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Asymmetric synthesis of pentenomycin I, epipentenomycin I, and their analogs

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Dedicated to Professor Dieter Seebach on the occasion of his 70th birthday

ABSTRACT

The synthetic utility of the intramolecular acylation of α-sulfinyl carbanions as an efficient and general synthetic approach for the preparation of (−)-pentenomycin I (**1**) and (−)-epipentenomycin I (**5**) and their enantiomers (*ent*-**1** and *ent*-**5**), starting from chiral (2*S*,5*S*,6*S*)-ester **6** and *ent*-**6**, respectively, has been demonstrated. Easy accesses to pentenomycin analogs have also been demonstrated through the Pummerer, Suzuki–Miyaura, and Sonogashira reactions.

1. Introduction

Natural products containing highly oxygenated cyclopentenoid skeleton, for example, cryptosporiopsin,[1] kjellmanianone,[2] reductiomycin,[3] and didemnenones,[4] have attracted considerable attention due to their interesting biological activities. Among these classes of compounds, pentenomycins I–III (**1**–**3**) and dehydropentenomycin (**4**) are representatives of small highly oxygenated cyclopentenone antibiotics (Fig. 1). Pentenomycin I (**1**) and pentenomycin II (**2**) were first isolated from aerobic culture broths of a mutant strain of *Streptomyces eurythermus*.[5] Pentenomycin III (**3**)[6a] and dehydropentenomycin (**4**)[6b] (antibiotic G-2201-C) were isolated from *Streptoverticillium eurocidicum* SF-1768 and *Streptomyces cattleya*, respectively. (+)-Epipentenomycin I (*ent*-**5**) was found in carpophores of *Perziza* sp. collected from horse manure.[7] Pentenomycins I and II (**1** and **2**) exhibit moderate to strong activity in vitro against a variety of both Gram-positive and Gram-negative bacteria.[5] Because of their important biological activities as well as their highly oxygenated structures, there have been several studies directed toward the synthesis of pentenomycins and analogs in both enantiomeric and racemic forms.[8,9]

2. Results and discussion

Previously, we reported intramolecular acylation of α-sulfinyl carbanions as general strategies for the preparation of highly functionalized cyclopentenones,[10] cyclohexenones,[11] and α,β-unsaturated-γ- and δ-butyrolactones.[12] The method was successfully applied to the racemic synthesis of (±)-pentenomycin I (**1**) and (±)-epipentenomycin I (**5**) as well as dehydropentenomycin I (**4**), starting from (±)-methyl glycerate acetonide.[13] We report herein asymmetric synthesis of pentenomycin I and epipentenomycin I and their analogs starting from an appropriate chiral ester **6** or *ent*-**6**.[14] A retrosynthetic analysis of (−)-pentenomycin I (**1**) and (−)-epipentenomycin I (**5**) and their enantiomers is presented in Figure 2. Of interest to our laboratory is the convergent synthesis of highly functionalized cyclopentenones via intramolecular acylation of α-sulfinyl carbanions.[10,13] Accordingly, we anticipated that the key feature of our retrosynthetic analysis is a diastereoselective hydroxyalkylation of the enolate anion derived from chiral ester **6** with 3-phenylsulfanylpropanal, which, after oxidation, leads to the expected equatorial-sulfoxide **8**. The sulfinylcyclopentanone **9** would be constructed via the intramolecular acylation of α-sulfinyl carbanion generated from sulfinylester **8**. Finally, pyrolysis followed by hydrolysis should provide the required pentenomycin I (**1**) and epipentenomycin I (**5**) with high enantioselectivity. In the forward synthetic sense, (−)-pentenomycin I (**1**) and (−)-epipentenomycin I (**5**) are derived from chiral ester **6** while *ent*-**6** provides (+)-pentenomycin I (*ent*-**1**) and (+)-epipentenomycin I (*ent*-**5**).

Efforts toward the synthesis of (−)-pentenomycin I (**1**) and (−)-epipentenomycin I (**5**) began with the chiral ester **6** (Scheme 1).

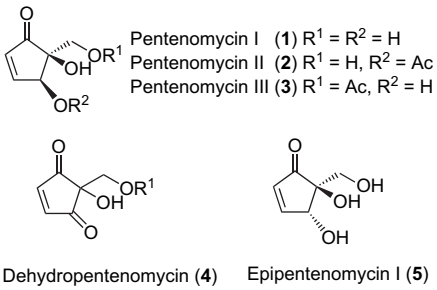

Figure 1. Pentenomycins, dehydropentenomycin, and epipentenomycin I.

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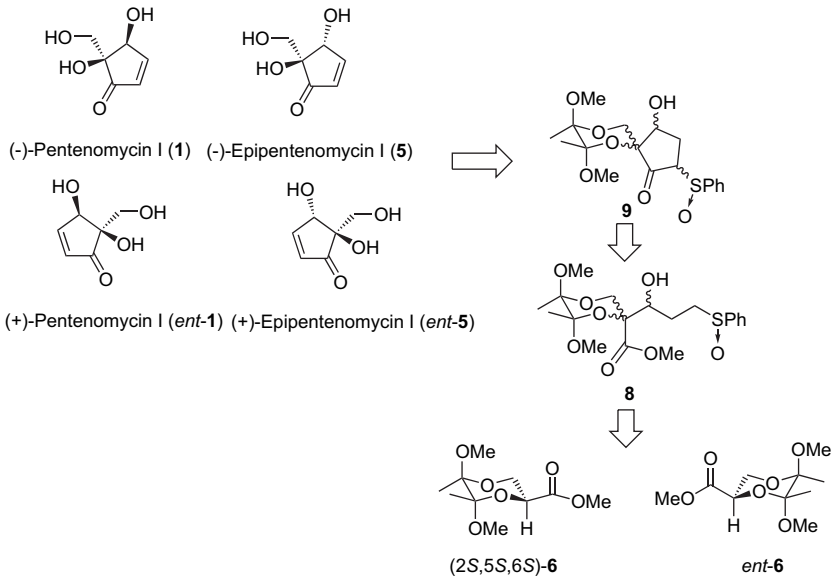
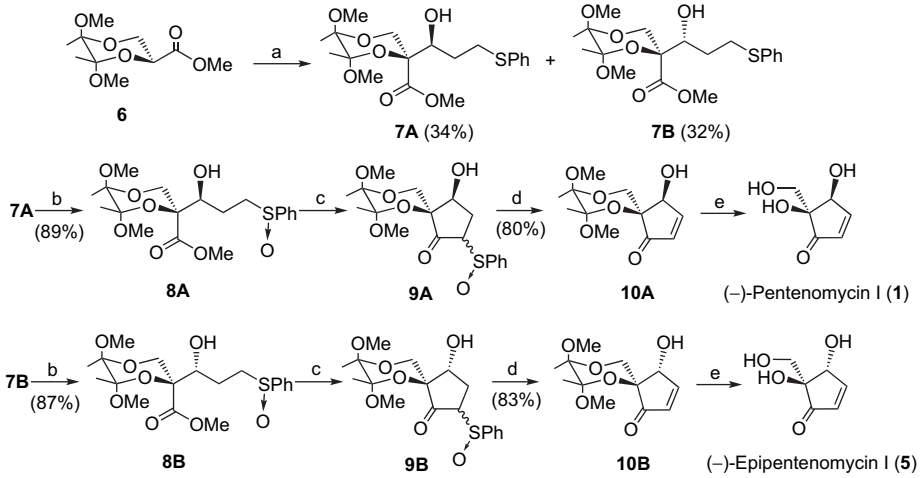


Figure 2. Retrosynthetic analysis.

Ley and co-workers previously reported that the enolate anions of (2*S*,5*S*,6*S*)-ester **6** and *ent*-**6** reacted with electrophiles at the equatorial position with high stereoselectivity.[14,15] Thus, treatment of (2*S*,5*S*,6*S*)-ester **6** with lithium diisopropylamide (LDA) (1.25 equiv) followed by reaction with 3-phenylsulfanylpropanal afforded the expected sulfide **7** in 66% yield as a mixture of diastereomers. Separation of the diastereomers was made by column chromatography to give **7A** and **7B** in 34 and 32% yields, respectively. It is worth mentioning that axial adducts were not observed as revealed by ^{1}H NMR, ^{13}C NMR as well as TLC analysis. Oxidation of sulfides **7A** and **7B** with sodium metaperiodate ($NaIO_4$, 1.2 equiv) in aqueous methanol at 0 °C to room temperature overnight gave the corresponding sulfoxides **8A** and **8B** in 89 and 87% yields, respectively, each as a mixture of diastereomers. Treatment of **8A** or **8B** with LDA (3.5 equiv) in THF at −78 °C for 2 h and 0 °C for 2 h followed by quenching with saturated ammonium chloride solution afforded spiroketosulfoxide **9A** or **9B**, each as a mixture of diastereomers in quantitative yield. Subsequent sulfoxide elimination of the crude products **9A** and **9B** in refluxing toluene in the presence of $CaCO_3$ for 15 h yielded the corresponding hydroxylspirocyclopentenones **10A** and **10B** in 80 and 83% yields, respectively. Eventually, hydrolysis of the butanediacetal (BDA) protecting group of **10A** and **10B** using 90% TFA at 0 °C for 5 h readily afforded (−)-pentenomycin I (**1**) and (−)-epipentenomycin I (**5**) in quantitative yield. Chemical structures and optical properties of the synthesized (−)-pentenomycin I (**1**) and (−)-epipentenomycin I (**5**) were established and confirmed by comparing the ^{1}H NMR and ^{13}C NMR as well as the sign of the optical rotations with those reported in the literature. The data are in good agreement with the reported values.[5,9]

Having accomplished the synthesis of (−)-pentenomycin I (**1**) and (−)-epipentenomycin I (**5**), the syntheses of their corresponding enantiomers, i.e., (+)-pentenomycin I (*ent*-**1**) and (+)-epipentenomycin I (*ent*-**5**), respectively, were straightforward starting from *ent*-**6** using the reaction conditions described in Scheme 1. Yields in each step were comparable to those obtained in the prior synthetic route starting from (2*S*,5*S*,6*S*)-ester **6**. The spectroscopic data and optical properties of (+)-pentenomycin I (*ent*-**1**) and (+)-epipentenomycin I (*ent*-**5**) were in agreement with those reported in the literature (Fig. 3).[7]

At this stage, we would like to demonstrate the synthetic versatility of our synthesis by preparing some pentenomycin analogs from common intermediates isolated from our synthetic approach to the pentenomycins. Accordingly, spiroketosulfoxide *ent*-**9A** was



Scheme 1. Synthesis of (−)-pentenomycin I (**1**) and (−)-epipentenomycin I (**5**). Reagents and conditions: (a) LDA, THF, −78 °C, then $PhS(CH_2)_2CHO$; (b) $NaIO_4$, MeOH, H_2O; (c) LDA (3.5 equiv), THF, −78 °C, 2 h then 0 °C, 2 h; (d) toluene, $CaCO_3$, reflux, 15 h; (e) 90% TFA, 0 °C, 5 h.

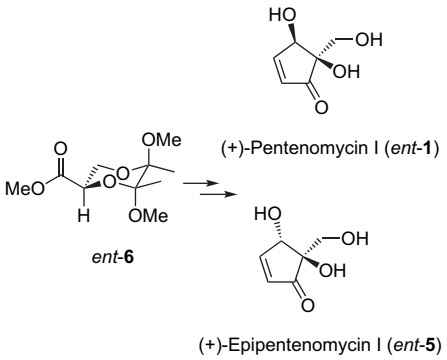
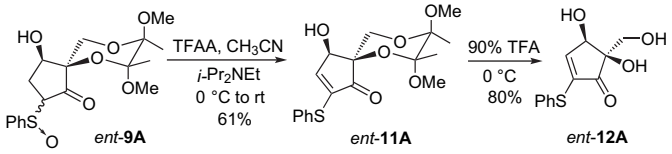


Figure 3. Synthetic approach to *ent*-**1** and *ent*-**5**.

subjected to the Pummerer rearrangement.[16] Reaction employing acetic anhydride led to the recovery of the starting material. Gratifyingly, treatment of *ent*-**9A** with trifluoroacetic anhydride (1.1 equiv) and ethyldiisopropylamine in acetonitrile at 0 °C to room temperature overnight, after chromatography, provided *ent*-**11A** in 61% yield (Scheme 2). Subsequent standard hydrolysis of the BDA-protecting group (90% aqueous TFA, 0 °C, 5 h) provided α-phenylsulfanylpentenomycin (*ent*-**12A**) in 80% yield as colorless crystals. Highly oxygenated cyclopentenones of type *ent*-**11A** and *ent*-**12A** may be useful as starting materials for further synthetic manipulation.



Scheme 2. Preparation of *ent*-α-phenylsulfanylpentenomycin I (*ent*-**12A**).

Compound *ent*-**10A** has proven to be a crucial intermediate for the synthesis of α-aryl- and α-alkynyl-substituted pentenomycin derivatives by employing the Suzuki–Miyaura and Sonogashira reactions, respectively (Scheme 3). Initially, α-iodo derivative *ent*-**13A** was prepared by treatment of *ent*-**10A** with I_2 in the presence of an amine base such as DMAP and pyridine. Under optimal conditions, I_2/pyridine in CCl_4,[17] *ent*-**13A** was obtained in 97% yield from *ent*-**10A**.

The Suzuki–Miyaura coupling reaction[18] of *ent*-**13A** with phenylboronic acid was carried out by treatment of *ent*-**13A** with phenylboronic acid in THF in the presence of 10 mol % $PdCl_2(PPh_3)_2$ and Na_2CO_3 at 40 °C for 15 h under an argon atmosphere to afford the expected α-phenyl-substituted derivative *ent*-**14A** in 70% yield together with 25% yield of the recovered starting material. The reaction employing K_2CO_3 in THF and DMF provided low yield of *ent*-**14A**. α-Phenylspirocyclopentenone *ent*-**14A** was hydrolyzed under standard conditions to give the corresponding α-phenylpentenomycin *ent*-**15A** as a white solid in 84% yield after chromatography.

Our success of the Suzuki–Miyaura coupling reaction of *ent*-**14A** led us to further investigate the Sonogashira coupling reaction.[19] The optimum conditions were found to employ $PdCl_2(PPh_3)_2$, CuI, and diisopropylamine in THF. The reactions of *ent*-**13A** with both phenylacetylene and *tert*-butylacetylene were completed within 45 min and gave good yields of the corresponding coupling products *ent*-**16Aa**,**b** (Scheme 3).

3. Conclusion

The work described in this article demonstrated the synthetic utility of the intramolecular acylation of α-sulfinyl carbanions as an efficient and general synthetic approach for the preparation of both enantiomers of pentenomycin I and epipentenomycin I, starting from readily available chiral ester (2*S*,5*S*,6*S*)-**6** and *ent*-**6**. Syntheses of pentenomycin analogs have been carried out via the Pummerer, Suzuki–Miyaura, and Sonogashira reactions. Compound *ent*-**10A**, a precursor for *ent*-pentenomycin I (*ent*-**1**), was employed as a versatile starting material for the preparation of α-alkynyl- and α-phenyl-substituted pentenomycins.

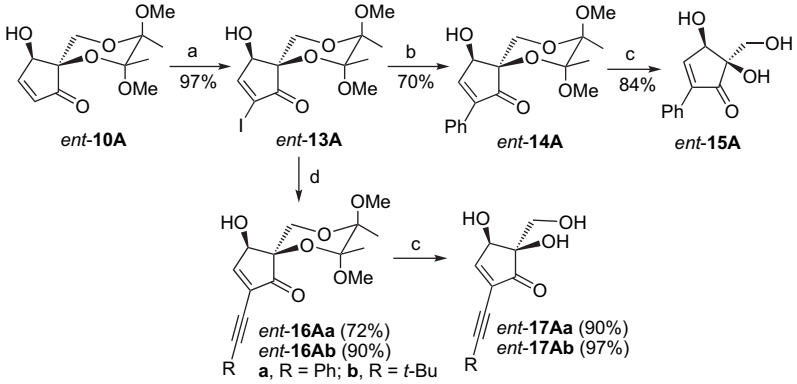
4. Experimental

4.1. General

^{1}H NMR and ^{13}C NMR were recorded on a Bruker DPX-300 or a Bruker DPX-500 spectrometer. IR spectra were recorded either with a Jasco A-302 or a Perkin–Elmer 683 infrared spectrometer. Mass spectra were performed on a Thermo Finnigan Polaris Q mass spectrometer. Microanalyses were performed with a Perkin–Elmer Elemental analyzer 2400 CHN. High resolution MS were obtained from either HR-TOF-MS Micromass model VQ-TOF2 or Finnigan MAT 95 mass spectrometer. All chemicals used are of commercial grade.

4.2. (2*S*,5*S*,6*S*)-2-(1′-Hydroxy-3′-(phenylsulfanyl)propyl)-5,6-dimethoxy-5,6-dimethyl-[1,4]dioxane-2-carboxylic acid methyl ester (7)

General procedure A: a THF (15 mL) solution of (2*S*,5*S*,6*S*)-ester **6** (5.39 g, 23.00 mmol) was added slowly to a THF (25 mL) solution



Scheme 3. Preparation of *ent*-**15A** and *ent*-**17A**. Reagents and conditions: (a) I_2, pyridine, CCl_4; (b) $PhB(OH)_2$, $PdCl_2(PPh_3)_2$, Na_2CO_3, THF, 60 °C; (c) 90% TFA, 0 °C, 5 h; (d) phenylacetylene or *tert*-butylacetylene, $PdCl_2(PPh_3)$, CuI, *i*-Pr_2NH, THF, 0 °C, 45 min.

of LDA [(28.75 mmol), prepared by reacting *N*,*N*-diisopropylamine (4.53 mL, 32.2 mmol) with *n*-BuLi (1.35 M in hexane, 22.0 mL, 28.75 mmol)] at −78 °C. The mixture was stirred at −78 °C for 2 h. To this solution was added a THF (5.75 mL) solution of 3-phenylsulfanylpropanal [freshly prepared by reacting of Et_3N (4.0 mL, 28.75 mmol), thiophenol (4.57 mL, 36.0 mmol) with acrolein (1.90 mL, 28.75 mmol)]. The resulting mixture was stirred at −78 °C for 2 h and quenched with saturated aqueous NH_4Cl solution (30 mL). Layers were separated and the aqueous phase was extracted with ethyl acetate (3×25 mL). The combined organic layers were washed with water, brine, and dried over anhydrous Na_2SO_4. The organic phase was concentrated (aspirator then in vacuo) to give a crude pale yellow liquid, which was purified by column chromatography (silica gel, 25% ethyl acetate in hexanes). The less polar fraction was **7A** (3.129 g, 34% yield): ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.28–7.00 (m, 5H, Ar*H*), 3.98 (d, *J*=11.6 Hz, 1H, C–CH*H*), 3.96–3.89 (m, 1H, C–C*H*), 3.86 (d, *J*=11.6 Hz, 1H, C–C*H*H), 3.53 (s, 3H, CO_2CH_3), 3.15 (s, 3H, OCH_3), 3.12 (s, 3H, OCH_3), 3.10–3.05 (m, 2H, CH*H*–CH_2 and br O*H*), 2.90–2.78 (m, 1H, C*H*H–CH_2), 1.50–1.35 (m, 1H, CH–CH*H*), 1.35–1.20 (m, 4H, CH_3, CH–C*H*H), 1.20 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.7 (C=O), 135.6 (C), 129.2 (2×CH), 128.7 (2×CH), 125.8 (CH), 99.7 (C), 97.6 (C), 76.1 (CH), 72.6 (CH), 56.4 (CH_2), 52.1 (CH), 50.2 (CH), 48.0 (CH_3), 30.0 (CH_3), 28.4 (CH_3), 17.5 (CH_3), 17.4 (CH_3). IR (neat): ν_{max} 3480 m, 1739 s, 1584 m, 1482 s, 1375 s, 1148 s, 1037 s, 740 m, 692 m cm^{-1}. MS: *m*/*z* (% relative intensity): 400 (M^+, 0.6), 337 (46), 143 (100), 136 (81), 123 (62), 110 (58), 93 (45). HRMS (ESI-TOF) calcd for $C_{19}H_{28}O_7SNa$: 423.1453; found: 423.1454. $[\alpha]_D^{29}$ +139.7 (*c* 0.9, $CHCl_3$). The more polar fraction was **7B** (2.945 g, 32% yield): ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.20–7.06 (m, 5H, Ar*H*), 4.05 (d, *J*=11.7 Hz, 1H, CH*H*), 3.76 (dd, *J*=8.8, 3.9 Hz, 1H, C*H*O), 3.69 (s, 3H, CO_2CH_3), 3.65 (d, *J*=11.7 Hz, 1H, C*H*H), 3.19 (s, 2×3H, OCH_3), 3.11–3.03 (m, 1H, C*H*H–CH_2), 2.96–2.85 (m, 1H, C*H*H–CH_2), 2.10–1.85 (br s, 1H, O*H*), 1.61–1.49 (m, 2H, CH–CH_2), 1.24 (s, 3H, CH_3), 1.20 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.8 (C=O), 135.9 (C), 129.4 (2×CH), 128.8 (2×CH), 126.0 (CH), 99.4 (C), 97.9 (C), 75.3 (C), 73.3 (CH), 59.5 (CH_2), 52.1 (CH_3), 50.5 (CH_3), 48.2 (CH_3), 30.4 (CH_2), 30.3 (CH_2), 17.7 (CH_3), 17.6 (CH_3). IR (neat): ν_{max} 3480 m, 1739 s, 1634 w, 1585 m, 1482 m, 1440 s, 1252 s, 1147 s, 1101 s, 1050 s, 1037 m cm^{-1}. MS: *m*/*z* (% relative intensity): 400 (M^+, 0.2), 251 (47), 220 (45), 192 (49), 143 (100), 136 (92), 123 (76), 110 (82). HRMS (ESI-TOF) calcd for $C_{19}H_{28}O_7SNa$: 423.1453; found: 423.1450. $[\alpha]_D^{29}$ +60.6 (*c* 1.75, $CHCl_3$).

4.3. (2*R*,5*R*,6*R*)-2-(1′-Hydroxy-3′-(phenylsulfanyl)propyl)-5,6-dimethoxy-5,6-dimethyl-[1,4]dioxane-2-carboxylic acid methyl ester (*ent*-7)

According to the general procedure A, a THF (15 mL) solution of (2*R*,5*R*,6*R*)-ester *ent*-**6** (4.683 g, 20.0 mmol) was treated with a THF (20 mL) solution of LDA (25 mmol) at −78 °C. The resulting solution was reacted with a THF (5 mL) solution of 3-phenylsulfanylpropanal [freshly prepared from Et_3N (3.48 mL, 25.0 mmol), thiophenol (3.98 mL, 31.25 mmol) and acrolein (1.65 mL, 25.0 mmol)]. The crude product was purified by column chromatography (silica gel, 25% ethyl acetate in hexanes) to give two separable diastereomers of *ent*-**7**. A less polar fraction was *ent*-**7A** (2.637 g, 33% yield): ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.28–7.00 (m, 5H, Ar*H*), 3.98 (d, *J*=11.6 Hz, 1H, C–CH*H*), 3.96–3.89 (m, 1H, C–C*H*), 3.86 (d, *J*=11.6 Hz, 1H, C–C*H*H), 3.53 (s, 3H, CO_2CH_3), 3.15 (s, 3H, –OCH_3), 3.12 (s, 3H, OCH_3), 3.10–3.05 (m, 1H, CH*H*–CH_2), 2.90–2.78 (m, 2H, C*H*H–CH_2 and br O*H*), 1.50–1.35 (m, 1H, CH–CH*H*), 1.35–1.20 (m, 4H, CH_3, CH–C*H*H), 1.20 (s, 3H, CH_3). $[\alpha]_D^{29}$ −110.6 (*c* 0.98, $CHCl_3$). A more polar fraction was *ent*-**7B** (liquid, 2.482 g, 31% yield): ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.20–7.06 (m, 5H, Ar*H*), 4.05 (d, *J*=11.7 Hz, 1H, CH*H*), 3.76 (dd, *J*=8.8, 3.9 Hz, 1H, C–C*H*), 3.66 (s, 3H, CO_2CH_3), 3.65 (d, *J*=11.7 Hz, 1H, C*H*H), 3.19 (s, 2×3H, OCH_3), 3.11–3.03 (m, 1H, C*H*H–CH_2), 2.96–2.85 (m, 1H, C*H*H–CH_2), 1.56–1.49 (m, 3H, CH–CH_2 and br O*H*), 1.24 (s, 3H, CH_3), 1.20 (s, 3H, CH_3). $[\alpha]_D^{29}$ −67.0 (*c* 1.76, $CHCl_3$).

4.4. (2*S*,5*S*,6*S*,1′*S*)-2-(1′-Hydroxy-3′-(phenylsulfinyl)propyl)-5,6-dimethoxy-5,6-dimethyl-[1,4]dioxane-2-carboxylic acid methyl ester (8A)

General procedure B: a solution of (2*S*,5*S*,6*S*,1′*S*)-**7A** (3.00 g, 7.48 mmol) in methanol (36 mL) was added dropwise to a suspension of $NaIO_4$ (0.942 g, 8.976 mmol) in water (10 mL) at 0 °C. The resulting mixture was stirred at 0 °C to room temperature overnight. The precipitate of $NaIO_3$ was filtered and washed several times with ethyl acetate. The organic layer was separated and the aqueous layer was extracted with ethyl acetate (3×20 mL). The combined organic layers were washed with water (20 mL) and brine (20 mL), and dried over anhydrous Na_2SO_4. Filtration followed by evaporation (aspirator then in vacuo) gave a yellow liquid of the crude product, which was purified by column chromatography (silica gel, 80% ethyl acetate in hexanes) to furnish a pale yellow liquid of (2*S*,5*S*,6*S*,1′*S*)-**8A** (2.776 g, 89% yield) as a 1:1 mixture of two diastereomers. ^{1}H NMR (300 MHz, $CDCl_3$, data are reported for both diastereomers): δ 7.60–7.42 (m, 2×5H, Ar*H*), 4.12 (d, *J*=11.5 Hz, 1H, OC*H*H), 4.04 (d, *J*=11.5 Hz, 1H, OCH*H*), 3.81 (d, *J*=11.5 Hz, 1H, OCH*H*), 3.77 (d, *J*=11.5 Hz, 1H, OC*H*H), 3.69–3.61 (br s, 4H, OCH_3 and C*H*OH), 3.62 (s, 3H, OCH_3), 3.30 (br, 1H, O*H*), 3.16 (s, 3H, OCH_3), 3.14 (s, 3H, OCH_3), 3.12 (s, 3H, OCH_3), 3.07 (s, 3H, OCH_3), 3.20–3.02 (m, 3×1H, C*H*H–CH_2 and C*H*OH), 2.85 (br, 1H, O*H*), 2.83–2.65 (m, 2×1H, CH*H*–CH_2), 1.80–1.40 (m, 2×2H, CH_2–CH), 1.21 (s, 2×3H, CH_3), 1.17 (s, 2×3H, –CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.4 (C=O), 171.3 (C=O), 143.1 (C), 142.7 (C), 130.8 (2×CH), 129.06 (2×CH), 129.02 (2×CH), 123.9 (2×CH), 123.8 (2×CH), 99.64 (C), 99.61 (C), 97.69 (C), 97.67 (C), 75.6 (C), 75.4 (C), 73.7 (CH), 73.3 (CH), 58.0 (CH_2), 57.5 (CH_2), 54.0 (CH_2), 53.9 (CH_2), 53.3 (2×C), 52.3 (CH_3), 52.1 (CH_3), 50.2 (2×CH_3), 48.0 (CH_3), 47.9 (CH_3), 23.2 (CH_2), 22.8 (CH_2), 17.5 (CH_3), 17.4 (CH_3). IR (neat): ν_{max} 3364 m, 1738 s, 1732 s, 1445 s, 1374 s, 1251 s, 1146 s, 1046 m, 883 s, 751 m, 692 m cm^{-1}. MS: *m*/*z* (% relative intensity): 416 (M^+, 0.3), 143 (87), 125 (65), 109 (64), 93 (48), 83 (59), 73 (100). HRMS (ESI-TOF) calcd for $C_{19}H_{28}O_8SNa$: 439.1403; found: 439.1390.

4.5. (2*S*,5*S*,6*S*,1′*R*)-2-(1′-Hydroxy-3′-(phenylsulfinyl)propyl)-5,6-dimethoxy-5,6-dimethyl-[1,4]dioxane-2-carboxylic acid methyl ester (8B)

According to the general procedure B, a solution of (2*S*,5*S*,6*S*,1′*R*)-**7B** (2.019 g, 5.00 mmol) in methanol (24.00 mL) was treated with $NaIO_4$ (0.634 g, 6.0 mmol) in water (24 mL) at 0 °C to room temperature overnight to give a crude product, which was purified by column chromatography (silica gel, 80% ethyl acetate in hexanes) to furnish a yellow syrup of (2*S*,5*S*,6*S*,1′*R*)-**8B** (1.828 g, 87% yield) as 1:1 mixture of diastereomers. ^{1}H NMR (300 MHz, $CDCl_3$, data are reported for both diastereomers): δ 7.58–7.31 (m, 2×5H, Ar*H*), 4.15 (d, *J*=11.5 Hz, 1H, O–C*H*H), 4.12 (d, 1H, *J*=11.5 Hz, O–CH*H*), 3.71 (s, 3H, OCH_3), 3.69 (m, 2×1H, C*H*–OH), 3.68 (s, 3H, CO_2CH_3), 3.56 (d, *J*=11.5 Hz, 2×1H, OCH*H*), 3.18 (s, 3H, OCH_3), 3.14 (s, 2×3H, OCH_3), 3.10 (s, 3H, OCH_3), 3.10–3.01 (m, 2×1H, CH*H*–CH_2), 2.90–2.62 (m, 2×2H, CH*H*–CH and br O*H*), 2.20–1.91 (m, 2×1H, C*H*H–CH), 1.69–1.61 (m, 2×1H, CH–CH*H*), 1.21 (s, 3H, CH_3), 1.13 (s, 3H, CH_3), 1.19 (s, 3H, CH_3), 1.17 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 172.4 (C=O), 172.1 (C=O), 143.1 (C), 142.0 (C), 131.0 (CH), 130.9 (CH), 129.2 (2×CH), 129.1 (2×CH), 124.2 (2×CH), 124.0 (2×CH), 99.37 (C), 99.32 (C), 97.9 (2×C), 75.0 (C), 74.9 (C), 74.1 (CH), 73.8 (CH), 58.6 (CH_2), 58.2 (CH_2), 54.7 (CH_2), 53.7 (CH_2), 52.3 (CH_3), 52.2 (CH_3), 50.35 (2×CH_3), 48.1 (CH_3), 48.0 (CH_3), 25.2 (CH_2), 24.7 (CH_2), 17.64 (2×CH_3), 17.58 (2×CH_3). IR (neat): ν_{max} 3554 s, 2923 s, 2583 s, 1726 s, 1455 s, 1377 s, 1303 m, 1253 m, 1145 s cm^{-1}. MS: *m*/*z* (% relative intensity): 416 (M^+, 0.1), 143 (78), 141.2 (78), 125 (55), 115 (100), 109

(48), 83 (74). HRMS (ESI) calcd for $C_{19}H_{28}O_8SNa$: 439.1403; found: 439.1400.

4.6. (2*R*,5*R*,6*R*,1′*R*)-2-(1′-Hydroxy-3′-(phenylsulfinyl)propyl)-5,6-dimethoxy-5,6-dimethyl-[1,4]dioxane-2-carboxylic acid methyl ester (*ent*-8A)

According to the general procedure B, a solution of (2*R*,5*R*,6*R*,1′*R*)-*ent*-**7A** (2.082 g, 5.20 mmol) in methanol (25 mL) was treated with $NaIO_4$ (0.654 g, 1.39 mmol) in water (10 mL) at 0 °C to room temperature overnight to give a crude product, which was purified by column chromatography (silica gel, 80% ethyl acetate in hexanes) to furnish a pale yellow syrup of (2*R*,5*R*,6*R*,1′*R*)-*ent*-**8A** (1.832 g, 87% yield) as a mixture of diastereomers. The ^{1}H NMR spectrum was identical to that of **8A**: ^{1}H NMR (300 MHz, $CDCl_3$, data are reported for both diastereomers): δ 7.60–7.42 (m, 2×5H, Ar*H*), 4.12 (d, *J*=11.5 Hz, 1H, OC*H*H), 4.04 (d, *J*=11.5 Hz, 1H, OCH*H*), 3.81 (d, *J*=11.5 Hz, 1H, OCH*H*), 3.77 (d, *J*=11.5 Hz, 1H, OC*H*H), 3.69 (s, 3H, OCH_3), 3.62 (s, 4H, OCH_3 and C*H*OH), 3.16 (s, 4H, OCH_3 and C*H*OH), 3.14 (s, 3H, OCH_3), 3.12 (s, 3H, OCH_3), 3.07 (s, 3H, OCH_3), 3.02 (m, 2×1H, C*H*H–CH_2), 2.83–2.75 (m, 2×1H, –CH*H*–CH_2), 2.70 (br s, 2×1H, O*H*), 1.80–1.40 (m, 2×2H, CH_2–CH), 1.21 (s, 2×3H, CH_3), 1.17 (s, 2×3H, CH_3).

4.7. (2*R*,5*R*,6*R*,1′*S*)-2-(1′-Hydroxy-3′-(phenylsulfinyl)propyl)-5,6-dimethoxy-5,6-dimethyl-[1,4]dioxane-2-carboxylic acid methyl ester (*ent*-8B)

According to the general procedure B, a solution of (2*R*,5*R*,6*R*,1′*S*)-*ent*-**7B** (2.403 g, 6.00 mmol) in methanol (38 mL) was treated with $NaIO_4$ (0.755 g, 1.60 mmol) and water (10 mL) at 0 °C to room temperature overnight to give a pale yellow syrup of a crude product, which was purified by column chromatography (silica gel, 80% ethyl acetate in hexanes) to furnish a pale yellow syrup of (2*R*,5*R*,6*R*,1′*S*)-*ent*-**8B** (2.125 g, 85% yield) as a mixture of diastereomers. The ^{1}H NMR spectrum was identical to that of **8B**: ^{1}H NMR (300 MHz, $CDCl_3$, data are reported for both diastereomers): δ 7.51–7.40 (m, 2×5H, Ar*H*), 4.22 (d, *J*=11.5 Hz, 1H, OC*H*H), 4.19 (d, *J*=11.5 Hz, 1H, OCH*H*), 3.78 (s, 3H, CO_2CH_3), 3.76 (m, 2×1H, C*H*OH), 3.75 (s, 3H, CO_2CH_3), 3.63 (d, 2×1H, *J*=11.5 Hz, OCH*H*), 3.25 (s, 3H, OCH_3), 3.21 (s, 2×3H, OCH_3), 3.17 (s, 3H, OCH_3), 3.05–2.75 (m, 2×2H, CH_2–CH_2 and br O*H*), 2.88 (m, 2×1H, CH*H*–CH), 2.04–1.98 (m, 2×1H, C*H*H–CH), 1.76–1.68 (m, 2×1H, CH–CH*H*), 1.28 (s, 3H, CH_3), 1.27 (s, 3H, CH_3), 1.26 (s, 3H, CH_3), 1.24 (s, 3H, CH_3).

4.8. (2*S*,5*S*,6*S*,5′*S*)-5′-Hydroxy-2′-oxo-3′-phenylsulfinyl spirocyclopentane-5,6-dimethoxy-5,6-dimethyl-[1,4]-dioxane (9A)

General procedure C: a THF (11 mL) solution of (2*S*,5*S*,6*S*,5′*S*)-**8A** (1.806 g, 5.00 mmol) was slowly added to a cooled (−78 °C) THF (12 mL) solution of LDA [(17.50 mmol), prepared by reacting *N*,*N*-diisopropylamine (2.76 mL, 19.6 mmol) with *n*-BuLi (1.35 M in hexane, 13.35 mL, 17.5 mmol)]. The reaction mixture was stirred at −78 °C for 2 h and at 0 °C for 2 h. The resulting dark-orange solution was quenched with saturated aqueous NH_4Cl solution (40 mL) and extracted with ethyl acetate (3×30 mL). The organic phase was washed with water (30 mL), brine (20 mL), and dried over anhydrous Na_2SO_4. The crude product obtained was purified by column chromatography (silica gel, 30–65% ethyl acetate in hexanes) to give two fractions of **9A**. Fraction I (less polar) was obtained as a white solid (0.317 g, 19% yield, mp 172–175 °C; a single diastereomer): ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.59–7.54 (m, 5H, Ar*H*), 4.25 (d, *J*=8.8 Hz, 1H, C–C*H*H), 4.00–3.95 (m, 2H, C–CH*H* and C*H*H–CHOH), 3.74 (d, *J*=11.6 Hz, 1H, SOC*H*), 3.28 (s, 3H, OCH_3), 3.15 (s, 3H, OCH_3), 2.72 (ddd, *J*=15.7, 11.6, 4.3 Hz, 1H, CH*H*–CHOH), 2.01 (d, *J*=15.7 Hz, 1H, C*H*OH), 1.65 (br s, 1H, O*H*), 1.32 (s, 3H, CH_3), 1.25 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 205.9 (C=O), 140.2 (C), 131.5 (CH), 129.5 (2×CH), 124.1 (2×CH), 99.5 (C), 97.9 (C), 77.0 (C), 71.9 (CH), 69.5 (CH), 57.1 (CH_2), 49.1 (CH_3), 48.2 (CH_3), 26.5 (CH_2), 18.1 (CH_3), 17.7 (CH_3). IR ($CHCl_3$): ν_{max} 3290 w, 1755 s, 1445 m, 1146 s, 1114 s, 1032 m, 969 m cm^{-1}. MS: *m*/*z* (% relative intensity): 384 (M^+, 0.7), 227 (66), 195 (61), 126 (53), 115 (99), 101 (55), 73 (100). HRMS (ESI-TOF) calcd for $C_{18}H_{24}O_7SNa$: 407.1140; found: 407.1140. $[\alpha]_D^{29}$ +375.0 (*c* 0.60, $CHCl_3$). Fraction II (more polar) was obtained as a pale yellow viscous liquid (0.716 g, 43% yield; a mixture of two diastereomers): ^{1}H NMR (300 MHz, $CDCl_3$, data are reported for both diastereomers): δ 7.61–7.42 (m, 10H, Ar*H*), 4.19 (br, 1H), 3.95 (br, 1H), 3.95 (d, *J*=12.3 Hz, 1H), 3.78–3.73 (m, 3H), 3.44 (dd, *J*=12.2, 10.4 Hz, 2H), 3.19 (s, 3H, OCH_3), 3.18 (s, 3H, OCH_3), 3.16 (s, 3H, OCH_3), 2.89 (s, 3H, OCH_3), 2.81 (d, *J*=15.5 Hz, 1H), 2.42 (br d, *J*=15.5 Hz, 1H), 1.51 (dd, *J*=13.7, 10.0 Hz, 2H), 1.40–1.10 (br, 2H, O*H*), 1.25 (s, 3H, CH_3), 1.21 (s, 3H, CH_3), 1.17 (s, 3H, CH_3), 1.14 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 205 (C=O), 203.8 (C=O), 142.5 (C), 138 (C), 131.4 (CH), 131.0 (2×CH), 129.2 (2×CH), 128.9 (2×CH), 124.7 (CH), 123.8 (2×CH), 99.4 (C), 99.1 (C), 98.2 (C), 97.9 (C), 76.6 (C), 75.4 (C), 74.4 (CH), 72.7 (CH), 69.1 (CH), 63.3 (CH), 57.3 (CH_2), 56.5 (CH_2), 49.5 (CH_3), 48.7 (CH_3), 48.3 (CH_3), 48.1 (CH_3), 31.4 (CH_2), 23.2 (CH_2), 18.2 (2×CH_3), 17.7 (CH_3), 17.6 (CH_3). IR ($CHCl_3$): ν_{max} 3368 w, 3028 m, 1755 s, 1445 m, 1147 s, 1112 s, 1036 m cm^{-1}. MS: *m*/*z* (% relative intensity): 384 (M^+, 0.4), 227 (43), 195 (56), 125 (77), 115 (74), 111 (88), 109 (48), 99 (61), 97 (43), 73 (100). HRMS (ESI-TOF) calcd for $C_{18}H_{24}O_7SNa$: 407.1132; found: 407.1108.

4.9. (2*S*,5*S*,6*S*,5′*R*)-5′-Hydroxy-2′-oxo-3′-phenylsulfinyl spirocyclopentane-5,6-dimethoxy-5,6-dimethyl-[1,4]-dioxane (9B)

According to the general procedure C, a THF (10 mL) solution of (2*S*,5*S*,6*S*,5′*R*)-**8B** (1.611 g, 4.45 mmol) was added slowly to a cooled (−78 °C) THF (10 mL) solution of LDA (15.60 mmol). After stirring at −78 °C for 2 h, the mixture was stirred at 0 °C for 2 h and quenched with saturated aqueous NH_4Cl solution (40 mL) and extracted with ethyl acetate (3×30 mL). The organic phase was washed with water (30 mL), brine (20 mL), and dried over anhydrous Na_2SO_4. The crude product obtained was purified by column chromatography (silica gel, 30–65% ethyl acetate in hexanes) to give two fractions of **9B**. Fraction I (less polar) was obtained as a white solid of (0.267 g, 18% yield, 165–168 °C; a single diastereomer): ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.58–7.34 (m, 5H, Ar*H*), 4.19 (dd, *J*=5.0, 3.0 Hz, 1H, C*H*OH), 4.03 (d, *J*=11.9 Hz, 1H, OC*H*H), 3.74 (d, *J*=11.9 Hz, 1H, OCH*H*), 3.56 (t, *J*=9.1 Hz, 1H, CH_2–C*H*), 3.28 (s, 3H, OCH_3), 3.48 (s, 3H, OCH_3), 2.56 (ddd, *J*=14.5, 9.1, 5.0 Hz, 1H, C*H*H), 1.80 (ddd, *J*=15.6, 11.9, 3.0 Hz, 1H, CH*H*), 1.6 (br s, 1H, O*H*), 1.36 (s, 3H, CH_3), 1.34 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 207.3 (C=O), 141.3 (C), 131.2 (CH), 129.3 (2×CH), 123.8 (2×CH), 100.6 (C), 99.3 (C), 81.1 (C), 70.9 (CH), 67.7 (CH), 58.3 (CH_2), 48.9 (CH_3), 48.1 (CH_3), 21.5 (CH_2), 18.6 (CH_3), 18.3 (CH_3). IR ($CHCl_3$): ν_{max} 3288 m, 1749 s, 1460 m, 1377 m, 1145 m, 1032 m cm^{-1}. MS: *m*/*z* (% relative intensity): 384 (M^+, 0.5), 153 (57), 149 (54), 126 (71), 111 (90), 109 (55), 73 (100). HRMS (ESI-TOF) calcd for $C_{18}H_{24}O_7Na$: 407.1140; found: 407.1140. $[\alpha]_D^{29}$ +305.9 (*c* 0.35, $CHCl_3$). Fraction II (more polar) was obtained as a pale yellow liquid (0.654 g, 44% yield; mixture of two diastereomers): ^{1}H NMR (300 MHz, $CDCl_3$, data are reported for both diastereomers): δ 7.63–7.45 (m, 10H, Ar*H*), 4.20 (dd, *J*=10.1, 6.0 Hz, 1H), 3.74–3.65 (m, 3H), 3.42–3.30 (m, 1H), 3.30 (s, 3H, OCH_3), 3.27–3.05 (m, 5H), 3.23 (s, 3H, OCH_3), 3.21 (s, 3H, OCH_3), 3.13 (s, 3H, OCH_3), 2.71–2.65 (m, 1H), 2.56–2.40 (m, 1H), 2.39–2.29 (m, 1H), 1.90–1.74 (m, 1H), 1.31 (s, 3H, CH_3), 1.28 (s, 3H, CH_3), 1.23 (s, 3H, CH_3), 1.21 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 205.3 (C=O), 204.8 (C=O), 142.6 (C), 139.6 (C), 131.9 (CH), 131.2 (CH), 129.3 (2×CH), 129.1 (2×CH), 125.2 (2×CH), 123.9 (2×CH),

100.2 (C), 99.7 (C), 98.6 (C), 98.4 (C), 78.3 (C), 75.6 (C), 71.0 (CH), 70.2 (CH), 69.1 (CH), 66.8 (CH), 58.1 (CH_2), 57.5 (CH_2), 49.6 (CH_3), 48.9 (CH_3), 48.3 (CH_3), 48.0 (CH_3), 25.8 (CH_2), 22.9 (CH_2), 18.3 (CH_3), 18.1 (CH_3), 17.9 (CH_3), 17.8 (CH_3). IR ($CHCl_3$): ν_{max} 3386 m, 1754 s, 1445 m, 1376 m, 1147 s, 1112 s, 1055 m, 1036 m cm^{-1}. MS: *m*/*z* (% relative intensity): 385 (M^++1, 0.6), 227 (61), 195 (47), 126 (75), 115 (79), 109 (51), 69 (100). HRMS (ESI-TOF) calcd for $C_{18}H_{24}O_7Na$: 407.1140; found: 407.1136.

4.10. (2*R*,5*R*,6*R*,5′*R*)-5′-Hydroxy-2′-oxo-3′-phenylsulfinyl spirocyclopentane-5,6-dimethoxy-5,6-dimethyl-[1,4]dioxane (*ent*-9A)

According to the general procedure C, a THF (10 mL) solution of (2*R*,5*R*,6*R*,5′*R*)-*ent*-**8A** (1.695 g, 4.69 mmol) was treated with a THF (12 mL) solution of LDA (16.42 mmol) to provide a crude product, which was purified by column chromatography (silica gel, 30–65% ethyl acetate in hexanes) to give two fractions of *ent*-**9A**. Fraction I (less polar) was obtained as a white solid (0.3129 g, 20% yield, mp 174–175 °C; a single diastereomer): ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.59–7.54 (m, 5H, Ar*H*), 4.25 (d, *J*=8.8 Hz, 1H, C–C*H*H), 4.00–3.95 (m, 1H, C–CH*H*), 3.74 (d, *J*=11.6 Hz, 1H, S(O)C*H*), 4.00–3.90 (m, 1H, C*H*H–CHOH), 3.28 (s, 3H, OCH_3), 3.15 (s, 3H, OCH_3), 2.72 (ddd, *J*=15.7, 11.6, 4.3 Hz, 1H, CH*H*–CHOH), 2.01 (d, *J*=15.7 Hz, 1H, C*H*OH), 1.75 (br s, 1H, O*H*), 1.32 (s, 3H, CH_3), 1.25 (s, 3H, CH_3). $[\alpha]_D^{29}$ −380.9 (*c* 0.31, $CHCl_3$). Fraction II (more polar) was obtained as a yellow liquid (0.655 g, 42% yield; mixture of two diastereomers): ^{1}H NMR (300 MHz, $CDCl_3$, data are reported for both diastereomers): δ 7.61–7.42 (m, 2×5H, Ar*H*), 4.15 (br, 1H), 3.95 (br, 1H), 3.81 (d, *J*=12.3 Hz, 1H), 3.80–3.61 (m, 3H), 3.44 (dd, *J*=12.2, 10.4 Hz, 2H), 3.19 (s, 3H, OCH_3), 3.18 (s, 3H, OCH_3), 3.16 (s, 3H, OCH_3), 2.89 (s, 3H, OCH_3), 2.81 (d, *J*=14.5 Hz, 1H), 2.42 (d, *J*=15.5 Hz, 1H), 1.51 (dd, *J*=13.7, 10.0 Hz, 2H), 1.30–1.11 (br, 2×1H, O*H*), 1.25 (s, 3H, CH_3), 1.21 (s, 3H, CH_3), 1.17 (s, 3H, CH_3), 1.14 (s, 3H, CH_3).

4.11. (2*R*,5*R*,6*R*,5′*S*)-5′-Hydroxy-2′-oxo-3′-phenylsulfinyl spirocyclopentane-5,6-dimethoxy-5,6-dimethyl-[1,4]dioxane (*ent*-9B)

According to the general procedure C, a THF (10 mL) solution of (2*R*,5*R*,6*R*,5′*S*)-*ent*-**8B** (2.080 g, 5.00 mmol) was treated with a THF (12 mL) solution of LDA (17.47 mmol) to provide a crude product, which was purified by column chromatography (silica gel, 30–65% ethyl acetate in hexanes) to give two fractions of *ent*-**9B**. Fraction I (less polar) was obtained as a white solid (0.439 g, 17% yield, mp 167–169 °C; a single diastereomer): ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.58–7.34 (m, 5H, Ar*H*), 4.19 (dd, *J*=5.0, 3.0 Hz, 1H, C*H*OH), 4.03 (d, *J*=11.9 Hz, 1H, OC*H*H), 3.74 (d, *J*=11.9 Hz, 1H, OCH*H*), 3.56 (t, *J*=9.1 Hz, 1H, CH_2–C*H*), 3.28 (s, 3H, OCH_3), 3.48 (s, 3H, OCH_3), 2.56 (ddd, *J*=14.5, 9.1, 5.0 Hz, 1H, C*H*H), 1.80 (ddd, *J*=15.6, 11.9, 3.0 Hz, 1H, CH*H*), 1.68 (br, 1H, O*H*), 1.36 (s, 3H, CH_3), 1.34 (s, 3H, CH_3). $[\alpha]_D^{29}$ −306.86 (*c* 0.35, $CHCl_3$). Fraction II (more polar) was obtained as a pale yellow liquid (0.712 g, 43% yield; a mixture of diastereomers): ^{1}H NMR (300 MHz, $CDCl_3$, data are reported for both diastereomers): δ 7.63–7.45 (m, 2×5H, Ar*H*), 4.20 (dd, *J*=10.1, 6.0 Hz, 1H), 3.75–3.68 (m, 2H), 3.37 (d, *J*=11.9 Hz, 1H), 3.30 (s, 3H, OCH_3), 3.23 (s, 3H, OCH_3), 3.25–3.18 (m, 2H), 3.21 (s, 3H, OCH_3), 3.13 (s, 3H, OCH_3), 3.10 (d, *J*=11.9 Hz, 1H), 3.09 (d, *J*=16.2 Hz, 1H), 2.71–2.65 (m, 1H), 2.56–2.40 (m, 1H), 2.39–2.29 (m, 1H), 2.81–1.94 (m, 1H), 1.80–1.78 (br, 2×1H, O*H*), 1.31 (s, 3H, CH_3), 1.28 (s, 3H, CH_3), 1.23 (s, 3H, CH_3), 1.21 (s, 3H, CH_3).

4.12. (2*S*,5*S*,6*S*,5′*S*)-5′-Hydroxy-2′-oxospirocyclopent-3′-ene-5,6-dimethoxy-5,6-dimethyl-[1,4]dioxane (10A)

A mixture of diastereomers of (2*S*,5*S*,6*S*,5′*S*)-**9A** (0.385 g, 1.00 mmol) and anhydrous $CaCO_3$ (3.0 g) in dry toluene (15 mL) was refluxed at 110 °C for 10 h under an argon atmosphere. After removal of toluene (aspirator then in vacuo), the residue was purified by column chromatography (silica gel, 23% ethyl acetate in hexanes) to give a single diastereomer of (2*S*,5*S*,6*S*,5′*S*)-**10A** as a white solid (0.205 g, 80% yield, mp 96–99 °C). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.63 (dd, *J*=6.1 Hz, 1H, =CH_β), 6.28 (dd, *J*=6.1 Hz, 1H, =CH_α), 4.59 (s, 1H, CC*H*), 4.22 (d, *J*=10.9 Hz, 1H, CH*H*), 3.46 (s, 3H, OCH_3), 3.34 (d, *J*=10.9 Hz, 1H, C*H*H), 3.31 (s, 3H, OCH_3), 1.34 (s, 3H, CH_3), 1.33 (br s, 1H, O*H*), 1.31 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 203.1 (C=O), 161.1 (CH), 133.6 (CH), 133.9 (CH), 100.9 (C), 99.98 (C), 77.1 (C), 63.6 (CH_2), 48.6 (CH_3), 48.0 (CH_3), 18.78 (CH_3), 18.73 (CH_3). IR (Nujol): ν_{max} 3501 m, 1728 s, 1596 w, 1463 m, 1150 s, 1114 s, 1075 s cm^{-1}. MS: *m*/*z* (% relative intensity): 258 (M^+, 0.8), 195 (76), 110 (71), 109 (20), 101 (37), 89 (36), 82 (52), 73 (100), 55 (23), 53 (23). HRMS (ESI-TOF) calcd for $C_{12}H_{18}O_6Na$: 281.1001; found: 281.1002. $[\alpha]_D^{29}$ +58.6 (*c* 1.33, $CHCl_3$).

4.13. (2*S*,5*S*,6*S*,5′*R*)-5′-Hydroxy-2′-oxospirocyclopent-3′-ene-5,6-dimethoxy-5,6-dimethyl-[1,4]dioxane (10B)

A mixture of diastereomers of (2*S*,5*S*,6*S*,5′*R*)-**9B** (0.365 g, 0.95 mmol) and anhydrous $CaCO_3$ (3.0 g) in dry toluene (15 mL) was refluxed at 110 °C for 10 h under an argon atmosphere. After removal of toluene (aspirator then in vacuo), the residue was purified by column chromatography (silica gel, 27% ethyl acetate in hexanes) to give a single diastereomer of (2*S*,5*S*,6*S*,5′*R*)-**10B** as a colorless liquid (0.201 g, 83% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.43 (dd, *J*=5.9 Hz, 1H, =CH_β), 6.14 (dd, *J*=5.9 Hz, 1H, =CH_α), 4.87 (s, 1H, CC*H*), 4.11 (d, *J*=10.9 Hz, 1H, CH*H*), 3.77 (d, *J*=10.9 Hz, 1H, C*H*H), 3.41 (s, 3H, OCH_3), 3.36 (s, 3H, OCH_3), 3.32 (br s, 1H, O*H*), 1.45 (s, 3H, CH_3), 1.36 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 202.4 (C=O), 160.5 (CH), 132.9 (CH), 100.58 (C), 100.52 (C), 81.1 (C), 79.9 (CH), 60.3 (CH_2), 49.2 (CH_3), 48.4 (CH_3), 18.8 (CH_3), 18.6 (CH_3). IR ($CHCl_3$): ν_{max} 3565 w, 1725 s, 1597 w, 1456 w, 1376 m, 1153 s, 1141 s cm^{-1}. MS: *m*/*z* (% relative intensity): 258 (M^+, 0.8), 110 (71), 89 (36), 82 (52), 74 (100). HRMS (ESI-TOF) calcd for $C_{12}H_{18}O_6Na$: 281.1001; found: 281.1001. $[\alpha]_D^{29}$ +76.2 (*c* 0.18, $CHCl_3$).

4.14. (2*R*,5*R*,6*R*,5′*R*)-5′-Hydroxy-2′-oxospirocyclopent-3′-ene-5,6-dimethoxy-5,6-dimethyl-[1,4]dioxane (*ent*-10A)

A mixture of (2*R*,5*R*,6*R*,5′*R*)-*ent*-**9A** (0.351 g, 0.91 mmol) and anhydrous $CaCO_3$ (3.0 g) was refluxed in dry toluene (15 mL) for 10 h under an argon atmosphere. The crude product was purified by column chromatography (silica gel, 23% ethyl acetate in hexanes) to give a single diastereomer of (2*R*,5*R*,6*R*,5′*R*)-*ent*-**10A** as a white solid (0.189 g, 80% yield, mp 97–101 °C). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.63 (dd, *J*=6.1 Hz, 1H, =CH_β), 6.28 (dd, *J*=6.1 Hz, 1H, =CH_α), 4.59 (s, 1H, CC*H*), 4.30 (d, *J*=10.9 Hz, 1H, CH*H*), 3.52 (s, 3H, OCH_3), 3.40 (d, *J*=10.9 Hz, 1H, C*H*H), 3.39 (s, 3H, OCH_3), 1.80 (br s, 1H, O*H*), 1.42 (s, 3H, CH_3), 1.41 (s, 3H, CH_3). $[\alpha]_D^{29}$ −52.8 (*c* 0.175, $CHCl_3$).

4.15. (2*R*,5*R*,6*R*,5′*S*)-5′-Hydroxy-2′-oxospirocyclopent-3′-ene-5,6-dimethoxy-5,6-dimethyl-[1,4]dioxane (*ent*-10B)

A mixture of (2*R*,5*R*,6*R*,5′*S*)-*ent*-**9B** (0.2176 g, 0.57 mmol) and anhydrous $CaCO_3$ (3.0 g) in dry toluene (10 mL) was refluxed at 110 °C for 10 h under an argon atmosphere. The crude product was purified by column chromatography (silica gel, 27% ethyl acetate in hexanes) to give a single diastereomer of (2*R*,5*R*,6*R*,5′*S*)-*ent*-**10B** as a colorless liquid (0.1227 g, 84%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.50 (dd, *J*=5.9 Hz, 1H, =CH_β), 6.23 (dd, *J*=5.9 Hz, 1H, =CH_α), 4.95 (s, 1H, CC*H*), 4.18 (d, *J*=10.9 Hz, 1H, CH*H*), 3.85 (d, *J*=10.9 Hz, 1H, C*H*H), 3.49 (s, 3H, OCH_3), 3.44 (s, 3H, OCH_3), 1.80 (br s, 1H, O*H*), 1.45 (s, 3H, CH_3), 1.36 (s, 3H, CH_3). $[\alpha]_D^{29}$ −74.1 (*c* 0.2053, $CHCl_3$).

4.16. (−)-Pentenomycin I (1)

(2*S*,5*S*,6*S*,5′*S*)-**10A** (0.118 g, 0.45 mmol) was treated with 90% trifluoroacetic acid (7 mL) at 0 °C. The mixture was slowly warmed up to room temperature for 5 h. The solvents were freeze-dried overnight to give a crude product, which was purified by preparative thin layer chromatography (PLC, silica gel, 1% MeOH in EtOAc) to give (−)-pentenomycin I (**1**) (54 mg, 83% yield) as an amorphous powder (viscous liquid or syrup on standing). ^{1}H NMR (300 MHz, D_2O): δ 7.73 (dd, J=4.4, 2.7 Hz, 1H, =CH_β), 6.32 (d, J=4.4 Hz, 1H, =CH_α), 4.73 (s, 1H, C*H*OH), 3.72 (ABq, J=11.8 Hz, 1H, CH_AH$_B$–OH), 3.69 (ABq, J=11.8 Hz, 1H, CH$_A$$H_B$–OH). ^{13}C NMR (75 MHz, D_2O): δ 210.1 (C=O), 164.9 (CH), 133.7 (CH), 76.6 (C), 71.9 (CH), 63.3 (CH_2). IR (neat): ν_{max} 3416 s, 1712 s, 1636 m, 1385 m, 1262 m, 1162 m, 1047 m cm^{-1}. MS: m/z (% relative intensity): 145 (M^++1, 12), 125 (100), 99 (70), 95 (56), 81 (77), 67 (71). $[\alpha]_D^{29}$ −31.2 (*c* 1.50, EtOH) (lit.[5] $[\alpha]_D$ −32.0 (*c* 0.3, EtOH)).

4.17. (+)-Pentenomycin I (*ent*-1)

(2*R*,5*R*,6*R*,5′*R*)-*ent*-**10A** (0.135 g, 0.52 mmol) was treated with 90% trifluoroacetic acid (8 mL) at 0 °C to room temperature for 5 h. The solvents were freeze-dried overnight to give a crude product, which was purified by PLC (silica gel, 2% MeOH in EtOAc) to give [(+)-pentenomycin I (*ent*-**1**) (61 mg, 82% yield) as an amorphous powder (viscous liquid or syrup on standing). ^{1}H NMR (300 MHz, D_2O): δ 7.73 (dd, J=4.4, 2.7 Hz, 1H, =CH_β), 6.32 (d, J=4.4 Hz, 1H, =CH_α), 4.73 (s, 1H, C*H*OH), 3.72 (ABq, J=11.8 Hz, 1H, CH_AH$_B$–OH), 3.69 (ABq, J=11.8 Hz, 1H, CH$_A$$H_B$–OH). $[\alpha]_D^{29}$ +37.1 (*c* 0.28, EtOH) (lit.[9e] $[\alpha]_D$ +30.0 (*c* 0.1, EtOH)).

4.18. (+)-Epipentenomycin I (*ent*-5)

(2*R*,5*R*,6*R*,5′*S*)-*ent*-**10B** (0.153 g, 0.59 mmol) was treated with 90% trifluoroacetic acid (9 mL) at 0 °C to room temperature for 5 h. The solvents were freeze-dried overnight to give a crude product, which was purified by PLC (silica gel, 4% MeOH in EtOAc) to give (+)-epipentenomycin I (*ent*-**5**) (69 mg, 81% yield) as a colorless viscous liquid. ^{1}H NMR (300 MHz, D_2O): δ 7.79 (dd, J=6.1, 2.3 Hz, 1H, =CH_β), 6.47 (d, J=6.1 Hz, 1H, =CH_α), 4.85–4.60 (m, 1H, C*H*OH), 3.84 (d, J=12.0 Hz, 1H, C*H*H), 3.63 (d, J=12.0 Hz, 1H, CH*H*). $[\alpha]_D^{29}$ +68.9 (*c* 0.25, EtOH) (lit.[7] $[\alpha]_D$ +130.0 (*c* 0.51, H_2O)).

4.19. (−)-Epipentenomycin I (5)

(2*S*,5*S*,6*S*,5′*R*)-**10B** (0.086 g, 0.33 mmol) was treated with 90% trifluoroacetic acid (5 mL) at 0 °C. The mixture was slowly warmed up to room temperature for 5 h. The solvents were freeze-dried overnight to give a crude product, which was purified by PLC (silica gel, 1% MeOH in EtOAc) to give (−)-epipentenomycin I (**5**) (40 mg, 80% yield) as a colorless viscous liquid. ^{1}H NMR (300 MHz, D_2O): δ 7.79 (dd, J=6.1, 2.3 Hz, 1H, =CH_β), 6.47 (d, J=6.1 Hz, 1H, =CH_α), 4.85–4.60 (m, 1H, C*H*OH), 3.84 (d, J=12.0 Hz, 1H, C*H*H), 3.63 (d, J=12.0 Hz, 1H, CH*H*). ^{13}C NMR (75 MHz, D_2O): δ 215.9 (C=O), 161.7 (CH), 135.6 (CH), 102.3 (C), 79.3 (CH), 65.0 (CH_2). IR (neat): ν_{max} 3449 s, 1722 m, 1638 s, 1259 m, 1106 s, 1044 m, 925 s cm^{-1}. MS: m/z (% relative intensity): 145 (M^++1, 12), 135 (23), 121 (32), 113 (100), 97 (46), 95 (53), 81 (57). $[\alpha]_D^{29}$ −74.1 (*c* 0.20, EtOH) (lit.[9f] $[\alpha]_D$ −75.3 (*c* 1.15, MeOH)).

4.20. (2*R*,5*R*,6*R*,5′*R*)-5′-Hydroxy-2′-oxo-3′-phenylsulfanyl spirocyclopentene-5,6-dimethoxy-5,6-dimethyl-[1,4]dioxane (*ent*-11A)

Trifluoroacetic anhydride (0.14 mL, 1.10 mmol) was added to a cooled (0 °C) solution of (2*R*,5*R*,6*R*,5′*R*)-*ent*-**9A** (0.258 g, 1.00 mmol) in acetonitrile (5 mL) followed by the addition of diisopropylethylamine (0.11 mL, 0.8 mmol). After stirring at room temperature overnight (12 h), a dark-brown solution was quenched with 1 M HCl and extracted with ethyl acetate. The organic phase was washed with water (20 mL) and brine (20 mL), and dried over anhydrous Na_2SO_4. The crude product obtained was purified by PLC (silica gel, 22% ethyl acetate in hexanes) to give (2*R*,5*R*,6*R*,5′*R*)-*ent*-**11A** as a pale yellow viscous liquid (0.285 g, 61% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.45–7.40 (m, 2H, Ar*H*), 7.40–7.33 (m, 3H, Ar*H*), 6.65 (d, J=3.1 Hz, 1H, C*H*=C), 4.42 (d, J=3.1 Hz, 1H, C*H*OH), 4.27 (d, J=5.5 Hz, 1H, CH*H*), 3.44 (s, 3H, OCH_3), 3.35 (d, J=5.5 Hz, 1H, CH*H*), 3.26 (s, 3H, OCH_3), 1.50 (br s, 1H, O*H*), 1.35 (s, 3H, CH_3), 1.32 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 195.9 (C=O), 148.3 (CH), 143.6 (C), 134.6 (2×CH), 129.7 (2×CH), 129.4 (CH), 128.8 (C), 99.6 (C), 98.1 (C), 82.2 (CH), 77.1 (C), 61.1 (CH_2), 50.0 (CH_3), 48.2 (CH_3), 17.74 (CH_3), 17.71 (CH_3). IR (neat): ν_{max} 3427 m, 1731 s, 1558 w, 1384 m, 1124 s, 1043 s, 754 s cm^{-1}. MS: m/z (% relative intensity): 367 (M^++1, 0.5), 139 (56), 123 (56), 123 (100), 111 (68). HRMS (ESI-TOF) calcd for $C_{18}H_{22}O_6SNa$: 389.1027; found: 389.1015. $[\alpha]_D^{29}$ −85.35 (*c* 1.14, $CHCl_3$).

4.21. (+)-4,5-Dihydroxy-2-phenylsulfanyl-5-hydroxymethyl-2-cyclopentenone (*ent*-12A)

(2*R*,5*R*,6*R*,5′*R*)-*ent*-**11A** (0.122 g, 0.34 mmol) was stirred with 90% trifluoroacetic acid (4 mL) at 0 °C. The mixture was slowly warmed up to room temperature for 3.5 h. The solvent was freeze-dried overnight to give a crude product, which was purified by PLC (silica gel, 77% EtOAc in hexanes) to give *ent*-**12A** as colorless crystals (67.2 g, 80% yield, mp 134–136 °C). ^{1}H NMR (300 MHz, acetone-d_6): δ 7.61–7.44 (m, 5H, Ar*H*), 6.71 (d, J=2.8 Hz, 1H, =C*H*), 4.57 (d, J=2.8 Hz, 1H, C*H*OH), 3.83 (d, J=11.6 Hz, 1H, CH*H*), 3.65 (d, J=11.6 Hz, 1H, CH*H*), 2.9 (br s, 3H O*H*). ^{13}C NMR (75 MHz, $CDCl_3$): δ 200.7 (C=O), 147.9 (CH), 146.8 (C), 134.9 (2×CH), 130.8 (2×CH), 130.3 (CH), 102.0 (C), 78.6 (CH), 76.5 (C), 65.6 (CH_2). IR (Nujol): ν_{max} 3528 m, 1723 s, 1456 m, 1115 s, 1040 m, 769 s cm^{-1}. MS: m/z (% relative intensity): 252 (M^++1, 45), 250 (34), 234 (100), 91 (31), 69 (34). HRMS (ESI-TOF) calcd for $C_{12}H_{12}O_4SNa$: 275.0333; found: 275.0346. $[\alpha]_D^{29}$ +81.8 (*c* 0.17, $CHCl_3$).

4.22. (2*R*,5*R*,6*R*,5′*R*)-5′-Hydroxy-2′-oxo-3′-iodospiro-cyclopent-3′-ene-5,6-dimethoxy-5,6-dimethyl-[1,4]dioxane (*ent*-13A)

A solution of (2*R*,5*R*,6*R*,5′*R*)-*ent*-**10A** (0.625 g, 2.41 mmol), pyridine (5 mL), and carbon tetrachloride (5 mL) was added to a solution of iodine (2.43 g, 9.64 mmol) in pyridine (5 mL) and carbon tetrachloride (5 mL). After stirring for 1 h at room temperature in the dark, the mixture was diluted with Et_2O (3×15 mL) and washed successively with water (20 mL), 1 M HCl (5 mL), saturated $Na_2S_2O_3$ (20 mL), and brine (15 mL). The aqueous layer was extracted with Et_2O and the combined organic layers were dried over anhydrous Na_2SO_4. After filtration and evaporation, the residue was purified by column chromatography on silica gel (silica gel, 20% EtOAc in hexanes) to give *ent*-**13A** as a white solid (0.901 g, 97% yield, mp 98–100 °C), which was unstable on standing at room temperature. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.92 (d, J=2.7 Hz, 1H, =C*H*), 4.49 (d, J=2.7 Hz, 1H, C*H*OH), 4.24 (d, J=11.2 Hz, 1H, C*H*H), 3.99–3.89 (br, 1H, O*H*), 3.43 (s, 3H, OCH_3), 3.37 (d, J=11.2 Hz, 1H, CH*H*), 3.30 (s, 3H, OCH_3), 1.34 (s, 3H, CH_3), 1.33 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 198.0 (C=O), 166.4 (CH), 104.4 (C), 101.1 (C), 99.9 (C), 75.2 (CH), 74.7 (C), 63.1 (CH_2), 48.7 (CH_3), 48.1 (CH_3), 18.68 (CH_3), 18.60 (CH_3). IR (Nujol): ν_{max} 3388 s, 1715 s, 1631 m, 1452 m, 1115 m, 1049 m cm^{-1}. MS: m/z (% relative intensity): 384 (M^+, 0.27), 250 (45), 141 (41), 110 (100). HRMS (ESI-TOF) calcd for $C_{12}H_{17}O_6NaI$: 406.9968; found: 406.9969. $[\alpha]_D^{29}$ −27.29 (*c* 0.98, $CHCl_3$).

4.23. (2*R*,5*R*,6*R*,5′*R*)-2′-Oxo-3′-phenylspirocyclopent-3′-ene-5,6-dimethoxy-5,6-dimethyl-[1,4]dioxane (*ent*-14A)

A round-bottomed flask was charged with phenylboronic acid (46 mg, 0.38 mmol), (2*R*,5*R*,6*R*,5′*R*)-*ent*-**13A** (96 mg, 0.249 mmol), and $PdCl_2(PPh_3)_2$ (10 mg, 0.012 mmol, 5 mol %). THF (1.5 mL) was added followed by 2 M Na_2CO_3 (0.7 mL, 1.8 mmol). The resulting reaction mixture was heated at 40 °C under an argon atmosphere overnight. The mixture was cooled to room temperature and ethyl acetate (10 mL) was added followed by saturated $NaHCO_3$ (20 mL) and water (15 mL). The aqueous layer was extracted with EtOAc (2×10 mL). The combined organic layers were washed with 0.5 N NaOH (2×10 mL), brine (2×10 mL) and dried over anhydrous Na_2SO_4. Filtration followed by evaporation gave the a crude product, which was purified by column chromatography (silica gel, 25% EtOAc in hexanes) to give (2*R*,5*R*,6*R*,5′*R*)-*ent*-**14A** as a white solid (58.5 g, 70% yield, mp 171–172 °C). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.80–7.75 (m, 2H, Ar*H*), 7.71 (d, *J*=2.1 Hz, 1H, =C*H*), 7.38–7.30 (m, 3H, Ar*H*), 4.87 (d, *J*=2.1 Hz, 1H, C*H*OH), 3.89 (d, *J*=11.1 Hz, 1H, CH*H*), 3.74 (d, *J*=11.1 Hz, 1H, CH*H*), 3.43 (s, 3H, OCH_3), 3.31 (s, 3H, OCH_3), 1.47 (s, 3H, CH_3), 1.35 (br s, 1H, O*H*), 1.34 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 198.6 (C=O), 153.4 (CH), 141.1 (C), 130.0 (C), 129.3 (CH), 128.5 (2×CH), 127.1 (2×CH), 99.5 (C), 98.0 (C), 83.2 (C), 76.3 (CH), 61.2 (CH_2), 50.1 (CH_3), 48.2 (CH_3), 17.7 (2×CH_3). IR (neat): ν_{max} 3522 s, 1722 s, 1449 s, 1104 s, 1032 s, 997 s cm^{-1}. MS: *m*/*z* (% relative intensity): 334 (M^++1, 1), 234 (54), 142 (24), 140 (100), 114 (73). HRMS (ESI-TOF) calcd for $C_{18}H_{22}O_6Na$: 357.1313; found: 387.1304. $[\alpha]_D^{29}$ −290.7 (*c* 0.15, $CHCl_3$).

4.24. (+)-4,5-Dihydroxy-5-hydroxymethyl-2-phenyl-2-cyclopentenone (*ent*-15A)

(2*R*,5*R*,6*R*,5′*R*)-*ent*-**14A** (50 mg, 0.176 mmol) was treated with 90% trifluoroacetic acid (1 mL) at 0 °C. The mixture was slowly warmed up to room temperature for 3.5 h. The solvent was freeze-dried overnight to give a crude product, which was purified by PLC (silica gel, 67% EtOAc in hexanes) to give *ent*-**15A** as a white solid (27 mg, 90% yield, mp 127–130 °C). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.73–7.71 (m, 3H, Ar*H* and =C*H*), 7.43–7.39 (m, 3H, Ar*H*), 4.83 (d, *J*=2.6 Hz, 1H, C*H*OH), 3.91 (d, *J*=11.7 Hz, 1H, C*H*H), 3.77 (d, *J*=11.7 Hz, 1H, CH*H*), 2.40 (s, 3H, O*H*). ^{13}C NMR (75 MHz, $CDCl_3$): δ 202.7 (C=O), 151.8 (CH), 143.7 (C), 129.5 (C), 128.7 (CH), 128.0 (2×CH), 127.3 (2×CH), 101.4 (C), 76.5 (CH), 65.7 (CH_2). IR (Nujol): ν_{max} 3417 m, 1704 s, 1597 m, 1571 m, 1449 m, 1038 m, 759 s, 701 m cm^{-1}. MS: *m*/*z* (% relative intensity): 221 (M^+, 0.54), 189 (100), 115 (34), 91 (57), 77 (13). HRMS (ESI-TOF) calcd for $C_{12}H_{12}O_4Na$: 463.1360; found: 463.1347. $[\alpha]_D^{29}$ +23.8 (*c* 0.31, EtOH).

4.25. (2*R*,5*R*,6*R*,5′*R*)-5′-Hydroxy-2′-oxo-3′-phenylacetylenyl spirocyclopent-3′-ene-5,6-dimethoxy-5,6-dimethyl-[1,4]dioxane (*ent*-16Aa)

General procedure D: a mixture of (2*R*,5*R*,6*R*,5′*R*)-*ent*-**13A** (132 mg, 0.342 mmol), phenylacetylene (0.174 mL, 1.71 mmol), $PdCl_2(PPh_3)_2$ (12.3 mg, 0.015 mmol, 5 mol %), and CuI (8.6 mg, 0.034 mmol) was treated with *N*,*N*-diisopropylamine (0.14 mL, 1.026 mmol) at 0 °C. The resulting yellow to dark-brown solution was stirred at 0 °C for 1 h. The mixture was partitioned with Et_2O and 1 M HCl. The aqueous layer was extracted with Et_2O (3×20 mL). The combined organic layers were washed with brine and dried over anhydrous Na_2SO_4. Filtration and concentration gave the crude reaction mixture, which was purified by column chromatography (silica gel, 21% EtOAc in hexanes) to give *ent*-**16Aa** as a pale yellow viscous liquid (88.8 mg, 72% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.57 (d, *J*=2.07 Hz, 1H, =C*H*), 7.61–7.50 (m, 2H, Ar*H*), 7.34–7.30 (m, 3H, Ar*H*), 5.00 (d, *J*=2.07 Hz, 1H, C*H*OH), 4.25 (d, *J*=10.71 Hz, 1H, C*H*H), 3.90 (d, *J*=10.71 Hz, 1H, CH*H*), 3.51 (s, 3H, OCH_3), 3.44 (s, 3H, OCH_3), 1.44 (s, 3H, CH_3), 1.36 (s, 3H, CH_3), 1.33 (br s, 1H, O*H*). ^{13}C NMR (75 MHz, $CDCl_3$): δ 198.9 (C=O), 159.5 (CH), 132.0 (2×CH), 129.2 (CH), 128.9 (C), 128.3 (2×CH), 121.9 (C), 109.79 (C), 100.74 (C), 97.5 (C), 81.6 (C), 78.6 (CH), 60.4 (CH_2), 49.4 (CH_3), 48.6 (CH_3), 29.6 (CH), 18.9 (CH_3), 18.7 (CH_3). IR (neat) ν_{max} 3497 s, 2221 m, 1732 s, 1615 m, 1457 m, 1039 m, 755 m cm^{-1}. MS: *m*/*z* (% relative intensity): 358 (M^+, 0.3), 336 (26), 220 (100), 149 (29), 93 (34), 73 (51). HRMS (ESI-TOF) calcd for $C_{20}H_{22}O_6Na$: 381.1409; found: 381.1442. $[\alpha]_D^{29}$ −29.87 (*c* 0.23, $CHCl_3$).

4.26. (2*R*,5*R*,6*R*,5′*R*)-3′-*tert*-Butylacetylenyl-5′-hydroxy-2′-oxospirocyclopentene-5,6-dimethoxy-5,6-dimethyl-[1,4]dioxane (*ent*-16Ab)

According to the general procedure D as described for *ent*-**16Aa**, the reaction of (2*R*,5*R*,6*R*,5′*R*)-*ent*-**13A** (173 mg, 0.450 mmol), *tert*-butylacetylene (0.164 mL, 2.25 mmol), $PdCl_2(PPh_3)_2$ (16 mg, 0.023 mmol, 5 mol %), CuI (9 mg, 0.045 mmol), and *N*,*N*-diisopropylamine (0.19 mL, 1.35 mmol) provided a crude product, which was purified by column chromatography (silica gel, 20% EtOAc in hexanes) to give *ent*-**16Ab** as a white solid (152.8 mg, 90% yield, 139–141 °C). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.33 (d, *J*=2.5 Hz, 1H, =C*H*), 4.85 (d, *J*=2.5 Hz, 1H, C*H*OH), 4.28 (d, *J*=10.8 Hz, 1H, –CH*H*), 3.77 (d, *J*=10.8 Hz, 1H, C*H*H), 3.42 (s, 3H, OCH_3), 3.36 (s, 3H, OCH_3), 1.60 (br s, 1H, O*H*), 1.35 (s, 3H, CH_3), 1.27 (s, 3H, CH_3), 1.23 (s, 3×3H, CCH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 199.4 (C=O), 158.8 (CH), 129.3 (C), 107.5 (C), 100.7 (C), 81.6 (C), 78.5 (CH), 77.2 (C), 68.9 (C), 60.5 (CH_2), 49.4 (CH_3), 48.6 (CH_2), 30.6 (3×CH_3), 28.1 (C), 18.9 (CH_3), 18.8 (CH_3). IR (film): ν_{max} 3479 m, 2222 w, 1731 s, 1455 m, 1265 s, 1114 s, 1036 s cm^{-1}. MS: *m*/*z* (% relative intensity): 338 (M^+, 0.6), 175 (100), 147 (33), 119 (24), 115 (47), 91 (60). HRMS (ESI-TOF) calcd for $C_{18}H_{26}O_6Na$: 361.1619; found: 361.1629. $[\alpha]_D^{29}$ −29.73 (*c* 0.4, $CHCl_3$).

4.27. (+)-4,5-Dihydroxy-5-(hydroxymethyl)-2-phenylacetylenyl-2-cyclopentenone (*ent*-17Aa)

(2*R*,5*R*,6*R*,5′*R*)-*ent*-**16Aa** (86 mg, 0.238 mmol) was treated with 90% trifluoroacetic acid (1 mL) at 0 °C. The mixture was slowly warmed up to room temperature for 3.5 h. The solvent was freeze-dried overnight to give a crude product, which was purified by PLC (silica gel, 70% EtOAc in hexanes) to give *ent*-**17Aa** as a colorless viscous liquid (45.5 mg, 90% yield). ^{1}H NMR (300 MHz, acetone-d_6): δ 7.65 (br s, 1H, =C*H*), 7.61–7.50 (m, 2H, Ar*H*), 7.40–7.28 (m, 3H, Ar*H*), 4.78 (br s, 1H, C*H*OH), 3.90–3.0 (m, 5H, CH_2 and 3×O*H*). ^{13}C NMR (75 MHz, $CDCl_3$): δ 205.2 (C=O), 161.9 (CH), 131.7 (C), 131.5 (2×CH), 129.4 (C), 129.1 (CH), 128.5 (2×CH), 102.6 (C), 90.9 (C), 77.0 (CH), 74.7 (C), 64.5 (CH_2). IR (film): ν_{max} 3424 s, 3019 m, 2241 m, 1730 m, 1620 m cm^{-1}. MS: *m*/*z* (% relative intensity): 243 (M^+−1, 0.9), 125 (67), 78 (100). HRMS (ESI-TOF) calcd for $C_{14}H_{12}O_4Na$: 267.0632; found: 267.0646. $[\alpha]_D^{29}$ +16.0 (*c* 0.50, EtOH).

4.28. (+)-*tert*-2-Butylacetylenyl-4,5-dihydroxy-5-(hydroxymethyl)-2-cyclopentenone (*ent*-17Ab)

(2*R*,5*R*,6*R*,5′*R*)-*ent*-**16Ab** (69 mg, 0.292 mmol) was treated with 90% trifluoroacetic acid (1 mL) at 0 °C. The crude product was purified by PLC (silica gel, 60% EtOAc in hexanes) to give (+)-*ent*-**17Ab** as a white solid (23.3 mg, 97% yield, mp 98–101 °C). ^{1}H NMR (300 MHz, acetone-d_6): δ 7.38 (d, *J*=2.2 Hz, 1H, =C*H*), 4.89 (br, 1H, O*H*), 4.64 (br, 1H, C*H*OH), 4.50 (br, 1H, O*H*), 3.62 (br, 2H, CH_2), 3.58 (br, 1H, O*H*), 3.05 (s, 3×3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 203.6 (C=O), 161.6 (CH), 129.9 (C), 106.6 (C), 81.6 (C), 77.8 (CH), 70.6 (C), 76.6 (C), 65.4 (CH_2), 30.5 (3×CH_3). IR (Nujol): ν_{max} 3418 s, 1714 s, 1633 s, 1465 m, 1050 s, 757 s cm^{-1}. MS: *m*/*z* (% relative intensity): 223 (M^+, 2), 167 (31), 149 (100), 125 (26), 91 (51), 81 (29). HRMS

(ESI-TOF) calcd for $C_{12}H_{16}O_4Na$: 247.0938; found: 247.0928. $[\alpha]_D^{29}$ +21.84 (*c* 0.2, $CHCl_3$).

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