Supplementary Information for

A fungal ketoreductase domain that displays substrate-dependent stereospecificity

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1. Supplementary Results

Supplementary Figure 1. The chiral HPLC traces (240 nm) of (i) the mixture of the chemical standards 4L and 4D, and the reductive products generated by (ii) Hpm8, (iii) Hpm8B2, (iv) Hpm8B4, (v) Hpm8B5 or (vi) Hpm8B9 starting from (S,E)-7-hydroxy-3-oxooct-4-enoyl SNAC 4.
Supplementary Figure 2. (i) The chiral HPLC traces of the mixture of the chemical standards $5D$ and $5L$, and the chiral HPLC traces of the reductive products by (ii) Hpm8 or (iii) Hpm8B4 with the substrate 5. The chromatograms above were obtained by monitoring at 240 nm.

Supplementary Figure 3. (i) The chiral HPLC traces of the mixture of the chemical standards $6D$ and $6L$, and the chiral HPLC traces of the reductive products by (ii) Hpm8 or (iii) Hpm8B4 with the substrate 6. The chromatograms above were obtained by monitoring at 240 nm.
Supplementary Figure 4. The LCMS analysis of the in vitro Hpm8 KR assay on substrate 3. The traces shown are the selected ion monitoring of desired ions in the positive ionization mode. Trace a is [M+H]$^+$ at 234 for 3D/L and trace b is [M+H]$^+$ at 232 for 3.

Supplementary Figure 5. The LCMS analysis of the in vitro Hpm8 KR assay on substrate 7. The traces shown are the selected ion monitoring of desired ions in the positive ionization mode. Trace a is [M+H]$^+$ at 290 for 7D/L and trace b is [M+H]$^+$ at 288 for 7.
Supplementary Figure 6. The LCMS analysis of the in vitro Hpm8 KR assay on substrate 8. The traces shown are the selected ion monitoring of desired ions in the positive ionization mode. Trace a is \([\text{M+H}]^+\) at 318 for 8D/L and trace b is \([\text{M+H}]^+\) at 316 for 8.

Supplementary Figure 7. (i) The chiral HPLC traces of the mixture of the chemical standards 3D and 3L, and the chiral HPLC traces of the reductive products by (ii) Hpm8 or (iii) Hpm8B4 assayed with the substrate 3. The chromatograms above were obtained by monitoring at 240 nm.
Supplementary Figure 8. (i) The chiral HPLC traces of the mixture of the chemical standards 7D and 7L, and the chiral HPLC traces of the reductive products by (ii) Hpm8 or (iii) Hpm8B4 working on the substrate 7. The chromatograms above were obtained by monitoring at 240 nm.

Supplementary Figure 9. (i) The chiral HPLC traces of the mixture of the chemical standards 8D and 8L, and the chiral HPLC traces of the reductive products by (ii) Hpm8 or (iii) Hpm8B4 working on the substrate 8. The chromatograms above were obtained by monitoring at 240 nm.
Supplementary Figure 10. a. Chemical structures of (R)-monocillin II and radicicol^1; b. The sequence alignment among the catalytic KR domain of DEBS module 1 KR (EryKR1, accession NO.: Q03131), Hpm8_cKR and Rdc5_cKR. The catalytic residues K, S, Y and N are labeled with asterisks. The conserved sequence patch for NADPH binding is underlined. The LDD motif symbolizing B-type KR is highlighted with dots. To match the numbering in entire HRPKS, a plus of 1969 is required for the residue numbers in the above sequence of Hpm8_cKR (a plus of 1994 is required for those in Rdc5_cKR). The catalytic EryKR1 shares 30% sequence similarity with either cKR.
Supplementary Figure 11. The HPLC traces of the in vivo metabolites profiles from the *S. cerevisiae* co-transformants expressing Hpm3 and (i) Hpm8, active site mutants (ii) Hpm8_K2088D, (iii) Hpm8_S2113A, (iv) Hpm8_Y2126A or (v) Hpm8_Y2118F. The chromatograms above were obtained by monitoring at 320 nm. Mutation of K2088, S2113 and Y2126 abolished the activities of Hpm8.
Supplementary Figure 12. The sequence alignment among the catalytic KR domain of AmpKR2 (PDB ID: 3MJE), Hpm8_cKR and Rdc5_cKR. The catalytic residues K, S, Y and N are labeled with asterisks. The conserved sequence patch for NADPH binding is underlined. The conserved W for A-type KR is highlighted with dot. To match the numbering in entire HRPKS, a plus of 1969 is required for the residue numbers in the above sequence of Hpm8_cKR (a plus of 1994 is required for those in Rdc5_cKR).
Supplementary Figure 13. The cartoon view of modeled structure of Hpm8_cKR in blue a: from side, b: from top. The cartoon view of modeled structure of Rdc5_cKR in green c: from side, d: from top. The catalytic residues are highlighted in red in all the structures. The conserved motifs (GXGXXG) for NADPH binding are in yellow. The LRD loops are shown in cyan color and the helix lid elements (corresponding to the αFG region in EryKR1) are in salmon pink. e: The topology diagram of the modeled structure of Hpm8_cKR. The secondary structures α4, β5, α5 and α6 are highlighted in salmon.
Supplementary Figure 14. High-resolution mass spectrum of compound 9. The calculated mass is 317.1389 Da.
Supplementary Figure 15. $^{13}$C NMR spectrum (125 MHz) of 9 in methanol-$d_4$. 
Supplementary Figure 16. $^1$H NMR spectrum of 9 (500 MHz) in methanol-$d_4$. 
Supplementary Figure 17. HSQC spectrum of 9 in methanol-\textit{d}_4 (\textit{H}: 500 MHz).
Supplementary Figure 18. HMBC spectrum of 9 in methanol-\textit{d}_4 (\textit{^1}H: 500 MHz).
Supplementary Figure 19. Phylogenetic tree of fungal HRPKS catalytic ketoreductase domain with a bacterial actKR as an outgroup. The evolutionary distances were computed using the Poisson correction method and are in the units of the number of amino acid substitutions per site. The branch lengths are also shown along the branches.
**Supplementary Table 1.** The list of products generated in the KR assay of Hpm8 on different β-keto acyl SNAC substrates.

| Substrate structure | D configuration product | L configuration product |
|---------------------|-------------------------|------------------------|
| Diketide, 2         | 2D, 8.8%                | 2L, 91.2%             |
| Triketide, 3        | 3D                      | Not Detected           |
| Tetraketide, 4      | 4D                      | Not Detected           |
| Tetraketide, 5      | 5D                      | Not Detected           |
| Tetraketide, 6      | 6D                      | Not Detected           |
| Pentaketide, 7      | 7D                      | Not Detected           |
| Hexaketide, 8       | 8D                      | Not Detected           |
Supplementary Table 2. NMR data comparison between 9 and 1.

| No. | $^{13}$C δ (ppm) | $^1$H δ (ppm) | $^{13}$C δ (ppm) | $^1$H δ (ppm) |
|-----|-----------------|----------------|-----------------|----------------|
|     |                 | (m, area, $J_{HH}$ (Hz)) |                 | (m, area, $J_{HH}$ (Hz)) |
| 1   | 171.0           | -              | 172.4           | -              |
| 2   | 103.4           | -              | 106.5           | -              |
| 3   | 162.0           | -              | 163.0           | -              |
| 4   | 101.5           | 6.44 (d, 1H, 2.4) | 102.5           | 6.40 (d, 1H, 3) |
| 5   | 164.1           | -              | 164.3           | -              |
| 6   | 106.2           | 6.19 (d, 1H, 2.4) | 107.6           | 6.20 (d, 1H, 3) |
| 7   | 142.7           | -              | 143.6           | -              |
| 1'  | 129.4           | 7.09 (d, 1H, 15.8) | 131.5           | 6.94 (d, 1H, 15.8) |
| 2'  | 131.4           | 6.06 (dt, 1H, 15.8, 5.4) | 133.3           | 5.94 (dt, 1H, 15.8, 6.28) |
| 3'  | 29.3            | 2.33-2.39 (m, 2H) | 31.6            | 2.14-2.28 (m, 2H) |
|     |                 | 2.15 (1H, m)    |                 |                 |
| 4'  | 22.4            | 1.61-1.66 (m, 2H) | 22.6            | 1.74-1.84 (m, 2H) |
| 5'  | 34.2            | 1.49-1.54 (m, 1H) | 34.7            | 1.52-1.71 (m, 2H) |
|     |                 | 1.67-1.73 (m, 1H) |                 |                 |
| 6'  | 72.9            | 3.95 (m, 1H)    | 72.8            | 4.23 (m, 1H)    |
| 7'  | 136.8           | 5.52-5.49 (m, 1H) | 137.5           | 5.59-5.72 (m, 2H) |
| 8'  | 125.1           | 5.80 (m, 2H)    | 126.6           | 5.59-5.72 (m, 2H) |
| 9'  | 36.5            | 2.42-2.44 (m, 1H) | 38.8            | 2.53 (dt, 1H, 15.8, 4.2) |
|     |                 | 2.50-2.56 (m, 1H) |                 |                 |
| 10' | 71.2            | 5.44-5.48 (m, 1H) | 73.2            | 2.33 (m, 1H)    |
| 11' | 17.2            | 1.39 (d, 3H, 6.5) | 19.8            | 5.30 (m, 1H)    |

* Spectra were obtained at 500 MHz for proton and 120 MHz for carbon and were recorded in methanol-$d_4$. 
2. Supplementary Methods

2.1. Molecular cloning

*E. coli* XL1-Blue and *E. coli* TOP10 (Invitrogen) were used for cloning following standard recombinant DNA techniques. DNA restriction enzymes were used as recommended by the manufacturer (New England Biolabs). PCR was performed using Phusion® DNA Polymerase (New England Biolabs). The constructs of pCR-Blunt vector (Invitrogen) containing desired PCR products were confirmed by DNA sequencing (Laragen, CA). *Saccharomyces cerevisiae* strain BJ5464-NpgA (MATa ura3-52 his3-Δ200 leu2-Δ1 trp1 pep4::HIS3 prb1 Δ1.6R can1 GAL) was used as the yeast expression hosts. The genome integrated *npgA* gene encodes a phosphopantetheinyl transferase required for post-translational activation of the PKS proteins by the addition of phosphopantetheine.

The expression plasmid of N-terminus hexa histidine-tagged wild type Hpm8 was constructed based on pKJ31, a 2µ-based yeast-*E.coli* shuttle plasmid with *URA3* auxotrophic marker. The *hpm8* was flanked by 5’-*Nde*I and 3’-*Pml*I sites in this plasmid (pZH126). The cloning vector for constructing all the Hpm8 mutants was prepared by digesting pZH126 with *Age*I (The *Age*I site is located in the ER domain of Hpm8, around 2.1kb upstream of the stop codon) and *Pml*I (The *Pml*I site follows the stop codon of *hpm8*). The inserts for site-directed mutation were amplified by two-piece slice-overlap extension PCR (SOE). The inserts for the chimeric Hpm8 enzymes (Hpm8B1 to Hpm8B9) were similarly prepared by three-piece SOE PCR. Taking the construction of the expression plasmid pZH327 for the mutant Hpm8_Y2126F as an example, the primer pair of P1-for/P1-Y2126F-rev and the pair of P2-Y2126F-for/P3-rev were used to
amplify fragment I and fragment II. SOE PCR was performed to link these two fragments together, which was ligated into pCR Blunt vector for sequencing. The corresponding insert carrying the $\text{Y}^{2126}\text{F}$ mutation was cut out by AgeI and PmeI and ligated back to pZH126 derived vector for the construction of pZH327. The Hpm8$_{S}^{2113}\text{A}$, Hpm8$_{K}^{2088}\text{D}$ and Hpm8$_{Y}^{2118}\text{F}$ mutants were constructed similarly to Hpm8$_{Y}^{2126}\text{F}$. The primer pairs for fragment I replication are P1-for/P1- S2113A-rev, P1-for/P1-K2088D-rev and P1-for/ P1-Y2118F-rev, respectively. The primer pairs for the amplification of fragment II are P2- S2113A-for/P3-rev, P2-K2088D-for/P3-rev and P2-Y2118F-for/P3-rev, respectively.

Similar strategy was applied to construct Hpm8B1 to Hpm8B9. Three pieces SOE PCR was utilized to obtain the insert carrying different regions of Rdc5_cKR. Taking the construction of the expression plasmid pZH213 for Hpm8B1 as an example, fragment I and fragment III were amplified by two pairs of primers including P1-for/ P1-B1-rev and P3-B1-for/P3-rev, respectively. The template gene is wild type $\text{hpm8}$. The middle fragment II is replicated by primer pair P2-B1-for/ P2-B1-rev based on the $\text{rdc5}$ gene as template. After SOE PCR, the insert was ligated into pCR Blunt vector for sequencing. Recovered by cleavage with AgeI and PmeI, the insert was ligated into pZH126-derived vector for the completion of pZH213. The other chimeric Hpm8 enzymes in KR domain were constructed accordingly. The corresponding primers are named with the number of the hybrid enzymes. For instance, the primer pair P2-B2-for/P2-B2-rev are employed for the amplification of fragment II for the insert of Hpm8B2.

**Supplementary Table 3.** List of primers.
| Primer Name | 5'-Primer sequence-3' |
|------------|----------------------|
| P1-for     | agaaccgggtgcgaagctacca |
| P1-Y2126F-rev | atctcggtgaatttgccagctgcgcAattgagccgctgtgggataac |
| P2-Y2126F-for | gttatccagctgctcaatTCgcaActggtgcacaaacactacaggat |
| P1-S2113A-rev | aataccgtagataacccggagctAGCggagccagtgaccatgaagtc |
| P2-S2113A-for | gcaccttcgcagctcgcGCTgaccttcgctttctgctgc |
| P1-Y2126A-rev | tctectgttagttgcegcgcGctagctgcagctgggataaccc |
| P2-Y2126A-for | gttatccagctgctcaataGCcgcGgctggcaacactacaggat |
| P1-K2088D-rev | caagttccagtaaccttgggAGTCggagcagatgaccatgaagtc |
| P2-K2088D-for | tgtcgccgttcgctgccccGGTCggagcagatgaccatgaagtc |
| P1-Y2118F-rev | tgtcgccgttcgctgccccGGTCggagcagatgaccatgaagtc |
| P2-Y2118F-for | gttatccagctgctcaataGCcgcGgctggcaacactacaggat |
| P1-B2-rev     | ggacttcatggtcatgctccGCTgacctccggtatctacggttat |
| P2-B2-for     | gttatccagctgctcaataGCcgcGgctggcaacactacaggat |
| P1-B3-rev     | gcagcacatccacccggcagcGCTGACGGCCAGGGCTCTGC |
| P2-B3-for     | ggtcgccgttcgctgccccGGTCggagcagatgaccatgaagtc |
| P1-B4-rev     | gttatccagctgctcaataGCcgcGgctggcaacactacaggat |
| P2-B4-for     | gttatccagctgctcaataGCcgcGgctggcaacactacaggat |
| P1-B5-rev     | gttatccagctgctcaataGCcgcGgctggcaacactacaggat |
| P2-B5-for     | gttatccagctgctcaataGCcgcGgctggcaacactacaggat |
| P1-B6-rev     | gttatccagctgctcaataGCcgcGgctggcaacactacaggat |
| P2-B6-for     | gttatccagctgctcaataGCcgcGgctggcaacactacaggat |
| P1-B7-rev     | gttatccagctgctcaataGCcgcGgctggcaacactacaggat |
| P2-B7-for     | gttatccagctgctcaataGCcgcGgctggcaacactacaggat |
2.2. Protein expression and purification

The expression plasmids harboring the Hpm8 mutants and chimeric HRPKSs were all transformed into *S. cerevisiae* strain BJ5464-NpgA for expression, respectively. For 1 L of yeast culture, the cells were grown at 28°C in YPD media with 1% dextrose for 72 hours. The cells were harvested by centrifugation (4000 rpm, 10 minutes, 4°C), resuspended in 20 mL lysis buffer (50mM NaH$_2$PO$_4$ pH = 8.0, 0.15 M NaCl, 10 mM imidazole) and lysed with sonication on ice. Cellular debris was removed by centrifugation (17000 g, 1 hour, 4°C). Ni-NTA agarose resin was added to the supernatant (2 mL/L of culture) and the solution was rotated at 4°C for at least 2 hours. The protein/resin mixture was loaded into a gravity flow column. Buffer A (50 mM Tris-HCl, pH=7.9, 2 mM EDTA, 2 mM DTT) with increasing concentrations of imidazole (10 mM, 20 mM and 30 mM) was used as washing buffers. The desired proteins were eluted with Buffer A containing 250 mM imidazole. Purified proteins were concentrated and buffered exchanged into Buffer A+10% glycerol, concentrated, aliquoted and flash frozen. Protein concentrations were determined using the Bradford dye-binding assay (Biorad).
Supplementary Table 4. List of enzymes constructed in this work.

| Enzyme name     | Plasmid No. | Expression level (mg/L culture) |
|-----------------|-------------|---------------------------------|
| Hpm8B1          | pZH213      | Not solubly expressed           |
| Hpm8B2          | pZH305      | 1.8                             |
| Hpm8B3          | pZH303      | Not solubly expressed           |
| Hpm8B4          | pZH255      | 1.9                             |
| Hpm8B5          | pZH315      | 1.7                             |
| Hpm8B6          | pZH288      | Not solubly expressed           |
| Hpm8B7          | pZH276      | 0.9                             |
| Hpm8B8          | pZH316      | 1.5                             |
| Hpm8B9          | pZH254      | 1.6                             |
| Hpm8\_Y^{2126}F | pZH327      | 0.8                             |
| Hpm8\_S^{2113}A | pZH330      | 0.38                            |
| Hpm8\_K^{2088}D | pZH329      | 1.3                             |
| Hpm8\_Y^{2118}F | pZH172      | 1.0                             |

2.3. Homology modeling

Homology modeling of the catalytic KRs of both Hpm8 and Rdc5 are performed by using the online server HHpred\(^7\). The best template identified by HHpred for both Hpm8\_cKR
and Rdc5_cKR is EryKR1 (PDB ID 2FR1). Single-template homology models are constructed for both Hpm8_cKR and Rdc5_cKR based on the same template. In the modeled structure, the distance between catalytic Ser and Tyr (4.7 Å in Hpm8 and 4.4 Å in Rdc5) or Tyr and Lys (4.2 Å in Hpm8 and 3.5 Å in Rdc5) are comparable to the distance of Ser-Tyr (4.5 Å) or Tyr-Lys (4.3 Å) in the crystal structure of EryKR1 (SI Fig. 14).

2.4. In vitro assays

For a typical in vitro KR assay, a 100 μL reaction was set up containing 2 μM HRPKS, 2 mM NADPH and 100 mM NaH₂PO₄, pH=7.4. After 6 hour incubation, the reactions were quenched and extracted twice with 99% ethyl acetate (EA)/1% acetic acid (AcOH). The resultant organic extracts were evaporated to dryness, redissolved in methanol, and then analyzed by LC-MS. For the chiral HPLC analysis, the dried organic extracts were dissolved in 2-propanol (IPA). In the in vitro assay for Hpm3, 2 mM chemically synthesized hexaketide SNAC thioester 12 and 2 mM malonyl-CoA were co-incubated with 100 μM Hpm3 for an overnight reaction. The same extraction procedure was performed for this assay as the one for KR assays.

2.5. Heterologous reconstitution

The expression plasmids for HRPKSs were co-transformed with Hpm3 (NRPKS) in S. cerevisiae strain BJ5464-NpgA. 200 μL of the third day culture was extracted with 99% ethyl acetate (EA)/1% acetic acid (AcOH). The resultant organic extracts were evaporated to dryness, redissolved in methanol, and then analyzed by LC-MS.
2.6. HPLC analysis

LC-MS was conducted with a Shimadzu 2010 EV Liquid Chromatography Mass Spectrometer by using both positive and negative electrospray ionization, and a Phenomenex Luna 5µ 2.0 x 100 mm C18 reverse-phase column. Samples were separated on a linear gradient of 5 to 95% or 5 to 40% CH₃CN (vol/vol) in H₂O supplemented with 0.05% (vol/vol) formic acid at a flow rate of 0.1 ml/min. Chiral compound was analyzed by normal phase HPLC (Lux 3µ Cellulose-1, 150×4.60 mm) under different isocratic condition of IPA in n-Hexane (v/v). All the standard chemicals and reaction extracts were all dissolved in IPA for chiral HPLC analysis. The mixture of each pair of chiral standards contains 10 µl of 5 mM each standard.

For the separation by chiral HPLC, the solvent ratios and flow rates for different pairs of chemical standards are listed in Table 5. The difference in the retention time (ΔRT) for each pair of standards is also calculated.

**Supplementary Table 5.** Solvent ratios for chiral HPLC and retention time difference.

| Pair of standards | IPA/hexane% | flow rate v, ml/min | ΔRT     |
|-------------------|-------------|---------------------|---------|
| 2L, 2D            | 15          | 1.0                 | 1.2 min |
| 3L, 3D            | 10          | 0.8                 | 2.3 min |
| 4L, 4D            | 15          | 1.5                 | 1.9 min |
| 5L, 5D            | 15          | 1.0                 | 1.0 min |
| 6L, 6D            | 10          | 0.6                 | 2.8 min |
| 7L, 7D            | 10          | 0.6                 | 2.5 min |
| 8L, 8D            | 10          | 0.5                 | 1.5 min |
2.7. Phylogenetic analysis of HRPKS catalytic KR domains

Besides Hpm8, Rdc5 and PKS4, the sequences of 42 other HRPKSs (Table 6) were retrieved from National Center for Biotechnology Information (NCBI). The catalytic KR domain of each HRPKS was accordingly identified based on the boundary of Hpm8_cKR. The sequence alignment was then conducted with ClustalW\textsuperscript{9}, where the sequence of bacterial ketoreductase actKR\textsuperscript{10,11} from type II PKs pathway was also included as an out-group. The phylogeny reconstruction was performed on MEGA version 5.0\textsuperscript{12} using both the bootstrap minimum evolution method and maximum likelihood method. The evolutionary history was estimated by Minimum Evolution method\textsuperscript{13} and by using the Maximum Likelihood method based on the JTT matrix-based model\textsuperscript{14}. As shown in SI Fig. 19, the phylogenetic analysis of fungal HRPKS KRMs established their phylogenetic relationship that they may co-evolve with their cognate KS domain. While the correlation between sequence and stereochemistry of fungal IPKS KRMs is still implicit due to lack of complete stereochemical data for most of the KRMs.
**Supplementary Table 6.** List of HRPKSs used in the phylogenetic analysis.

| Protein name                        | Strain Name                  | Accession No.   |
|-------------------------------------|------------------------------|-----------------|
| *Alternaria solani* PKSF            | *Alternaria solani*          | BAE80697        |
| *Alternaria solani* PKSN            | *Alternaria solani*          | BAD83684        |
| LovB                                | *Aspergillus Terreus*        | Q9Y8A5          |
| LovF                                | *Aspergillus Terreus*        | AAD34559        |
| PsoA                                | *Aspergillus fumigatus* Af293| ABS87601        |
| ApdA                                | *Aspergillus nidulans* FGSC A4 | XP 681681     |
| EasB_AN2547                         | *Aspergillus nidulans* FGSC A4 | CBF87072       |
| AfoG                                | *Aspergillus nidulans* FGSC A4 | XP 658640     |
| TenS                                | *Beauveria bassiana*         | AM409327        |
| Botryotinia fuckeliana PKS1         | *Botryotinia fuckeliana*     | AAR90237        |
| Botryotinia fuckeliana PKS3         | *Botryotinia fuckeliana*     | AAR90239        |
| Botryotinia fuckeliana PKS4         | *Botryotinia fuckeliana*     | AAR90240        |
| Botryotinia fuckeliana PKS6         | *Botryotinia fuckeliana*     | AAR90242        |
| Botryotinia fuckeliana PKS8         | *Botryotinia fuckeliana*     | AAR90244        |
| Botryotinia fuckeliana PKS11        | *Botryotinia fuckeliana*     | AAR90247        |
| Cochliobolus heterostrophus Fum1    | *Cochliobolus heterostrophus*| AAR90266        |
| Cochliobolus heterostrophus PKS2    | *Cochliobolus heterostrophus*| AAR90257        |
| Cochliobolus heterostrophus PKS3    | *Cochliobolus heterostrophus*| AAR90258        |
| Cochliobolus heterostrophus PKS5    | *Cochliobolus heterostrophus*| AAR90260        |
| Cochliobolus heterostrophus PKS6    | *Cochliobolus heterostrophus*| AAR90261        |
| Cochliobolus heterostrophus PKS8    | *Cochliobolus heterostrophus*| AAR90263        |
| Cochliobolus heterostrophus PKS9    | *Cochliobolus heterostrophus*| AAR90264        |
| Cochliobolus heterostrophus PKS10   | *Cochliobolus heterostrophus*| AAR90265        |
| Cochliobolus heterostrophus PKS12   | *Cochliobolus heterostrophus*| AAR90267        |
| Cochliobolus heterostrophus PKS14   | *Cochliobolus heterostrophus*| AAR90268        |
| Cochliobolus heterostrophus PKS17   | *Cochliobolus heterostrophus*| AAR90271        |
| Gibberella moniliformis PKS1        | *Gibberella moniliformis*    | AAR92208        |
| Gibberella moniliformis PKS2        | *Gibberella moniliformis*    | AAR92208        |
| Gibberella moniliformis PKS5        | *Gibberella moniliformis*    | AAR92212        |
| Gibberella moniliformis PKS6        | *Gibberella moniliformis*    | AAR92213        |
| Gibberella moniliformis PKS7        | *Gibberella moniliformis*    | AAR92214        |
| Gibberella moniliformis PKS8        | *Gibberella moniliformis*    | AAR92215        |
| Gibberella moniliformis PKS9        | *Gibberella moniliformis*    | AAR92216        |
| Gibberella moniliformis PKS10       | *Gibberella moniliformis*    | AAR92217        |
| Gibberella moniliformis PKS13       | *Gibberella moniliformis*    | AAR92220        |
| Gibberella moniliformis PKS14       | *Gibberella moniliformis*    | AAR92221        |
| Gibberella moniliformis PKS15       | *Gibberella moniliformis*    | AAR92222        |
| PKS4                                | *Gibberella zeae*            | ABB90283        |
| Hpm8                                | *Hypomyces subiculosus*      | ACD39758        |
| RdC5                                | *Pochonia chlamydospora*     | ACD39774        |
| Neurospora crassa PKS1              | *Neurospora crassa*          | XP_325868       |
| Neurospora crassa PKS2              | *Neurospora crassa*          | XP_324368       |
| Neurospora crassa PKS3              | *Neurospora crassa*          | XP_324222       |
| Neurospora crassa PKS4              | *Neurospora crassa*          | XP_329445       |
2.8. Compounds syntheses and characterization

**General Synthetic Procedures.** All reactions involving air or moisture sensitive reactants were conducted under a positive pressure of dry argon. All solvents and chemicals were reagent grade and used as supplied unless otherwise stated. For anhydrous reactions, solvents were dried according to the procedures detailed in Perrin and Armarego. Removal of solvent was performed under reduced pressure, below 40 °C, using a Büchi rotary evaporator. Chemical reagents were purchased from Sigma-Aldrich Chemical Company. All reactions and fractions from column chromatography were monitored by thin layer chromatography (TLC). Analytical TLC was done on glass plates (5 × 1.5 cm) precoated (0.25 mm) with silica gel (normal SiO₂, Merck 60 F254). Compounds were visualized by exposure to UV light and by dipping the plates in 1% Ce(SO₄)₂·4H₂O 2.5% (NH₄)Mo₇O₂₄·4H₂O in 10% H₂SO₄ followed by heating on a hot plate. Flash chromatography was performed on silica gel (EM Science, 60Å, 230-400 mesh).

**Spectroscopic Analyses.** Nuclear magnetic resonance (NMR) spectra for 2, 2D, 2L and 9 were obtained on a Bruker 500 MHz spectrometer. ¹H NMR chemical shifts are reported in parts per million (ppm) using the residual proton resonance of solvents as reference: CD₃OD δ 3.30 and CDCl₃ δ 7.26. ¹³C NMR chemical shifts are reported relative to CD₃OD δ 49.0 and CDCl₃ δ 77.0. NMR spectra of the rest compounds were obtained on a Varian Inova 500 MHz and 600 MHz spectrometers. ¹H NMR chemical shifts are reported in parts per million (ppm) using the residual proton resonance of solvents as reference: CDCl₃ δ 7.26, and CD₃OD δ 3.30. ¹³C NMR chemical shifts are
reported relative to CDCl$_3$ δ 77.0, and CD$_3$OD δ 49.0. Infrared spectra (IR) were recorded on a Nicolet Magna 750 or a 20SX FT-IR spectrometer. Film Cast refers to the evaporation of a solution on a NaCl plate. Mass spectra were recorded on a Waters LCT-Premier (high resolution, electron impact ionization (EI)), a Kratos IMS-50 (high resolution, electron impact ionization (EI)), and a ZabSpec IsoMass VG (high resolution. Electrospray (ES)).

The known compound 2 was synthesized by the literature procedures$^{16}$. The main substrate 2, 2, 6-trimethyl-l, 3-dioxin-4-one 13 (95%) was obtained from Sigma-Aldrich. All spectroscopic data and physical properties matched those previously reported.

3-(R)-hydroxybutyric acid 14 ($\geq 98\%$) and 3-(S)-hydroxybutyric acid 15 ($\geq 97\%$) were also purchased from Sigma-Aldrich. 2D and 2L were prepared by combining the free acid, diphenylphosphoryl azide, and the free thiol in DMF/triethylamine. Taking the synthesis of 2D as an example, 14 (104 mg, 1.00 mmol) was dissolved in 10 mL DMF at 0 °C and then treated with diphenylphosphoryl azide (325 μl, 1.50 mmol) and triethylamine (278 μl, 2.00 mmol) for 2 hours with stirring. $N$-acetylcysteamine (HSNAC, 128.4 μl, 1.20 mmol) was added to the solution. The mixture was stirred at
room temperature for additional 3 hours. The reaction was quenched with the addition of 50 ml H2O and extracted twice with ethyl acetate. The organic layer was dried over Na2SO4 and the solvent was removed in vacuo. The residue was purified with silica gel chromatograph to give 98.4 mg of a light yellow oil.

2D: 98.4 mg, light yellow oil, 48% yield. 1H NMR (500 MHz, CDCl3) δ 5.75 (s, 1H, NH), 4.23 (m, 1H, H-2), 3.44 (m, 2H, H-6), 3.03 (m, 2H, H-5), 2.69-2.72 (m, 2H, H-3), 1.95 (s, 3H, H-8), 1.22 (d, 3H, J = 6.30 Hz, H-1); 13C NMR (125 MHz, CDCl3) 199.7, 170.9, 65.3, 52.6, 39.5, 29.1, 23.5, 22.9. IR (CHCl3, cast film) 3295, 3087, 2970, 2929, 1686, 1657, 15552 cm⁻¹; αD25 = -33.8 (c = 0.13, CHCl3); HRMS (ES) m/z calculated for C8H15NSO3Na 228.0670, found 228.0668 [M+Na]+.

2L: 100 mg, light yellow oil, 49% yield. 1H NMR (500 MHz, CDCl3) δ 5.95 (s, 1H, NH), 4.23 (m, 1H, H-2), 3.41 (m, 2H, H-6), 3.01 (m, 2H, H-5), 2.67-2.70 (m, 2H, H-3), 1.93 (s, 3H, H-8), 1.20 (d, 3H, J = 6.30 Hz, H-1); 13C NMR (125 MHz, CDCl3) 199.5, 170.7, 65.2, 52.8, 39.4, 29.0, 23.4, 22.9. IR (CHCl3, cast film) 3295, 3087, 2970, 2929, 1686, 1657, 15552 cm⁻¹; αD25 = 28.0 (c = 0.49, CHCl3); HRMS (ES) m/z calculated for C8H15NSO3Na 228.0670, found 228.0700 [M+Na]+.
Supplementary Scheme 1: Synthesis of triketides 3, 3D and 3L

To a stirred solution of (S)-4-isopropyl-N-acetyl-1, 3-thiazolidine-2-thione (380 mg, 1.87 mmol) in dry dichloromethane (10 mL) was added TiCl$_4$ (1.0 M solution in CH$_2$Cl$_2$, 2.05 mL, 2.05 mmol) at 0 °C under Ar. The reaction mixture was stirred for 5 min and then cooled to -78 °C. A solution of DIPEA (291 mg, 2.24 mmol) in dichloromethane (2 mL) was added. The reaction mixture was stirred at -78 °C for 2 h. A solution of aldehyde 16 (333 mg, 1.65 mmol)$^6$ was added to the reaction mixture, which was then stirred for 15 min at -78 °C. The reaction was quenched with 10 mL saturated ammonium chloride. The layers were separated and the aqueous layer was extracted with EtOAc (3x10 mL). The combined organic layers were washed with brine (20 mL) and dried over Na$_2$SO$_4$. 
The solvent was removed in vacuo and the residue was purified using flash column chromatography (1:6 EtOAc/hexanes) to give two diastereomers 17 (98.0 mg, 45% yield) and 18 (40 mg, 18% yield) as yellow oils.

**17**: 98.0 mg, yellow oil, 45% yield. IR (CHCl₃, cast film) 3447, 2961, 2932, 2873, 1694, 1467 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.17 (ddd, 1H, J = 7.71, 6.33, 0.92 Hz, H-9), 4.12 (m, 1H, H-4), 3.63 (dd, 1H, J = 17.7, 2.38 Hz, H-5), 3.53 (dd, 1H, J = 11.5, 7.98 Hz, H-8), 3.12 (dd, 1H, J = 17.7, 9.44 Hz, H-5), 3.03 (dd, 1H, J = 11.5, 1.01 Hz, H-8), 2.35 (ABX₅, 1H, J = 6.78 Hz, H-10), 1.58 - 1.35 (m, 4H, H-2, H-3), 1.05 (d, 3H, J = 6.78 Hz, H-11), 0.98 (d, 3H, J = 6.97 Hz, H-11), 0.93 (t, 3H, J = 7.15Hz, H-1); ¹³C NMR (125 MHz, CDCl₃) 203.1, 173.3, 71.4, 67.7, 45.5, 38.5, 30.8, 30.6, 19.1, 18.7, 17.8, 14.0; [α]₂⁵⁺ = 269 (c = 0.480, CHCl₃); HRMS (ES) m/z calculated for C₁₂H₂₁NS₂O₂Na 298.0906, found 298.0907 [M+Na]⁺.

**18**: 40.0 mg, yellow oil, 18% yield. IR (CHCl₃, cast film) 3452, 2961, 2931, 2873, 1697, 1467 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.17 (ddd, 1H, J = 7.61, 6.42, 1.01 Hz, H-9), 4.03 (m, 1H, H-4), 3.51 (dd, 1H, J = 11.6, 7.98 Hz, H-8), 3.43 (dd, 1H, J = 17.4, 9.35 Hz, H-5), 3.32 (dd, 1H, J = 17.4, 2.65 Hz, H-5), 3.03 (dd, 1H, J = 11.6, 1.10 Hz, H-8), 2.35 (ABX₅, 1H, J = 6.78 Hz, H-10), 1.58 - 1.33 (m, 4H, H-2, H-3), 1.05 (d, 3H, J = 6.88 Hz, H-11), 0.98 (d, 3H, J = 6.77 Hz, H-11), 0.92 (t, 3H, J = 6.97 Hz, H-1); ¹³C NMR (125 MHz, CDCl₃) 203.1, 173.8, 71.4, 68.2, 45.2, 38.8, 30.8, 30.6, 19.1, 18.7, 17.8, 14.0; [α]₂⁵⁺ = 233 (c = 0.360, CHCl₃); HRMS (ES) m/z calculated for C₁₂H₂₁NS₂O₂Na 298.0906, found 298.0907 [M+Na]⁺.
3L: To a stirred solution of 17 (56.2 mg, 0.204 mmol) in 5 mL MeCN was added K$_2$CO$_3$ (109 mg, 0.715 mmol) and N-acetylcysteamine (37.8 mg, 0.196 mmol). The reaction mixture was stirred until the yellow color disappeared. The reaction was quenched with 5 mL saturated ammonium chloride. The layers were separated and the aqueous layer was extracted with EtOAc (3x10 mL). The combined organic layers were washed with brine (20 mL) and dried over Na$_2$SO$_4$. The solvent was removed *in vacuo* and the residue was purified using flash column chromatography (EtOAc) to give 3L (32.0 mg, 67% yield) as a white solid. IR (CHCl$_3$, cast film) 3295, 3085, 2959, 2932, 2873, 1687, 1658, 1553 cm$^{-1}$; $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 6.01 (s, 1H, NH), 4.05 (m, 1H, H-4), 3.45 (m, 1H, H-8), 3.03 (m, 2H, H-3), 2.80 (d, 1H, $J = 4.40$ Hz, OH), 2.73 (dd, 1H, $J = 15.4$, 3.49 Hz, H-5), 2.67 (dd, 1H, $J = 15.3$, 8.62 Hz, H-5), 1.96 (s, 3H, H-10), 1.53 - 1.33 (m, 4H, H-2, H-3), 0.92 (t, 3H, $J = 7.09$ Hz, H-1); $^{13}$C NMR (125 MHz, CDCl$_3$) 199.5, 170.5, 68.5, 51.1, 39.3, 38.9, 28.8, 23.2, 18.6, 13.9; $\alpha$$_D^{25}$ = 19.1 (c = 0.640, CHCl$_3$); HRMS (ES) m/z calculated for C$_{10}$H$_{19}$NSO$_3$Na 256.0978, found 256.0979 [M+Na]$^+$.  

3D: 54.6 mg, white solid, yield 66%. IR (CHCl$_3$, cast film) 3290, 3082, 2959, 2933, 2873, 1657, 1553 cm$^{-1}$; $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 6.20 (s, 1H, NH), 4.04 (m, 1H, H-4),
3.43 (m, 1H, H-8), 3.03 (m, 3H, H-3, OH), 2.71 (dd, 1H, J = 15.2, 3.57 Hz, H-5), 2.63 (dd, 1H, J = 15.0, 7.20 Hz, H-5), 1.93 (s, 3H, H-10), 1.51 - 1.30 (m, 4H, H-2, H-3), 0.90 (t, 3H, J = 6.96 Hz, H-1); 13C NMR (125 MHz, CDCl3) 199.3, 170.6, 68.5, 51.2, 39.2, 38.9, 28.8, 23.2, 18.6, 13.9; \( \alpha_D^{25} = -14.8 \) (c = 1.10, CHCl3); HRMS (ES) m/z calculated for C\(_{10}\)H\(_{19}\)NSO\(_3\)Na 256.0978, found 256.0978 [M+Na]\(^+\).

3: To a stirred solution of 3L (30.0 mg, 0.129 mmol) in 5 mL CH\(_2\)Cl\(_2\) was added Dess-Martin periodinane (79 mg, 0.186 mmol). The resulting solution was stirred at 25 °C for 2 h. The reaction was quenched by addition of 5 mL of 1:1 10% Na\(_2\)S\(_2\)O\(_3\) : saturated aqueous NaHCO\(_3\). The layers were separated and the aqueous layer was extracted with EtOAc (3x10 mL). The combined organic layers were washed with brine (20 mL) and dried over Na\(_2\)SO\(_4\). The solvent was removed \textit{in vacuo} and the residue was purified using flash column chromatography (EtOAc) to give 3 (8.00 mg, 27% yield, keto:enol = 3:1) as a white solid. IR (CHCl\(_3\), cast film) 3283, 3103, 2958, 2933, 2876, 1716, 1684, 1637, 1562 cm\(^{-1}\); 1H NMR (500 MHz, CDCl3) \( \delta \) 5.95 (s, 1H, NH), 5.49 (s, 0.25H, enol-H-5), 3.71 (s, 1.5H, keto-H-5), 3.48 (m, 2H, H-8), 3.11 (m, 2H, H-7), 2.53 (t, 1.5H, J = 7.24 Hz, keto-H-3), 2.18 (m, 0.5H, enol-H-3), 2.00 (m, 3H, H-10), 1.65 (m, 2H, H-2), 0.94 (m, 3H, H-1); 13C NMR (125 MHz, CDCl3) 202.1, 194.3, 192.4, 177.4, 170.6, 170.4, 99.3, 57.2, 45.3, 39.9, 39.3, 36.8, 29.2, 27.8, 23.3, 23.2, 19.6, 16.9, 13.6, 13.5; HRMS (ES) m/z calculated for C\(_{10}\)H\(_{17}\)NSO\(_3\)Na 254.0821, found 254.0821 [M+Na]\(^+\).
Supplementary Scheme 2: Synthesis of tetraketides 6, 6L, 6D.

Compounds 20 and 21 were synthesized from 1-hexanal by the method for synthesizing 17 and 18.

20: 240 mg, yellow oil, 50% yield. IR (CHCl₃, cast film) 3441, 2959, 2930, 2858, 1690, 1466 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.18 (ddd, 1H, J = 7.43, 6.32, 0.91 Hz, H-11), 4.15 (m, 1H, H-6), 3.66 (dd, 1H, J = 17.7, 2.39 Hz, H-7), 3.55 (dd, 1H, J = 11.5, 7.89 Hz, H-10), 3.15 (dd, 1H, J = 17.7, 9.36 Hz, H-7), 3.05 (dd, 1H, J = 11.6, 1.10 Hz, H-10), 2.79 (s, 1H, OH), 2.38 (ABX₆, 1H, J = 6.78 Hz, H-12), 1.62 - 1.30 (m, 8H, H-2, H-3, H-4, H-5), 1.09 (d, 3H, J = 6.79 Hz, H-13), 1.02 (d, 3H, J = 6.97 Hz, H-13), 0.86 (t, 3H, J = 6.79
$^{13}$C NMR (125 MHz, CDCl$_3$) 203.1, 173.4, 71.4, 68.1, 45.6, 36.4, 31.8, 30.9, 30.6, 25.2, 22.6, 19.1, 17.9, 14.1; $\alpha_{D}^{25} = 233.76$ (c = 1.45, CHCl$_3$); HRMS (ES) $m/z$ calculated for C$_{14}$H$_{25}$NS$_2$O$_2$Na 326.1219, found 326.1225 [M+Na$^+$].

21: 110 mg, yellow oil, 23% yield. IR (CHCl$_3$, cast film) 3450, 2959, 2930, 2858, 1687, 1466 cm$^{-1}$; $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 5.18 (ddd, 1H, $J = 7.61, 6.33, 1.10$ Hz, H-11), 4.03 (m, 1H, H-6), 3.52 (dd, 1H, $J = 11.6, 7.98$ Hz, H-10), 3.45 (dd, 1H, $J = 17.4, 9.35$ Hz, H-7), 3.32 (dd, 1H, $J = 17.4, 2.66$ Hz, H-7), 3.18 (s, 1H, OH), 3.04 (dd, 1H, $J = 11.6, 1.19$ Hz, H-10), 2.36 (ABX$_6$, 1H, $J = 6.79$ Hz, H-12), 1.58 - 1.25 (m, 8H, H-2, H-3, H-4, H-5), 1.07 (d, 3H, $J = 6.78$ Hz, H-13), 0.98 (d, 3H, $J = 6.97$ Hz, H-13), 0.86 (t, 3H, $J = 6.93$ Hz, H-1); $^{13}$C NMR (125 MHz, CDCl$_3$) 203.2, 173.9, 71.4, 68.5, 45.2, 36.6, 31.8, 30.8, 30.6, 25.2, 22.6, 19.1, 17.9, 14.1; $\alpha_{D}^{25} = 239.47$ (c = 0.700, CHCl$_3$); HRMS (ES) $m/z$ calculated for C$_{14}$H$_{25}$NS$_2$O$_2$Na 326.1219, found 326.1225 [M+Na$^+$].

Compound 6L was synthesized from 20 by the method for synthesizing 3L.

6L: 80.0 mg, white solid, 66% yield. IR (CHCl$_3$, cast film) 3297, 3086, 2955, 2931, 2859, 1688, 1658, 1553 cm$^{-1}$; $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 6.18 (s, 1H, NH), 4.02 (m, 1H, H-6), 3.39 (m, 1H, H-10), 3.10 (s, 1H, OH), 3.00 (m, 2H, H-9), 2.68 (dd, 1H, $J = 15.2, 3.67$ Hz, H-7), 2.64 (dd, 1H, $J = 15.2, 8.12$ Hz, H-7), 1.92 (s, 3H, H-12), 1.53 - 1.23 (m, 8H, H-2, H-3, H-4, H-5), 0.84 (t, 3H, $J = 6.87$ Hz, H-1); $^{13}$C NMR (125 MHz, CDCl$_3$) 199.3, 170.7, 68.7, 51.1, 39.2, 36.7, 31.6, 28.7, 25.1, 23.1, 22.5, 13.9; $\alpha_{D}^{25} = 12.31$ (c = 3.01,
CHCl₃); HRMS (ES) m/z calculated for C₁₂H₂₃NSO₃Na 284.1291, found 284.1295 [M+Na]+.

Compound 6D was synthesized from 21 by the method for synthesizing 3L.

6D: 56.7 mg, white solid, 80% yield. IR (CHCl₃, cast film) 3295, 3084, 2955, 2930, 2859, 1687, 1658, 1552 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 6.18 (s, 1H, NH), 4.03 (m, 1H, H-6), 3.42 (m, 1H, H-10), 3.02 (m, 2H, H-9), 2.95 (s, 1H, OH), 2.72 (dd, 1H, J = 15.3, 3.57 Hz, H-7), 2.66 (dd, 1H, J = 15.2, 8.53 Hz, H-7), 1.95 (s, 3H, H-12), 1.53 - 1.23 (m, 8H, H-2, H-3, H-4, H-5), 0.86 (t, 3H, J = 6.88 Hz, H-1); ¹³C NMR (125 MHz, CDCl₃) 199.4, 170.6, 68.8, 51.1, 39.2, 36.8, 31.6, 28.8, 25.1, 23.2, 22.6, 14.0; αD₂⁵ = -20.09 (c = 0.43, CHCl₃); HRMS (ES) m/z calculated for C₁₂H₂₃NSO₃Na 284.1291, found 284.1293 [M+Na]+.

Compound 6 was synthesized from 6L by the method for synthesizing 3.

6: 8.2 mg, white solid, 46% yield, keto:enol = 1.85:1. IR (CHCl₃, cast film) 3283, 3103, 2958, 2952, 2931, 2867, 1717, 1685, 1637, 1563 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ
5.92 (s, 1H, NH), 5.46 (s, 0.35H, enol-H-7), 3.69 (s, 1.3H, keto-H-7), 3.46 (m, 2H, H-10),
3.09 (m, 2H, H-9), 2.52 (t, 1.3H, J = 7.34 Hz, keto-H-5), 2.17 (t, 0.7H, J = 7.61 Hz, enol-
H-5), 1.96 (m, 3H, H-12), 1.59 (m, 2H, H-4), 1.30 (m, 4H, H-2, H-3), 0.89 (m, 3H, H-1);
$^{13}$C NMR (125 MHz, CDCl$_3$) 202.3, 194.3, 192.4, 177.7, 170.5, 170.4, 99.1, 57.2, 43.4,
39.9, 39.2, 34.9, 31.3, 31.1, 29.2, 27.8, 25.9, 23.2, 23.1, 22.4, 22.3, 13.9, 13.8;
HRMS (ES) m/z calculated for C$_{12}$H$_{21}$NSO$_3$Na 282.1134, found 282.1137 [M+Na]$^+$.

Supplementary Scheme 3: Synthesis of tetraketides 5, 5L and 5D.

Compounds 23 and 24 were synthesized from hex-2-enal by the method for synthesizing
17 and 18.
23: 112 mg, yellow oil, 50% yield. IR (CHCl₃, cast film) 3426, 2961, 2872, 1695, 1465 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.75 (m, 1H, H-5), 5.56 (ddt, 1H, J = 15.4, 6.42, 1.47 Hz, H-5), 5.17 (ddd, 1H, J = 7.43, 6.60, 0.83 Hz, H-11), 4.64 (m, 1H, H-6), 3.63 (dd, 1H, J = 17.5, 2.94 Hz, H-7), 3.51 (dd, 1H, J = 11.5, 7.88 Hz, H-10), 3.33 (dd, 1H, J = 17.6, 8.90 Hz, H-7), 3.05 (dd, 1H, J = 11.5, 0.92 Hz, H-10), 2.38 (ABX₆, 1H, J = 6.79 Hz, H-12), 2.15 (m, 2H, H-3), 1.43 (AB₂X₃, 1H, J = 7.43 Hz, H-2), 1.09 (d, 3H, J = 6.88 Hz, H-13), 1.01 (d, 3H, J = 6.97 Hz, H-13), 0.92 (t, 3H, J = 7.42 Hz, H-1); ¹³C NMR (125 MHz, CDCl₃) 202.9, 172.6, 132.5, 130.6, 71.4, 68.8, 45.5, 34.3, 30.8, 30.6, 22.2, 19.1, 17.8, 13.7; αD²⁵ = 293 (c = 0.470, CHCl₃); HRMS (ES) m/z calculated for C₁₄H₂₃NS₂O₃SiNa 324.1062, found 324.1063 [M+Na]⁺.

24: 33.0 mg, yellow oil, 14% yield. IR (CHCl₃, cast film) 3427, 2961, 2872, 1694, 1465 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.76 (m, 1H, H-5), 5.55 (ddt, 1H, J = 15.4, 6.42, 1.37 Hz, H-5), 5.20 (ddd, 1H, J = 7.43, 6.33, 1.1 Hz, H-11), 4.56 (m, 1H, H-6), 3.63 (dd, 1H, J = 17.3, 8.99 Hz, H-7), 3.53 (dd, 1H, J = 11.5, 7.98 Hz, H-10), 3.38 (dd, 1H, J = 17.3, 3.21 Hz, H-7), 3.06 (dd, 1H, J = 11.5, 1.19 Hz, H-10), 2.38 (ABX₆, 1H, J = 6.88 Hz, H-12), 2.15 (m, 2H, H-3), 1.43 (AB₂X₃, 1H, J = 7.25 Hz, H-2), 1.09 (d, 3H, J = 6.78 Hz, H-13), 1.01 (d, 3H, J = 6.87 Hz, H-13), 0.93 (t, 3H, J = 7.33 Hz, H-1); ¹³C NMR (125 MHz, CDCl₃) 203.1, 173.1, 132.5, 130.7, 71.4, 69.3, 45.3, 34.3, 30.8, 30.6, 22.2, 19.1, 17.8, 13.7; αD²⁵ = 257 (c = 0.500, CHCl₃); HRMS (ES) m/z calculated for C₁₄H₂₃NS₂O₃SiNa 324.1062, found 324.1063 [M+Na]⁺.
Compound 5L was synthesized from 23 by the method for synthesizing 3L.

5L: 80.0 mg, yellow oil, 61% yield. IR (CHCl₃, cast film) 3295, 3088, 2958, 2930, 2873, 1687, 1657, 1553 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 6.06 (s, 1H, NH), 5.67 (m, 1H, H-4), 5.45 (m, 1H, H-5), 4.52 (m, 1H, H-6), 3.40 (m, 2H, H-10), 3.04 (m, 2H, H-9), 2.82 (s, 1H, OH), 2.75 (m, 2H, H-7), 1.97 (m, 2H, H-3), 1.95 (s, 3H, H-12), 1.37 (AB₂X₃, 1H, J = 7.33 Hz, H-2), 0.87 (t, 3H, J = 7.43 Hz, H-1); ¹³C NMR (125 MHz, CDCl₃) 198.6, 170.6, 132.8, 130.6, 69.6, 51.2, 39.3, 34.2, 28.7, 23.1, 22.1, 13.6; [α]D²⁵ = 14.3 (c = 0.430, CHCl₃); HRMS (ES) m/z calculated for C₁₂H₂₁NSO₃Na 282.1134, found 282.1136 [M+Na]⁺.

Compound 5D was synthesized from 24 by the method for synthesizing 3L.

5D: 52.0 mg, yellow oil, 74% yield. IR (CHCl₃, cast film) 3296, 3087, 2958, 2929, 2872, 1687, 1658, 1552 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 6.06 (s, 1H, NH), 5.67 (m, 1H, H-4), 5.45 (m, 1H, H-5), 4.52 (m, 1H, H-6), 3.40 (m, 2H, H-10), 3.04 (m, 2H, H-9), 2.87 (s, 1H, OH), 2.75 (m, 2H, H-7), 1.97 (m, 2H, H-3), 1.95 (s, 3H, H-12), 1.36 (AB₂X₃, 1H, J = 7.52 Hz, H-2), 0.87 (t, 3H, J = 7.45 Hz, H-1); ¹³C NMR (125 MHz, CDCl₃) 198.6, 170.6, 132.8, 130.6, 69.6, 51.2, 39.3, 34.2, 28.7, 23.1, 22.1, 13.6; [α]D²⁵ = -11.3 (c = 0.390, CHCl₃); HRMS (ES) m/z calculated for C₁₂H₂₁NSO₃Na 282.1134, found 282.1136 [M+Na]⁺.
Compound 5 was synthesized from 5L by the method for synthesizing 3L.

5: 18.0 mg, white solid, 60% yield, keto:enol = 1:5.6. IR (CHCl₃, cast film) 3298, 3078, 2958, 2956, 2918, 2870, 1650, 1597, 1556 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 6.90 (dt, 0.14H, J = 15.8, 6.87 Hz, keto-H-4), 6.75 (dt, 0.86H, J = 15.4, 7.25 Hz, enol-H-4), 6.15 (dt, 0.14H, J = 15.9, 1.56 Hz, keto-H-5), 6.08 (s, 1H, NH), 5.72 (dd, 0.86H, J = 15.4, 1.46 Hz, enol-H-5), 5.40 (s, 0.85H, enol-H-7), 3.82 (s, 0.3H, keto-H-7), 3.48 (m, 2H, H-10), 3.09 (m, 2H, H-9), 2.18 (m, 2H, H-3), 1.97 (s, 3H, H-12), 1.46 (m, 2H, H-2), 0.98 (t, 3H, J = 6.24 Hz, H-1); ¹³C NMR (125 MHz, CDCl₃) 194.5, 192.6, 191.6, 170.5, 170.4, 167.5, 150.8, 143.9, 129.6, 123.9, 99.7, 54.8, 39.9, 39.2, 34.8, 34.6, 29.2, 27.8, 23.2, 23.1, 21.6, 21.2, 13.7; HRMS (ES) m/z calculated for C₁₂H₁₉NSO₃Na 280.0978, found 280.0980 [M+Na]⁺.
Supplementary Scheme 4: Synthesis of tetraketides 4, 4D, 4L.

Compounds 26 and 27 were synthesized from 25 by the method for synthesizing 17 and 18.

26: 190 mg, yellow oil, 51% yield. IR (CHCl₃, cast film) 3452, 2959, 2928, 2894, 2856, 1695, 1471 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.74 (m, 1H, H-5), 5.55 (ddt, 1H, J = 15.5, 6.22, 1.15 Hz, H-5), 5.15 (ddd, 1H, J = 7.51, 6.59, 0.92 Hz, H-11), 4.64 (m, 1H, H-6), 3.83 (AB₂X₃, 1H, J = 6.04 Hz, H-2), 3.55 (dd, 1H, J = 17.6, 2.93 Hz, H-7), 3.51 (dd, 1H, J = 11.5, 7.97 Hz, H-10), 3.30 (dd, 1H, J = 17.6, 9.07 Hz, H-7), 3.05 (dd, 1H, J = 11.5, 1.01 Hz, H-10), 2.38 (m, 1H, H-3), 2.17 (m, 2H, H-3, H-12), 1.11 (d, 3H, J = 6.04 Hz, H-1), 1.06 (d, 3H, J = 6.87 Hz, H-13), 0.98 (d, 3H, J = 6.96 Hz, H-13), 0.88 (s, 9H,
Si-C(CH$_3$)$_3$), 0.05 (s, 6H, SiCH$_3$); $^{13}$C NMR (125 MHz, CDCl$_3$) 202.8, 172.5, 132.6, 129.1, 71.4, 68.7, 68.3, 45.4, 42.6, 30.8, 30.6, 25.8, 23.5, 19.1, 18.1, 17.8, -4.49, -4.64; $\alpha^D$ = 253 (c = 0.690, CHCl$_3$); HRMS (ES) $m/z$ calculated for C$_{20}$H$_{37}$NS$_2$O$_3$SiNa 454.1876, found 454.1878 [M+Na]$^+$. 

27: 90.0 mg, yellow oil, 24% yield. IR (CHCl$_3$, cast film) 3449, 2928, 2894, 2856, 1695, 1471 cm$^{-1}$; $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 5.76 (m, 1H, H-5), 5.58 (ddt, 1H, $J$ = 15.5, 6.14, 1.28 Hz, H-5), 5.20 (ddd, 1H, $J$ = 7.61, 6.24, 1.10 Hz, H-11), 4.56 (m, 1H, H-6), 3.86 (AB$_2$X$_3$, 1H, $J$ = 6.05 Hz, H-2), 3.65 (dd, 1H, $J$ = 17.3, 9.05 Hz, H-7), 3.54 (dd, 1H, $J$ = 11.5, 7.97 Hz, H-10), 3.38 (dd, 1H, $J$ = 17.3, 3.21 Hz, H-7), 3.05 (dd, 1H, $J$ = 11.5, 1.19 Hz, H-10), 2.38 (m, 1H, H-3), 2.17 (m, 2H, H-3, H-12), 1.18 (d, 3H, $J$ = 6.06 Hz, H-1), 1.05 (d, 3H, $J$ = 6.79 Hz, H-13), 1.00 (d, 3H, $J$ = 6.96 Hz, H-13), 0.88 (s, 9H, Si-C(CH$_3$)$_3$), 0.087 (s, 6H, SiCH$_3$); $^{13}$C NMR (125 MHz, CDCl$_3$) 203.0, 173.0, 132.7, 129.1, 71.4, 69.1, 68.4, 45.2, 42.6, 30.8, 30.6, 25.9, 23.5, 19.1, 18.2, 17.8, -4.4, -4.6; $\alpha^D$ = 197 (c = 0.290, CHCl$_3$); HRMS (ES) $m/z$ calculated for C$_{20}$H$_{37}$NS$_2$O$_3$SiNa 454.1876, found 454.1882 [M+Na]$^+$. 

Compound 28 was synthesized from 26 by the method for synthesizing 3L.

28: 196 mg, white solid, 77% yield. IR (CHCl$_3$, cast film) 3290, 2956, 2929, 2897, 2857, 1689, 1657 cm$^{-1}$; $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 5.80 (s, 1H, NH), 5.73 (m, 1H, H-4), 5.50 (ddt, 1H, $J$ = 15.5, 6.50, 1.28 Hz, H-5), 4.56 (m, 1H, H-6), 3.82 (AB$_2$X$_3$, 1H, $J$ = 6.04 Hz, H-2), 3.45 (m, 2H, H-10), 3.04 (m, 2H, H-9), 2.78 (m, 2H, H-7), 2.48 (s, 1H,
OH), 2.15 (m, 2H, H-3), 1.97 (s, 3H, H-12), 1.10 (d, 3H, J = 6.05 Hz, H-1), 0.88 (s, 9H, Si-C(CH₃)₃), 0.036 (s, 3H, SiCH₃), 0.032 (s, 3H, SiCH₃); ¹³C NMR (125 MHz, CDCl₃) 198.2, 170.7, 132.7, 129.1, 69.4, 68.2, 51.1, 42.4, 39.1, 28.7, 25.8, 23.3, 23.0, 18.0, -4.6, -4.8; αD²⁵ = 10.3 (c = 0.130, CHCl₃); HRMS (ES) m/z calculated for C₁₈H₃₅NSO₄SiNa 412.1948, found 412.1944 [M+Na]⁺.

Compound 29 was synthesized from 27 by the method for synthesizing 3L.

29: 37.0 mg, white solid, 70% yield. IR (CHCl₃, cast film) 3298, 2956, 2929, 2895, 2856, 1686, 1657 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.95 (s, 1H, NH), 5.73 (m, 1H, H-4), 5.50 (ddt, 1H, J = 15.4, 6.41, 1.19 Hz, H-5), 4.54 (m, 1H, H-6), 3.82 (AB₂X₃, 1H, J = 6.04 Hz, H-2), 3.45 (m, 2H, H-10), 3.04 (m, 2H, H-9), 2.76 (m, 2H, H-7), 2.71 (s, 1H, OH), 2.15 (m, 2H, H-3), 1.95 (s, 3H, H-12), 1.09 (d, 3H, J = 6.24 Hz, H-1), 0.88 (s, 9H, Si-C(CH₃)₃), 0.026 (s, 3H, SiCH₃), 0.021 (s, 3H, SiCH₃); ¹³C NMR (125 MHz, CDCl₃) 198.7, 170.5, 132.5, 129.5, 69.5, 68.2, 51.0, 42.5, 39.3, 28.8, 25.9, 23.5, 23.2, 18.2, -4.5, -4.7; αD²⁵ = -3.67 (c = 0.180, CHCl₃); HRMS (ES) m/z calculated for C₁₈H₃₅NSO₄SiNa 412.1948, found 412.1949 [M+Na]⁺.

4L: To a flask containing 28 (0.133 mmol) was added 5 mL of a solution of 3:3:1 AcOH/H₂O/THF. The resulting solution was stirred at 25 °C for 12 h. The solvent was
removed in vacuo and the residue was purified using flash column chromatography (EtOAc) to give 4L (6.0 mg, yield 95%) as a white solid. IR (CHCl₃, cast film) 3300, 3094, 2965, 2919, 1687, 1658, 1555 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 6.03 (s, 1H, NH), 5.76 (m, 1H, H-4), 5.60 (ddt, 1H, J = 15.5, 6.05, 1.19 Hz, H-5), 4.57 (m, 1H, H-6), 3.82 (m, 1H, H-2), 3.44 (q, 2H, J = 6.23 Hz, H-10), 3.04 (td, 2H, J = 6.06, 1.93, H-9), 2.87 (s, 1H, OH), 2.81 (m, 2H, H-7), 2.30 – 2.10 (m, 2H, H-3), 1.97 (s, 3H, H-12), 1.20 (d, 3H, J = 6.14 Hz, H-1); ¹³C NMR (125 MHz, CDCl₃) 198.6, 170.6, 134.0, 128.5, 69.4, 67.0, 50.9, 42.0, 39.2, 29.1, 23.2, 23.0; ¹H D₂O = 12.1 (c = 0.140, CHCl₃); HRMS (ES) m/z calculated for C₁₂H₂₁NSO₄Na 298.1082, found 298.1083 [M+Na]⁺.

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\text{Compound 4D was synthesized from 29 by the method for synthesizing 4L.}
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4D: 8.00 mg, white solid, 94% yield. IR (CHCl₃, cast film) 3296, 3094, 2967, 2925, 1687, 1658, 1555 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 6.00 (s, 1H, NH), 5.76 (m, 1H, H-4), 5.60 (ddt, 1H, J = 15.5, 6.33, 1.12 Hz, H-5), 4.58 (m, 1H, H-6), 3.82 (m, 1H, H-2), 3.44 (m, 2H, H-10), 3.04 (m, 2H, H-9), 2.87 (s, 1H, OH), 2.82 (m, 2H, H-7), 2.30 – 2.10 (m, 2H, H-3), 1.97 (s, 3H, H-12), 1.20 (d, 3H, J = 6.24 Hz, H-1); ¹³C NMR (125 MHz, CDCl₃) 198.5, 170.6, 134.1, 128.7, 69.6, 67.0, 51.0, 42.0, 39.2, 29.1, 23.2, 23.0; ¹H D₂O = 31.3 (c = 0.310, CHCl₃); HRMS (ES) m/z calculated for C₁₂H₂₁NSO₄Na 298.1082, found 298.1083 [M+Na]⁺.
Compound 30 was synthesized from 28 by the method for synthesizing 3.

30: 21.0 mg, white solid, 60% yield, keto:enol = 3:2. IR (CHCl₃, cast film) 3287, 3079, 2956, 2930, 2857, 1724, 1656, 1623, 1553 cm⁻¹; ℎ NMR (500 MHz, CDCl₃) δ 5.90 (s, 1H, NH), 5.49 (s, 0.4H, enol-H-5), 4.30 (m, 0.6H, keto-H-2), 4.18 (m, 0.4H, enol-H-2), 3.78 (d, 0.6H, J = 15.5 Hz, keto-H-5), 3.72 (d, 0.6H, J = 15.5 Hz, keto-H-5), 3.48 (m, 2H, H-8), 3.09 (m, 2H, H-7), 2.70 (dd, 0.6H, J = 15.1, 7.25 Hz, keto-H-3), 2.53 (dd, 0.6H, J = 15.1, 4.67Hz, keto-H-3), 2.24 (d, 0.8H, J = 6.24 Hz, enol-H-3), 1.98 (s, 1.8H, keto-H-10), 1.97 (s, 1.2H, enol-H-10), 1.19 (m, 3H, H-1), 0.88 – 0.89 (m, 9H, Si-C(CH₃)₃), 0.11 – 0.00 (m, 6H, SiCH₃); ℏ C NMR (125 MHz, CDCl₃) 201.4, 194.3, 192.2, 174.4, 170.5, 170.3, 101.3, 66.1, 65.4, 58.6, 52.6, 45.4, 39.9, 39.2, 29.1, 27.7, 25.8, 25.7, 24.1, 23.9, 23.2, 23.1, 18.0, 17.9, -4.5, -4.6, -4.9, -5.1; HRMS (ES) m/z calculated for C₁₆H₃₂NSO₄SiNa 384.1635, found 385.1635 [M+Na]⁺.

Compound 4 was synthesized from 30 by the method for synthesizing 4L.

4: 18.0 mg, white solid, 95% yield, keto:enol = 2:3. IR (CHCl₃, cast film) 3296, 3086, 2969, 2930, 1657, 1583 cm⁻¹; ℎ NMR (500 MHz, CDCl₃) δ 6.95 (dt, 0.4H, J = 15.9, 7.34 Hz, keto-H-4), 6.78 (dt, 0.6H, J = 15.2, 7.52 Hz, enol-H-4), 6.22 (dt, 0.4H, J = 15.9, 1.37 Hz, keto-H-5), 6.04 (s, 0.4H, NHH) 5.99 (s, 0.6H, NH), 5.82 (d, 0.6H, J = 15.5 Hz, enol-H-5), 5.46 (s, 0.6H, enol-H-7), 3.95 (m, 1H, H-2), 3.86 (s, 0.8H, keto-H-7), 3.48 (m,
2H, H-10), 3.09 (m, 2H, H-9), 2.40 (m, 2H, H-3), 1.97 (s, 1.8H, enol-H-12), 1.97 (s, 1.2H, keto-H-12), 1.25 (d, 1.2H, J = 6.24 Hz, keto-H-1), 1.23 (d, 1.8H, J = 6.23 Hz, enol-H-1); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) 194.8, 192.6, 191.5, 170.6, 170.5, 167.3, 147.1, 139.6, 131.8, 126.6, 100.3, 67.1, 66.8, 55.1, 42.6, 42.3, 40.0, 39.2, 29.5, 28.1, 23.6, 23.4, 23.4, 23.3; HRMS (ES) m/z calculated for C\(_{12}\)H\(_{19}\)NSO\(_4\)Na 269.0927, found 269.0929 [M+Na]\(^+\).

Supplementary Scheme 5: Synthesis of pentaketides 7, 7L and 7D.

Compounds 32 and 33 were synthesized from 31 by the method for synthesizing 17 and 18.
32: 136 mg, yellow oil, 49% yield. IR (CHCl₃, cast film) 3437, 2958, 2927, 2857, 1696, 1467 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.15 (ddd, 1H, J = 7.68, 6.23, 1.01 Hz, H-13), 4.11 (m, 1H, H-8), 3.61 (dd, 1H, J = 17.7, 2.48 Hz, H-9), 3.51 (dd, 1H, J = 11.5, 7.89 Hz, H-12), 3.11 (dd, 1H, J = 17.7, 9.45 Hz, H-9), 3.02 (dd, 1H, J = 11.5, 1.01 Hz, H-12), 2.34 (m, 1H, H-14), 1.58 - 1.125 (m, 12H, H-2, H-3, H-4, H-5, H-6, H-7), 1.05 (d, 3H, J = 6.79 Hz, H-15), 0.98 (d, 3H, J = 6.97 Hz, H-15), 0.85 (d, 3H, J = 6.88 Hz, H-1); ¹³C NMR (125 MHz, CDCl₃) 203.0, 173.3, 71.4, 68.0, 45.5, 36.4, 31.8, 30.9, 30.6, 29.5, 29.2, 25.5, 22.6, 19.1, 17.8, 14.1; [α]₂⁵D = 279 (c = 0.470, CHCl₃); HRMS (ES) m/z calculated for C₁₆H₂₉NS₂O₂Na 354.1532, found 354.1532 [M+Na]⁺.

33: 91.3 mg, yellow oil, 33% yield. IR (CHCl₃, cast film) 3448, 2958, 2927, 2855, 1697, 1467 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.17 (ddd, 1H, J = 7.69, 6.24, 1.10 Hz, H-13), 4.03 (m, 1H, H-8), 3.45 (dd, 1H, J = 11.5, 7.97 Hz, H-12), 3.45 (dd, 1H, J = 17.4, 9.36 Hz, H-9), 3.32 (dd, 1H, J = 17.3, 2.66 Hz, H-9), 3.02 (dd, 1H, J = 11.5, 1.10 Hz, H-12), 2.34 (m, 1H, H-14), 1.58 - 1.25 (m, 12H, H-2, H-3, H-4, H-5, H-6, H-7), 1.05 (d, 3H, J = 6.87 Hz, H-15), 0.98 (d, 3H, J = 6.97 Hz, H-15), 0.86 (t, 3H, J = 6.88 Hz, H-1); ¹³C NMR (125 MHz, CDCl₃) 203.0, 173.8, 71.3, 68.5, 45.1, 36.4, 31.8, 30.7, 30.6, 29.5, 29.2, 25.4, 22.6, 19.0, 17.8, 14.1; [α]₂⁵D = 212.47 (c = 0.470, CHCl₃); HRMS (ES) m/z calculated for C₁₆H₂₉NS₂O₂Na 354.1532, found 354.1531 [M+Na]⁺.

![Chemical Structure](image)

**7L**

Compound **7L** was synthesized from **32** by the method for synthesizing **3L**.
7L: 70.0 mg, white solid, 69% yield. IR (CHCl₃, cast film) 3405, 3313, 2955, 2918, 2851, 1685, 1643, 1546 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 6.0 (s, 1H, NH), 4.10 (m, 1H, H-8), 3.42 (m, 1H, H-12), 3.03 (m, 2H, H-11), 2.87 (d, 1H, J = 4.21 Hz OH), 2.72 (dd, 1H, J = 15.2, 3.39 Hz, H-9), 2.66 (dd, 1H, J = 15.3, 8.62 Hz, H-9), 1.97 (s, 3H, H-14), 1.53 - 1.23 (m, 12H, H-2, H-3, H-4, H-5, H-6, H-7), 0.86 (t, 3H, J = 6.78 Hz, H-1); ¹³C NMR (125 MHz, CDCl₃) 199.4, 170.6, 68.8, 51.1, 39.3, 36.8, 31.8, 29.4, 29.2, 28.8, 25.4, 23.2, 22.6, 14.1; [α]D²⁵ = 14.1 (c = 1.210, CHCl₃); HRMS (ES) m/z calculated for C₁₄H₂₇NSO₃Na 312.1604, found 312.1604 [M+Na]⁺. 

![Chemical Structure](image)

Compound 7D was synthesized from 33 by the method for synthesizing 3L.

7D: 45.0 mg, white solid, 65% yield. IR (CHCl₃, cast film) 3405, 3313, 2955, 2918, 2851, 1685, 1643, 1546 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 6.0 (s, 1H, NH), 4.04 (m, 1H, H-8), 3.43 (m, 1H, H-12), 3.03 (m, 2H, H-11), 2.80 (d, 1H, J = 4.13 Hz OH), 2.73 (dd, 1H, J = 15.3, 3.40 Hz, H-9), 2.66 (dd, 1H, J = 15.3, 8.62 Hz, H-9), 1.97 (s, 3H, H-14), 1.53 - 1.23 (m, 12H, H-2, H-3, H-4, H-5, H-6, H-7), 0.86 (t, 3H, J = 6.88 Hz, H-1); ¹³C NMR (125 MHz, CDCl₃) 199.5, 170.6, 68.8, 51.1, 39.3, 36.8, 31.8, 29.4, 29.2, 28.8, 25.4, 23.2, 22.6, 14.1; [α]D²⁵ = -14.3 (c = 1.000, CHCl₃); HRMS (ES) m/z calculated for C₁₄H₂₇NSO₃Na 312.1604, found 312.1603 [M+Na]⁺. 

![Chemical Structures](image)
Compound 7 was synthesized from 7L by the method for synthesizing 3.

7: 15.0 mg, white solid, 30% yield, keto:enol = 1.85:1. IR (CHCl₃, cast film) 3281, 3105, 2949, 2923, 2856, 1717, 1687, 1637, 1563 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.95 (s, 1H, NH), 5.45 (s, 0.35H, enol-H-9), 3.69 (s, 1.3H, keto-H-9), 3.46 (m, 2H, H-12), 3.09 (m, 2H, H-11), 2.52 (t, 1.3H, J = 7.33 Hz, keto-H-7), 2.17 (t, 0.7H, J = 7.62 Hz, enol-H-7), 1.98 (m, 3H, H-14), 1.58 (m, 2H, H-6), 1.33 -1.20 (m, 8H, H-2, H-3, H-4, H-5), 0.89 (m, 3H, H-1); ¹³C NMR (125 MHz, CDCl₃) 202.3, 194.3, 192.4, 177.7, 170.4, 170.2, 99.1, 57.2, 43.5, 39.9, 39.2, 34.9, 31.7, 31.6, 29.3, 29.1, 29.0, 28.9, 27.9, 26.3, 23.5, 23.3, 23.2, 22.67, 14.1; HRMS (ES) m/z calculated for C₁₄H₂₅NSO₃Na 310.1447, found 310.1447 [M+Na]^⁺.

Supplementary Scheme 6: Synthesis of hexaketides 8, 8L and 8D.
Compounds 35 and 36 were synthesized from 34 by the similar method for synthesizing 17 and 18 where the auxiliary was changed to (S)-4-benzyl-N-acetyl-1, 3-thiazolidine-2-thione.

35: 203 mg, yellow oil, 50% yield. IR (CHCl$_3$, cast film) 3451, 2925, 2854, 1695, 1496 cm$^{-1}$; $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.37 – 7.25 (m, 5H, Ph), 5.40 (ddd, 1H, $J = 10.6, 6.97, 4.04$ Hz, H-15), 4.05 (m, 1H, H-10), 3.64 (dd, 1H, $J = 17.7, 2.38$ Hz, H-11), 3.40 (dd, 1H, $J = 11.5, 7.3$ Hz, H-14), 3.23 (dd, 1H, $J = 13.2, 3.76$ Hz, H-16), 3.13 (dd, 1H, $J = 17.7, 9.36$ Hz, H-11), 3.05 (dd, 1H, $J = 13.1, 10.5$ Hz, H-16), 2.89 (d, 1H, $J = 11.6$ Hz, H-14), 1.60 - 1.22 (m, 16H, H-2, H-3, H-4, H-5, H-6, H-7, H-8, H-9), 0.86 (t, 3H, $J = 6.61$ Hz, H-1); $^{13}$C NMR (125 MHz, CDCl$_3$) 201.4, 173.4, 136.4, 129.5, 128.9, 127.3, 68.4, 67.9, 45.9, 36.9, 36.4, 32.1, 31.9, 29.6, 29.5, 29.3, 25.6, 22.7, 14.1; $^{\alpha_k}$ = 123 (c = 0.280, CHCl$_3$); HRMS (ES) m/z calculated for C$_{22}$H$_{33}$NS$_2$O$_2$Na 430.1845, found 430.1847 [M+Na]$^+$.

36: 38.0 mg, yellow oil, 10% yield. IR (CHCl$_3$, cast film) 3449, 2925, 2854, 1697, 1496 cm$^{-1}$; $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.37 – 7.27 (m, 5H, Ph), 5.40 (ddd, 1H, $J = 10.6, 6.97, 4.04$ Hz, H-15), 4.05 (m, 1H, H-10), 3.46 (dd, 1H, $J = 17.4, 9.26$ Hz, H-11), 3.40 (dd, 1H, $J = 11.5, 7.2$ Hz, H-14), 3.34 (dd, 1H, $J = 17.4, 2.56$ Hz, H-11), 3.23 (dd, 1H, $J = 13.3, 3.30$ Hz, H-16), 3.09 (s, 1H, O-H), 3.05 (dd, 1H, $J = 13.2, 10.5$ Hz, H-16), 2.91 (d, 1H, $J = 11.6$ Hz, H-14), 1.60 - 1.20 (m, 16H, H-2, H-3, H-4, H-5, H-6, H-7, H-8, H-9), 0.86 (t, 3H, $J = 6.90$ Hz, H-1); $^{13}$C NMR (125 MHz, CDCl$_3$) 201.5, 173.9, 136.4, 129.5, 128.9, 127.3, 68.5, 68.3, 45.5, 36.8, 36.7, 32.1, 31.9, 29.6, 29.5, 29.3, 25.5, 22.7,
Compound 8L were synthesized from 35 by the method for synthesizing 3L.

8L: 90.0 mg, white solid, 58% yield. IR (CHCl₃, cast film) 3408, 3281, 3230, 2954, 2917, 2849, 1683, 1658, 1631, 1557 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 6.02 (s, 1H, NH), 4.04 (m, 1H, H-10), 3.45 (m, 1H, H-14), 3.04 (m, 2H, H-13), 2.80 (d, 1H, J = 4.40 Hz, OH), 2.87 (d, 1H, J = 4.21 Hz OH), 2.73 (dd, 1H, J = 15.3, 3.40 Hz, H-11), 2.67 (dd, 1H, J = 15.3, 8.71 Hz, H-11), 1.97 (s, 3H, H-16), 1.53 - 1.23 (m, 16H, H-2, H-3, H-4, H-5, H-6, H-7, H-8, H-9), 0.86 (t, 3H, J = 6.87 Hz, H-1); ¹³C NMR (125 MHz, CDCl₃) 199.5, 170.5, 68.8, 51.1, 39.3, 36.8, 31.9, 29.6, 29.5, 29.5, 29.3, 28.9, 25.4, 23.2, 22.7, 14.1; α²⁵D = 29.2 (c = 0.150, CHCl₃); HRMS (ES) m/z calculated for C₁₆H₃₁NSO₃Na 340.1917, found 340.1919 [M+Na]^+.

Compound 8D was synthesized from 36 by the method for synthesizing 3L.

8D: 22.0 mg, white solid, yield 81%. IR (CHCl₃, cast film) 3406, 3313, 2954, 2917, 2845, 1683, 1659, 1638, 1557 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.86 (s, 1H, NH), 4.06 (m, 1H, H-10), 3.45 (m, 1H, H-14), 3.04 (m, 2H, H-13), 2.87 (d, 1H, J = 4.21 Hz OH), 2.75
(dd, 1H, $J = 15.4$, 3.30 Hz, H-11), 2.67 (dd, 1H, $J = 15.5$, 8.56 Hz, H-11), 2.66 (d, 1H, $J = 4.22$ Hz, OH), 1.97 (s, 3H, H-16), 1.53 - 1.23 (m, 16H, H-2, H-3, H-4, H-5, H-6, H-7, H-8, H-9), 0.86 (t, 3H, $J = 6.88$ Hz, H-1); $^{13}$C NMR (125 MHz, CDCl$_3$) 199.6, 170.5, 68.9, 51.1, 39.3, 36.8, 31.9, 29.6, 29.5, 29.5, 29.3, 28.9, 25.4, 23.2, 22.7, 14.1; $\alpha_D^{25} = -14.3$ (c = 0.260, CHCl$_3$); HRMS (ES) $m/z$ calculated for C$_{16}$H$_{31}$NSO$_3$Na 340.1917, found 340.1918 [M+Na]$^+$.

![8-keto](compound_8_keto.png)

![8-enol](compound_8_enol.png)

Compound 8 was synthesized from 8L by the method for synthesizing 3.

8: 35.0 mg, white solid, 64% yield. IR (CHCl$_3$, cast film) 3279, 3104, 2948, 2920, 2849, 1717, 1687, 1636, 1565 cm$^{-1}$; $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 5.86 (s, 1H, NH), 5.45 (s, 0.3H, enol-H-11), 3.69 (s, 1.4H, keto-H-11), 3.46 (m, 2H, H-14), 3.09 (m, 2H, H-13), 2.52 (t, 1.3H, $J = 7.43$ Hz, keto-H-9), 2.17 (t, 0.7H, $J = 7.65$ Hz, enol-H-9), 1.96 (m, 3H, H-16), 1.58 (m, 2H, H-8), 1.33 -1.20 (m, 12H, H-2, H-3, H-4, H-5, H-6, H-7), 0.89 (m, 3H, H-1); $^{13}$C NMR (125 MHz, CDCl$_3$) 202.3, 194.3, 192.4, 177.7, 170.4, 170.2, 99.1, 57.2, 43.5, 39.9, 39.2, 34.9, 31.9, 31.3, 29.4, 29.4, 29.3, 29.2, 29.2, 29.1, 29.0, 27.9, 26.3, 23.5, 23.3, 23.2, 22.7, 14.1; HRMS (ES) $m/z$ calculated for C$_{16}$H$_{29}$NSO$_3$Na 338.1760, found 338.1763 [M+Na]$^+$. 

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**Supplementary Scheme 7:** Synthesis of hexaketide 12. Conditions: (a) TBDMSCl, imidazole, DMF, Quant.; (b) Grubbs II, crotonaldehyde, CH₂Cl₂, reflux, 75%; (c) (-)-Ipc₂B(allyl)borane, -100 °C, then NaOH, H₂O₂, 25 °C, 73%; (d) TBDMSCl, imidazole, DMF, 25 °C, Quant.; (e) Grubbs II, ethyl acrylate, CH₂Cl₂, 25 °C, 76%; (f) Mg, MeOH, reflux, 90%; (g) DIBAL, CH₂Cl₂, -78 °C, 93%; (h) LiBr, Et₃N, 44, CH₂Cl₂, 78%; (i) AcOH/H₂O/THF = 3:3:1, 25 °C, 98%.

The synthetic scheme for 12 is the same as for its 2-\((S)\) diastereomer as reported by Zhou et al. The known compound 38 was prepared by a different procedure. All spectroscopic data and physical properties matched those previously reported.

39: 3.30 g, colorless liquid, 73% yield. IR (CHCl₃, cast film) 3354, 3077, 2957, 2929, 2897, 2858, 1472, 1466 cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ 5.80 (m, 1H, H-8), 5.66 (m, 1H, H-4), 5.52 (ddt, 1H, J = 15.3, 6.62, 1.21 Hz, H-5), 5.12 (m, 2H, H-9), 4.12 (m, 1H, H-6), 3.85 (AB₂X₃, 1H, J = 6.06 Hz, H-2), 2.30 – 2.15 (m, 4H, H-3, H-7), 1.12 (d, 3H, J = 6.06 Hz, H-1), 0.88 (s, 9H, Si-C(CH₃)₃), 0.05 (s, 3H, SiCH₃), 0.04 (s, 3H, SiCH₃); ¹³C
NMR (125 MHz, CDCl₃) δ 134.4, 134.3, 128.8, 118.0, 71.9, 68.5, 42.6, 41.9, 25.9, 23.5, 18.2, -4.5, -4.8; α_D = -12.7 (c = 1.13, CHCl₃); HRMS (ES) m/z calculated for C₁₅H₃₀SiO₂Na 293.1907, found 293.1906 [M+Na]+.

40: 2.10 g, colorless liquid, Quant. IR (CHCl₃, cast film) 3078, 2957, 2930, 2897, 2858, 1472, 1463, 1257 cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ 5.78 (m, 1H, H-8), 5.55 (m, 1H, H-4), 5.45 (ddt, 1H, J = 15.4, 6.51, 1.21 Hz, H-5), 5.03 (m, 2H, H-9), 4.09 (m, 1H), 3.80 (AB₂X₃, 1H, J = 6.07 Hz, H-2), 2.27–2.11 (m, 4H, H-3, H-7), 1.30 (td, 1H, J = 6.06 Hz, H-1), 0.88 (s, 18H, Si-C(CH₃)₃), 0.06 (s, 6H, SiCH₃), 0.05 (s, 3H, SiCH₃), 0.03 (s, 3H, SiCH₃); ¹³C NMR (125 MHz, CDCl₃) δ 135.4, 135.3, 126.9, 116.6, 73.5, 68.6, 43.1, 42.6, 26.0, 25.9, 23.2, 18.2, 18.1, -4.2, -4.5, -4.6, -4.7; α_D = -2.16 (c = 1.64, CHCl₃); HRMS (ES) m/z calculated for C₂₁H₄₄Si₂O₂Na 407.2772, found 407.2769 [M+Na]+.

41: 2.10 g, colorless liquid, 75% yield. IR (CHCl₃, cast film) 3057, 2957, 2930, 2897, 2858, 1725, 1657, 1472, 1463 cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ 6.94 (m, 1H, H-8), 5.83 (dt, 1H, J = 15.6, 1.32 Hz, H-9), 5.60 (m, 1H, H-4), 5.45 (ddt, 1H, J = 15.5, 6.61, 1.10 Hz, H-5), 4.18 (m, 3H, H-6, OCH₂CH₃), 3.82 (AB₂X₃, 1H, J = 6.0 Hz, H-2), 2.38–2.12 (m, 4H, H-3, H-7), 1.28 (t, 3H, J = 7.10 Hz, OCH₂CH₃) 1.10 (d, 3H, J = 6.06 Hz, H-1), 0.89 (s, 9H, Si-C(CH₃)₃), 0.88 (s, 9H, Si-C(CH₃)₃), 0.05 (s, 6H, SiCH₃), 0.04 (s, 3H, SiCH₃), 0.02
(s, 3H, SiCH₃); ¹³C NMR (125 MHz, CDCl₃) δ 166.5, 145.9, 134.9, 127.8, 123.6, 72.7, 68.7, 60.1, 42.8, 41.7, 26.1, 26.0, 23.6, 18.2, 18.1, 14.4, -4.3, -4.5, -4.7, -4.8; [α]₂⁵D = -3.34 (c = 1.39, CHCl₃); HRMS (ES) m/z calculated for C₂₄H₄₈Si₂O₄Na 479.2983, found 479.2987 [M+Na]⁺.

42: 100 mg, colorless liquid, 90% yield. IR (CHCl₃, cast film) 2956, 2930, 2897, 2858, 1744, 1472, 1463 cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ 5.55 (m, 1H, H-4), 5.42 (m, 1H, H-5), 4.08 (m, 1H, H-6), 3.82 (AB₂X₃, 1H, J = 6.06 Hz, H-2), 3.68 (s, 3H, OCH₃), 2.32 (t, 2H, J = 7.14 Hz, H-9), 2.15 (m, 2H, H-3), 1.70-1.45 (m, 4H, H-7, H-8), 1.11 (d, 3H, J = 6.06 Hz, H-1), 0.89 (s, 9H, Si-C(CH₃)₃), 0.88 (s, 9H, Si-C(CH₃)₃), 0.05 (s, 6H, SiCH₃), 0.04 (s, 3H, SiCH₃), 0.02 (s, 3H, SiCH₃); ¹³C NMR (125 MHz, CDCl₃) δ 174.1, 135.4, 126.8, 73.3, 68.5, 51.4, 42.5, 37.7, 34.0, 26.0, 25.8, 23.2, 20.9, 18.2, 18.1, -4.2, -4.6, -4.7, -4.8; [α]₂⁵D = -0.77 (c = 0.71, CHCl₃); HRMS (ES) m/z calculated for C₂₃H₄₈Si₂O₄Na 467.2983, found 467.2977 [M+Na]⁺.

43: 70.0 mg, colorless liquid, 93% yield. IR (CHCl₃, cast film) 2956, 2930, 2897, 2858, 2710, 1730, 1473, 1255 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 9.76 (t, 1H, J = 1.84 Hz, H-10), 5.55 (m, 1H, H-4), 5.40 (m, 1H, H-5), 4.08 (m, 1H, H-6), 3.82 (AB₂X₃, 1H, J = 6.07 Hz, H-2), 2.42 (td, 2H, J = 7.34, 1.84 Hz, H-9), 2.16 (m, 2H, H-3), 1.70-1.45 (m, 4H, H-7,
H-8), 1.11 (d, 3H, J = 6.05 Hz, H-1), 0.89 (s, 18H, Si-C(CH$_3$)$_3$), 0.06 (s, 3H, SiCH$_3$), 0.05 (s, 3H, SiCH$_3$) 0.04 (s, 3H, SiCH$_3$), 0.02 (s, 3H, SiCH$_3$); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 202.6, 135.4, 127.0, 73.2, 68.5, 43.8, 42.6, 37.7, 25.9, 25.8, 23.1, 18.1, 18.0, -4.2, -4.5, -4.7, -4.8; $\alpha_D^{25}$ = -5.64 (c = 0.33, CHCl$_3$); HRMS (ES) m/z calculated for C$_{22}$H$_{46}$Si$_2$O$_3$Na 437.2878, found 437.2872 [M+Na]$^+$. 

44: This known compound was synthesized by literature procedures$^6$. All spectroscopic data and physical properties matched those previously reported$^6,18$.

45: 150 mg, colorless liquid, 78% yield. IR (CHCl$_3$, cast film) 3289, 2955, 2929, 2896, 2857, 1664, 1635, 1558, 1472, 1289 cm$^{-1}$; $^1$H NMR (600 MHz, CDCl$_3$) δ 6.92 (dt, 1H, J = 15.4, 6.84 Hz, H-10), 6.13 (dt, 1H, J = 15.5, 1.54 Hz, H-11 5.86 (s, 1H, NH), 5.54 (m, 1H, H-4), 5.40 (ddt, 1H, J = 15.3, 6.73, 1.21 Hz, H-5), 4.05 (dt, 1H, J = 6.40, 6.40 Hz, H-6), 3.82 (AB$_2$X$_3$, 1H, J = 6.06 Hz, H-2), 3.47 (dt, 2H, J = 5.96, 5.96 Hz, H-14), 3.10 (t, 2H, J = 6.50 Hz, H-13), 2.25 - 2.10 (m, 4H, H-3, H-9), 1.97 (s, 3H, H-16), 1.45 - 1.56 (m, 4H, H-7, H-8), 1.10 (d, 3H, J = 6.18 Hz, H-1), 0.88 (s, 18H, Si-C(CH$_3$)$_3$), 0.05 (s, 3H, SiCH$_3$), 0.05 (s, 3H, SiCH$_3$), 0.04 (s, 3H, SiCH$_3$), 0.02 (s, 3H, SiCH$_3$); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 190.4, 170.2, 146.5, 135.5, 128.4, 126.9, 73.3, 68.5, 42.6, 39.8, 37.8, 32.2, 28.3, 25.9, 25.8, 23.6, 23.4, 23.2, 18.2, 18.1, -4.2, -4.5, -4.7, -4.8; $\alpha_D^{25}$ = -3.21 (c = 1.56, CHCl$_3$); HRMS (ES) m/z calculated for C$_{28}$H$_{55}$Si$_2$O$_4$SNa 580.3283, found 580.3280 [M+Na]$^+$. 

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12: 70.0 mg, colorless liquid, 98% yield. IR (CHCl₃, cast film) 3300, 3089, 2965, 2927, 2854, 1660, 1556, 1436, 1292 cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ 6.92 dt, 1H, J = 15.4, 6.84 Hz, H-10 6.13 (dt, 1H, J = 15.4, 1.44 Hz, H-11 5.96 (s, 1H, NH), 5.67 (m, 1H, H-4), 5.58 (m, 1H, H-5), 4.10 (dt, 1H, J = 6.40, 6.40 Hz, H-6), 3.85 (AB₂X₃, 1H, J = 6.17 Hz, H-2), 3.45 (dt, 2H, J = 5.96, 5.96 Hz, H-14), 3.09 (t, 2H, J = 6.23 Hz, H-13), 2.27-2.15 (m, 4H, H-3, H-9), 1.95 (s, 3H, H-16), 1.87 (s, 2H, OH), 1.62-1.48 (m, 4H, H-7, H-8), 1.10 (d, 3H, J = 6.28 Hz, H-1); ¹³C NMR (100 MHz, CDCl₃) δ 190.4, 170.4, 146.2, 136.3, 128.6, 128.0, 72.5, 67.3, 42.1, 39.8, 36.5, 32.1, 28.3, 23.9, 23.3, 23.1; αₒ = -5.58 (c = 0.24, CHCl₃); HRMS (ES) m/z calculated for C₁₆H₂₇SO₄Na 352.1553, found 352.1551 [M+Na]⁺.

Supplementary Scheme 8: The strategy for confirmation of the stereochemistry of 9. Hydrogenation of 9 lead to the production of 10, which is the enantiomer of a commercially available compound 11.

10: To a stirred solution of epi-DHZ (1.00 mg, 3.10 μmol) in 1 mL CD₃OD was added Rh on alumina (700 μg, 5 wt%). The resulting solution was stirred under 1 atm H₂. The reaction was monitored by NMR until all starting material consumed. The solvent was removed in vacuo and the residue was purified using preparative TLC (2:1 Hexane/
EtOAc) to give 10 (0.8 mg, 80% yield). IR (MeOH, cast film) 3362, 2924, 2854, 1646, 1610, 1582, 1436, 1259 cm⁻¹; HRMS (ES) m/z calculated for C₁₈H₂₅O₅Na 321.1707, found 321.1706 [M-H]⁻.

It is noticeable that the extra carbon signals in the ¹³C spectrum of 10 actually come from the contamination in blank solvent CD₃OD. Both the ¹H and ¹³C spectra of 10 match with the ones for commercially available 11 (SynInnova, 98%). The circular dichroism spectra of 10 and 11 are mirror imaged, confirming their enantiomeric property.
Supplementary Table 7. Proton and carbon NMR for 10.

![Chemical Structure]

| No. | $^{13}$C $\delta$ (ppm) | $^1$H $\delta$ (ppm) |
|-----|-------------------------|-----------------------|
| 1   | 173.0                   | -                     |
| 2   | 106.0                   | -                     |
| 3   | 166.0                   | -                     |
| 4   | 111.7                   | 6.19 (d, 1H, 2.40)    |
| 5   | 163.7                   | -                     |
| 6   | 102.0                   | 6.15 (d, 1H, 2.40)    |
| 7   | 149.1                   | -                     |
| 1’  | 37.6                    | 3.17 (td, 1H, 12.1, 4.19) |
|     |                         | 2.42 (td, 1H, 12.5, 5.18) |
| 2’  | 32.3                    | 1.20-1.30 (m, 1H)     |
|     |                         | 1.75-1.86 (m, 2H)     |
| 3’  | 28.2                    | 1.36-1.46 (m, 2H)     |
|     |                         | 1.46-1.56 (m, 4H)     |
| 4’  | 24.5                    | 1.36-1.46 (m, 2H)     |
|     |                         | 1.56-1.66 (m, 3H)     |
| 5’  | 32.6                    | 1.30-1.35 (m, 4H)     |
|     |                         | 1.66-1.72 (m, 1H)     |
| 6’  | 69.2                    | 3.75 (m, 2H)          |
| 7’  | 36.6                    | 1.46-1.56 (m, 4H)     |
|     |                         | 1.56-1.66 (m, 3H)     |
| 8’  | 22.7                    | 1.46-1.56 (m, 4H)     |
| 9’  | 36.2                    | 1.56-1.66 (m, 3H)     |
| 10’ | 74.3                    | 5.16 (m, 2H)          |
| 11’ | 21.5                    | 1.33 (d, 3H, 6.17)    |

Spectra were obtained at 500 MHz for proton and 125 MHz for carbon and were recorded in CD$_3$OD.
Supplementary Figure 21. The CD spectra of compound 10 (line a, solid) and 11 (line b, dashed). The amount of each compound is 0.67 mg in 1 ml methanol (0.2 mm cell and 5 scans).
Supplementary Figure 22. Proton NMR spectra for 10 and 11.
Supplementary Figure 23. Carbon NMR spectra for 10 (upper) and 11 (bottom). The extra carbon signals in the upper spectrum for 10 have been noted compared to Figure 24.
Supplementary Figure 24. The carbon NMR spectrum for solvent CD$_3$OD.
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