_{D}^{27}$ -410 (c 0.095, CHCl₃); IR (neat, cm⁻¹): 3342, 2961, 2930, 2874, 2851, 1747, 1715, 1693, 1682, 1454, 1371, 1188, 1140, 754; ¹H NMR (500 MHz, CDCl₃): 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)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); ¹³C NMR (150 MHz, CDCl₃): 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

Copies of ¹H- and ¹³C-NMR spectra. This materials is available free of charge via the Internet at http://pubs.acs.org.

AUTHOR INFORMATION

Corresponding Author

*E-mail: tokuyama@mail.pharm.tohoku.ac.jp.

isaka@biotec.or.th

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