Supplementary Information

The case for a Diels-Alderase-free, bis-pericyclic, [4+2] dimerization in the biosynthesis of (±)-paracaseolide A

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Contents

I. General Experimental Protocols .............................................................. S2
II. Preparation procedures and characterization data for all key compounds ...... S3
III. Computational Methods ........................................................................... S17
IV. References for Supplementary Information ............................................. S42
V. Copies of NMR spectra
   1H and 13C NMR spectra of S2.................................................................. S43
   1H and 13C NMR spectra of 5a.................................................................. S45
   1H and 13C NMR spectra of 3a.................................................................. S47
   1H and 13C NMR spectra of 1a.................................................................. S49
   1H NMR spectra of S3............................................................................... S51
   1H and 13C NMR spectra of S4.................................................................. S52
   1H and 13C NMR spectra of S5.................................................................. S54
   1H and 13C NMR spectra of S6.................................................................. S56
   1H and 13C NMR spectra of 5b.................................................................. S58
   1H and 13C NMR spectra of 6b.................................................................. S60
   1H and 13C NMR spectra of 3b.................................................................. S62
   1H and 13C NMR spectra of 10b................................................................. S64
   Crude 1H NMR for dimerization of 6b at 35°C ........................................ S66
   1H and 13C NMR HSQC spectra of 7b-h....................................................... S70
   H/D exchange of 7b-h monitored by 1H NMR spectra................................ S74
   Crude 1H NMR for dehydration of 7b-h to 1b............................................. S75
   1H and 13C NMR spectra of 1b.................................................................. S76
   1H and 13C NMR spectra of 11.................................................................. S78
   1H and 13C NMR spectra of 10a................................................................. S80
   1H and 13C NMR spectra of 7a-h ............................................................... S82
   H/D exchange of 7b-h monitored by 1H NMR spectra............................... S84
   Crude 1H NMR for dehydration of 7b-h to 1b............................................. S85
I. General Experimental Protocols

NMR ($^1$H and $^{13}$C) spectra were recorded on Bruker Avance 500 (500 MHz) or Varian Inova 500 (500 MHz) spectrometers. $^1$H NMR chemical shifts (CDCl$_3$, CD$_3$OD) are referenced to TMS (0.00 ppm) and CHD$_2$OD (3.31 ppm), respectively. The designation "nfom" is used to denote non-first order multiplets. $^{13}$C NMR chemical shifts are referenced to chloroform (77.23 ppm) and methanol (49.15 ppm). The following format is used to report each resonance: chemical shift in ppm (multiplicity, J values (coupling constant(s)) in Hz, integral value, and assignment). Coupling constant analysis was aided by protocols we have reported elsewhere. The skeleton of some of the more complex structures are numbered to simplify identification of the proton assignment.

Infrared (IR) spectra were recorded of thin film samples on a ZnSe plate (ATR) on a Prospect MIDAC FT-IR spectrometer. Bands are reported in cm$^{-1}$.

MPLC refers to medium pressure liquid chromatography (50-200 psi) using hand-packed silica gel columns (25-35 µm, 60 Å pores) and a Waters HPLC pump outfitted with a Waters R401 differential refractive index detector. Flash chromatography was carried out on columns packed with E. Merck silica gel (40-63 µm).

Mass spectrometric measurements were made: i) at low resolution on an Agilent 5975 GC-MS instrument using an electron impact ionization method at 70 eV and ii) at high resolution on a Bruker BioTOF II instrument using electrospray ionization and PEG as an internal calibrant.

Optical rotation values were measured on a Rudolph Research Analytical (Autopol III) instrument.

Reactions needing anhydrous conditions were carried out under an atmosphere of argon or nitrogen in flame- or oven-dried glassware. Anhydrous diethyl ether, THF, toluene, and methylene chloride were collected after being passed through a column of activated alumina immediately prior to use.
II. Preparation procedures and characterization data for all key compounds

Preparation of 4-bromo-2-methylfuran (4)

Furan (2 mL) was added to a solution of 5-(tetrahydro-2H-pyran-2-yloxy)pent-3-yn-2-one\(^1\) (495 mg, 2.72 mmol) in pentane (8 mL). The solution was cooled to 0 °C in an ice bath and concentrated aqueous hydrobromic acid (48%, 0.4 mL) was added. The reaction mixture was stirred at room temperature for 18 h and a solution of saturated aqueous NaHCO\(_3\) was added. The resulting mixture was extracted with pentane (5 mL x 2). The combined organic layers were directly applied to a silica gel column and eluted with pentane. The eluent was concentrated on a rotary evaporator in an ambient temperature bath to a volume of ca. 0.3 mL. NMR analysis of this colorless solution allowed estimation of the percent content of 4-bromo-2-methylfuran 4 (est. 286 mg, 1.78 mmol, 65%). The \(^1\)H NMR and MS data were consistent with the structure of this known compound.\(^1\) This material was carried forward into the next reaction.

Preparation of (E)-2-methyl-4-(tetradec-1-enyl)furan (S2) via (E)-2-(tetradec-1-enyl)benzo[d][1,3,2]dioxaborole (S1)

Under an Ar atmosphere, a 20 mL vial was charged with catecholborane (2.3 mL, 19.2 mmol) and tetradecyne (4.7 mL, 19.1 mmol) and then sealed with a Teflon cap. The mixture was heated to 55 °C for 15 h. The resulting colorless liquid sample of S1 was used directly without further purification.

To a solution of 4-bromo-2-methylfuran (4, 0.58 g, 3.6 mmol) in \(i\)-PrOH/H\(_2\)O (11.5 mL/5.6 mL) was added Pd(dppf)Cl\(_2\) (53.5 mg, 0.07 mmol, 2 mol%) and \(t\)-BuNH\(_2\) (1.15 mL, 10.9 mmol). (E)-2-(Tetradec-1-enyl)benzo[d][1,3,2]dioxaborole (S1, 3.8 mL) was added dropwise. The headspace was flushed with N\(_2\) and the vessel was sealed with a Teflon cap. The mixture was heated to 80 °C for 26 h. The resulting mixture was directly filtered through a short plug of Celite\(^\circledR\) (EtOAc elution), the filtrate concentrated, and the residue chromatographed on silica (pure hexanes) to afford (E)-2-methyl-4-(tetradec-1-enyl)furan (S2, 0.95 g, 3.44 mmol, 96%) as a colorless oil.

\(^1\)H NMR (CDCl\(_3\), 500 MHz) \(\delta\) 7.19 (d, \(J = 0.4\) Hz, 1H, \(H5\)), 6.16 (dt, \(J = 15.7, 1.6\) Hz, 1H, ArCH=CHCH\(_2\)), 6.10 (dq, \(J = 0.4\) and 1.0 Hz, 1H, \(H3\)), 5.86 (dt, \(J = 15.7, 6.9\) Hz, 1H, ArCH=CHCH\(_2\)), 2.25 (d, \(J = 1.0\) Hz, 3H, Ar-CH\(_3\)), 2.12 (ddt, \(J = 7.0, 1.5, 7.0\) Hz, 2H, ArCH=CHCH\(_2\)), 1.41 (br quintet, 2H, CH=CHCH\(_2\)CH\(_2\)), 1.34–1.19 (m, 18H), and 0.88 (t, \(J = 7.0\) Hz, 3H, CH\(_2\)CH\(_3\)).

\(^13\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 153.1, 137.9, 130.5, 125.7, 119.8, 103.7, 33.1, 32.2, 29.9 (4C), 29.8, 29.7, 29.6, 29.5, 22.9, 14.3, and 13.8.

IR (neat): 2924, 2853, 1687, 1606, 1544, 1464, 1381, 1126, 959, 917, 797, and 735 cm\(^{-1}\).

GC-LRMS (ES, 70 eV): \(t_R = 10.08\) min. \(m/z\): 276 (M\(^+\)), 135 (M\(^+\)-C\(_{10}\)H\(_{21}\)) and 121 (M\(^+\)-C\(_{11}\)H\(_{23}\)).
Preparation of (E)-trimethyl(5-methyl-3-(tetradec-1-enyl)furan-2-yl)silane (5a)

To a dry 100 mL flask was added (E)-2-methyl-4-(tetradec-1-enyl)furan (S2, 0.95 g, 3.44 mmol) and THF (20 mL). The headspace was flushed with N₂ and the mixture was cooled to -78 °C in a dry ice-acetone acetone bath. n-BuLi (2.7 mL, 6.75 mmol, 2.5 M solution in hexanes) was added dropwise. The mixture was allowed to warm to -10 °C over 40 min, and freshly distilled TMSCl (0.74 g, 6.8 mmol) was added. The mixture was allowed to stir at room temperature for 1 h and saturated aqueous NH₄Cl was added. The water layer was extracted with diethyl ether. The combined organic phase was dried over Na₂SO₄, filtered, and concentrated to give (E)-trimethyl(5-methyl-3-(tetradec-1-enyl)furan-2-yl)silane (5a, 1.0 g, 3.0 mmol, 86%) as a colorless oil that was used without further purification.

1H NMR (CDCl₃, 500 MHz) δ 6.31 (ddt, J = 15.6, 0.3, 1.5 Hz, 1H, ArCH=CH), 6.12 (br s, 1H, ArH), 5.86 (dt, J = 15.5, 7.0 Hz, 1H, Ar=CH), 2.27 (d, J = 0.9 Hz, 3H, Ar-C₃H₃), 2.13 (ddt, J = 7.0, 1.6, 7.0 Hz, 2H, CH=CHCH₂), 1.45–1.35 (m, 2H, CH=CHCH₂C₂H₅), 1.34–1.20 (m, 18H), and 0.88 (t, J = 6.9 Hz, 3H, CH₂C₃H₇), and 0.29 (s, 9H, Si(C₃H₃)₃).

13C NMR (125 MHz, CDCl₃) δ 156.4, 154.3, 135.5, 130.7, 104.0, 33.3, 32.2, 29.9 (2C), 29.8, 29.7 (2C), 29.6, 29.4 (2C), 22.9, 14.4, 13.9, and 0.6.

IR (neat): 2954, 2923, 2853, 1248, 957, 841, and 794 cm⁻¹.

GC-LRMS (ES, 70 eV): tR = 10.90 min. m/z: 348 (M⁺), 333 (M⁺-CH₃), 275 (M⁺-TMS), and 73 (TMS⁺).

Preparation of (±)-(E)-5-hydroxy-5-methyl-3-(tetradec-1-enyl)furan-2(5H)-one (3a)

Methylene blue (1 mg) was added to a solution of (E)-trimethyl(5-methyl-3-(tetradec-1-enyl)furan-2-yl)silane (5a, 0.90 g, 2.59 mmol) in CH₂Cl₂ (50 mL) in a round bottomed flask. The mixture was cooled to -40 °C in a dry ice-acetone bath. O₂ was introduced into the solution via a fritted glass tube. A 175 W mercury lamp was placed directly above the reaction flask (distance < 5 cm). After 1.5 h full consumption of furan 5a was confirmed by TLC analysis. The mixture was concentrated and purified by flash column chromatography to give (E)-5-hydroxy-5-methyl-3-(tetradec-1-enyl)furan-2(5H)-one (3a) as a colorless waxy solid (602 mg, 1.95 mmol, 76%), whose spectral data closely matched those reported for this butenolide.²,³,⁴,⁵,⁶

1H NMR (500 MHz, CDCl₃) δ 6.84 (br dt, J = 15.8, 7.1 Hz, 1H, CH=CHCH₂), 6.83 (br s, 1H, C(OH)(CH₃)CH=CHC), 6.07 (dt, J = 15.8, 1.7 Hz, 1H, CH=CHCH₂), 2.87 (br s, 1H, -OH), 2.17 (dt, J = 1.6, 7.1, 7.4 Hz, 2H, CH=CHCH₂), 1.71 (s, 3H, C(OH)-CH₃), 1.47–1.40 (m, 2H, CH=CHCH₂CH₂), 1.35–1.21 (m, 18H), and 0.88 (t, J = 7.0 Hz, 1H, CH₂CH₃).

1³C NMR (125 MHz, CDCl₃) δ 170.1, 144.0, 141.4, 131.1, 118.0, 104.1, 33.7, 32.1, 29.9 (3C), 29.8, 29.7, 29.6, 29.5, 28.9, 25.1, 22.9, and 14.3.

IR (neat): 3356, 2924, 2853, 1746, 1662, 1463, 1372, 1260, 1170, 1106, 1056, 971, and 931 cm⁻¹.

HRMS (ESI-TOF): Calcd for (C₁₉H₃₃O₃)⁺ 309.2424. Found: 309.2412

mp 36–42 °C.
Preparation of (±)-paracaseolide A

\((1\alpha R,5\alpha S,5aS,7aS,7bR,7cS)-\text{rel-(±)}-5\)-dodecyl-\(1\alpha,5,5a,7a,7b,7c\)-hexahydro-\(1\alpha,7a\)-dimethyl-\(5a\)-(1E)-1-tetr decen-1-yldifuro[2,3,4-cd:4',3',2'-hi]isobenzofuran-3,6-dione \([(±)-1a]\) and its C5-epimer

\((1\alpha R,5S,5aS,7aS,7bR,7cS)-\text{rel-(±)}-5\)-dodecyl-\(1\alpha,5,5a,7a,7b,7c\)-hexahydro-\(1\alpha,7a\)-dimethyl-\(5a\)-(1E)-1-tetr decen-1-yldifuro[2,3,4-cd:4',3',2'-hi]isobenzofuran-3,6-dione \([(±)-S3]\)

\((±)-(E)-5\)-Hydroxy-\(5\)-methyl-3-(tetradec-1-enyl)furan-2(5H)-one \((3a, 33.2 \text{ mg}, 0.11 \text{ mmol})\) was placed in a 1 mL vial with a Teflon cap. The headspace was flushed with Ar. The reaction vial was heated to 110 °C for 43 h. The crude mixture was directly subjected to flash column chromatography on silica gel (hexanes:ethyl acetate = 12:1, then 5:1, then 3:1) to give (±)-paracaseolide A \((1a, 13.4 \text{ mg}, 42\%)\) and (±)-\(5\)-epi-paracaseolide A \((S3, 2.0 \text{ mg}, 7\%)\), each as a white powder.

\((±)-5\)-epi-paracaseolide A \((S3):^{2,3,4,5,6,7}

\(^1\)H NMR (CDCl\(_3\), 500 MHz): \(\delta 7.25\) (dd, \(J = 7.6, 3.2\) Hz, 1H, \(H4\)), 5.83 (dt, \(J = 15.7, 6.9\) Hz, 1H, \(HC=CHCH2\)), 5.49 (dt, \(J = 15.8, 1.5\) Hz, 1H, \(HC=CHCH2\)), 3.37 (dd, \(J = 9.5, 3.3\) Hz, 1H, \(H5\)), 3.20 (d, \(J = 9.9\) Hz, 1H, \(H7b\)), 2.20–2.07 (m, 3H, \(H5, CH=CHCH2\)), 1.75–1.64 (m, many H), 1.20–1.05 [m, 1H, \(C(5)CH(CHa)Hb\)], 0.88 [t, \(J = 7.0\) Hz, 6H, \((CH3CH2)2\)].

\(^{13}\)C NMR (CDCl\(_3\), 125 MHz) \(δ 175.3, 166.4, 144.9, 135.3, 129.5, 126.5, 115.6, 114.0, 58.5, 50.5, 46.9, 45.3, 32.9, 32.1 (2x), 29.91, 29.88 (2x), 29.87 (2x), 29.86 (2x), 29.84 (2x), 29.77, 29.64 (2x), 29.58 (2x), 29.3, 29.2, 28.4, 28.2, 26.8, 25.9, 22.9 (2x), and 14.3 (2x).

IR (neat): 2923, 2853, 1774, 1465, 1390, 1312, 1272, 1129, 1056, and 913 cm\(^{-1}\).

HRMS (ESI-TOF): Calcd for \((C_{38}H_{62}NaO_5)^+\) 621.4489, Found: 621.4499.

mp 59–64 °C.

\((±)-5\)-epi-paracaseolide A \((S3):^{4,5}

\(^1\)H NMR (CDCl\(_3\), 500 MHz): \(δ 6.98\) (dd, \(J = 4.2, 3.5\) Hz, 1H, \(H4\)), 5.69 (dt, \(J = 15.7, 6.9\) Hz, 1H, \(HC=CHCH2\)), 5.43 (dt, \(J = 15.7, 1.4\) Hz, 1H, \(HC=CHCH2\)), 3.27 (ddd, \(J = 9.9, 3.3, 2.0\) Hz), 3.20 (d, \(J = 9.9\) Hz, 1H, \(H7b\)), 2.20–2.07 (m, 3H, \(H5, CH=CHCH2\)), 2.01 [ddd, \(J = 13.8, 12.1, 10.2, 4.6\) Hz, 1H, \(C(5)CH(CHa)Hb\)], 1.75 (ddd, \(J = 13.6, 10.6, 6.0, 3.0\) Hz, 1H, \(C(5)CH(CHa)Hb\)).
Preparation of 1-(5-methylfuran-3-yl)propan-1-ol (S4)

An oven-dried 250 mL round bottom flask was charged with dry THF (75 mL). The flask was cooled to -78 °C before dropwise addition of a solution of t-BuLi (38 mL, 1.7 M, in hexanes; 65 mmol).

4-Bromo-2-methylfuran (4) containing ca. 5 wt% of pentane (4.98 g, 29 mmol) was added dropwise at -78 °C to form an orange solution. This mixture was stirred at -78 °C for 10 min before dropwise addition of dry propionaldehyde (6 mL, 84 mmol). The reaction mixture was allowed to warm to room temperature, quenched with aqueous NH₄Cl solution, and extracted with ethyl acetate. The organic layer was washed with brine, dried with Na₂SO₄, filtered, concentrated, and subjected to flash column chromatography on silica gel (hexanes:ethyl acetate = 5:1) to give 1-(5-methylfuran-3-yl)propan-1-ol (S4, 3.8 g, 95% yield) as a colorless liquid.

1H NMR (500 MHz, CDCl₃) δ 7.22 (br s, 1H, H2), 5.98 (br s, 1H, H4), 4.49 (br t, J = 6.5 Hz, 1H, CH(OH)CH₂), 2.27 (s, 3H, ArCH₃), 1.75 (ddq, J = 14, 7.4, 7.4 Hz, 1H, CH₃CH(CH₃)₃), 1.71 (ddq, J = 14, 7.2, 7.2 Hz, 1H, CH₃CH₂CH₃), 1.71 (br s, 1H, OH), and 0.93 (t, J = 7.5 Hz, 3H, CH₂CH₃).

13C NMR (125 MHz, CDCl₃) δ 153.1, 137.4, 129.9, 104.6, 68.8, 30.8, 13.8, and 10.2.

IR (neat): 3384, 2964, 2933, 2877, 1555, 1452, 1381, 1266, and 1208 cm⁻¹.

HRMS (ESI-TOF): Calcd for (C₁₉H₃₃O₃)⁺ 309.2424. Found: 309.2412.

GC-LRMS (ES, 70 eV): tᵣ = 4.08 min. m/z: 140 (M⁺), 111 (M⁺-CH₂CH₃), and 83 (M⁺-COCH₂CH₃).

Preparation of tert-butyldimethyl(1-(5-methylfuran-3-yl)propoxy)silane (S5)

To a CH₂Cl₂ (150 mL) solution of 1-(5-methylfuran-3-yl)propan-1-ol (S4, 3.6 g, 26 mmol) was added TBSCI (8.8 g, 58 mmol) and imidazole (3.9 g, 58 mmol) at room temperature. The reaction mixture was stirred for 20 h, and the resulting slurry was filtered through a cotton plug, using DCM to wash the solid filter cake. The filtrate was concentrated and the residue redissolved in ethyl acetate. This solution was washed with deionized water, dried over Na₂SO₄, filtered, and concentrated. The residue was purified using flash column chromatography on silica gel (hexanes:ethyl acetate = 12:1) to give tert-butyldimethyl(1-(5-methylfuran-3-yl)propoxy)silane (S5, 5.9 g, 90% yield) as a colorless liquid.

1H NMR (500 MHz, CDCl₃) δ 7.11 (br s, 1H, H2), 5.90 (br s, 1H, H4), 4.51 (t, J = 6.0 Hz, 1H, CH(OTBS)CH₂CH₃), 2.25 (s, 3H, ArCH₃), 1.67 (ddq, J = 6.7, 13.9, 7.4 Hz, 1H, CH₃CH(CH₃)₃), 1.61 (ddq, J = 5.8, 13.9, 7.6 Hz, 1H, CH₂H₂CH₃), 0.88 (s, 9H, SiC(CH₃)₃), 0.86 (s, 9H, SiC(CH₃)₃), 0.04 (s, 3H, SiMe₃), and −0.04 (s, 3H, SiMe₃).

13C NMR (125 MHz, CDCl₃) δ 152.4, 137.1, 130.8, 105.0, 69.3, 32.4, 26.1, 18.5, 13.9, 9.9, −4.4, and −4.7.

IR (neat): 2958, 2930, 2858, 1473, 1255, 1059, 1017, 836, and 776 cm⁻¹.

GC-LRMS (ES, 70 eV): tᵣ = 6.09 min. m/z: 239 (M⁺-CH₃), 225 (M⁺-CH₂CH₃), and 197 (M⁺-C(CH₃)₃).
Preparation of 1-(2-(tert-butyldimethylsilyl)-5-methylfuran-3-yl)propan-1-ol (S6)

To a solution of tert-butyldimethyl(1-(5-methylfuran-3-yl)propoxy)silane (S5, 5.4 g, 21 mmol) in dry THF (330 mL) was added HPMA (4.2 mL, 24 mmol) at room temperature. The reaction flask was then cooled to 0 °C followed by dropwise addition of n-BuLi solution (15 mL, 2.5 M in hexanes). The reaction solution was allowed to warm to room temperature and stirred for 45 min before being quenched by the addition of Et2O and aqueous NH4Cl solution. The organic layer was washed with brine, dried with Na2SO4, and concentrated. The residue was purified using flash column chromatography on silica gel (hexanes:ethyl acetate = 5:1) to give 1-(2-(tert-butyldimethylsilyl)-5-methylfuran-3-yl)propan-1-ol (S6, 4.67 g, 86% yield) as an off-white solid.

$^1$H NMR (500 MHz, CDCl3) δ 6.05 (s, 1H, Ar-H), 4.58 (dt, $J = 2.4, 6.9$ Hz, 1H, CH(OH)), 2.28 (s, 3H, Ar-CH3), 1.82 (ddq, $J = 7.3, 14.3, 7.3$ Hz, 1H, CH(OH)CH=CH3), 1.66 (ddq, $J = 7.3, 14.3, 7.3$ Hz, 1H, CH(OH)CH3), 0.92 (s, 9H, SiC(CH3)3), 0.91 (t, $J = 7.3$ Hz, 3H, CH2C(CH3), 0.27 (s, 3H, SiMe3), and 0.25 (s, 3H, SiMe2).  

$^{13}$C NMR (125 MHz, CDCl3) δ 156.9, 152.7, 140.9, 104.2, 68.6, 31.2, 26.7, 17.4, 14.1, 10.83, –4.84 and –5.14.

IR (neat): 3366, 2956, 2930, 2858, 1606, 1523, 1471, 1463, 1249, 836, and 826 cm$^{-1}$.

HRMS (ESI-TOF): Calcd for (C14H26NaO2Si)$^+$ 277.1594. Found: 277.1596.

mp 52.1–56.5 °C.

Preparation of E- and Z-tert-butyldimethyl(5-methyl-3-(prop-1-en-1-yl)furan-2-yl)silanes (5b)

To a solution of 1-(2-(tert-butyldimethylsilyl)-5-methylfuran-3-yl)propan-1-ol (S6, 1.0 g, 4 mmol) in dry toluene (80 mL) was added $p$-toluenesulfonic acid (15 mg, 0.08 mmol) and 4 Å molecular sieves (ca. 1 g) at room temperature. A reflux condenser was attached and the reaction flask was placed in a 110 °C oil bath and stirred for 2 h. The reaction mixture was then cooled to room temperature and filtered through Celite. The filtrate was concentrated and the residue purified with flash column chromatography on silica gel (pure hexanes) to give a coeluting, 5:1 E/Z mixture of tert-butyldimethyl(5-methyl-3-(prop-1-en-1-yl)furan-2-yl)silane (5b, 0.73 g, 78% yield) as a colorless liquid.

(E)-tert-Butyldimethyl(5-methyl-3-(prop-1-en-1-yl)furan-2-yl)silane (E-5b):

$^1$H NMR (500 MHz, CDCl3) δ 6.33 (ddq, $J = 0.6, 15.5, 1.7$ Hz, 1H, CH=CHCH3), 6.11 (dq, $J = 0.5, 1.0$ Hz, 1H, Ar-H), 5.87 (dq, $J = 15.5, 6.6$ Hz, 1H, CH=CHCH3), 2.26 (d, $J = 0.9$ Hz, 3H, Ar-CH3), 1.81 (dd, $J = 1.7, 6.7$ Hz, 3H, CH=CHCH3), 0.90 (s, 9H, SiC(CH3)3), and 0.27 (s, 6H, Si(CH3)2).

$^{13}$C NMR (125 MHz, CDCl3) δ 156.5, 152.9, 136.5, 124.9, 122.9, 103.9, 26.7, 18.8, 17.8, 13.9, and –5.29.

GC-LRMS (ES, 70 eV): $t_R = 6.35$ min. $m/z$: 236 (M$^+$), and 179 (M$^+$-C(CH3)).

(Z)-tert-Butyldimethyl(5-methyl-3-(prop-1-en-1-yl)furan-2-yl)silane (Z-5b):

$^1$H NMR (500 MHz, CDCl3) δ 6.35 (ddq, $J = 0.6, 15.5, 1.7$ Hz, 1H, CH=CHCH3), 6.11 (dq, $J = 0.5, 1.0$ Hz, 1H, Ar-H), 5.87 (dq, $J = 15.5, 6.6$ Hz, 1H, CH=CHCH3), 2.26 (d, $J = 0.9$ Hz, 3H, Ar-CH3), 1.81 (dd, $J = 1.7, 6.7$ Hz, 3H, CH=CHCH3), 0.90 (s, 9H, SiC(CH3)3), and 0.27 (s, 6H, Si(CH3)2).
**1H NMR** (500 MHz, CDCl3) δ 6.33 (ddq, J = 0.5, 11.4, 1.8 Hz, 1H, CH=CHCH3), 6.18 (dq, J = 0.5, 0.9 Hz, 1H, Ar-H), 5.57 (dq, J = 7.1, 11.5 Hz, 1H, CH=CHCH3), 2.30 (d, J = 0.9 Hz, 3H, Ar-CH3), 1.84 (dd, J = 1.8, 7.1 Hz, 3H, CH=CHCH3), 0.90 (s, 9H, SiC(CH3)3), and 0.25 (s, 6H, Si(CH3)2).

**13C NMR** (125 MHz, CDCl3) δ 156.5, 152.9, 136.5, 125.2, 122.1, 107.3, 26.7, 18.8, 17.8, 14.9, and –5.29.

**GC-LRMS** (ES, 70 eV): tR = 6.22 min. m/z: 236 (M+), and 179 (M+-C(CH3)3).

**IR** (neat, of the E/Z mixture of alkenes): 2954, 2928, 2857, 1604, 1502, 1463, 1249, 1111, and 957 cm⁻¹.

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**Preparation of 5-hydroxy-5-methyl-3-(prop-1-en-1-yl)furan-2(5H)-one (3b) via (2Z)-tert-butyldimethylsilyl 4-oxo-2-(prop-1-en-1-yl)pent-2-enoate (6b).**

Methylene blue (5 mg) was added to a solution of tert-butyldimethyl(5-methyl-3-(prop-1-en-1-yl)furan-2-yl)silane (5b, 1.83 g, 7.7 mmol) in CH2Cl2 (250 mL) in a round bottomed flask. The mixture was cooled to 0 °C in an ice-water bath. O2 was introduced into the solution by slow bubbling through a fritted glass tube fitted into a stopper or septum that contained a vent needle. A common 75 W incandescent light bulb was placed directly above the reaction flask (distance < 5 cm). (See photo below of a typical set-up for the experiment.) Ice was periodically added to maintain sub-ambient temperature. After 7 h full consumption of furan 5b was confirmed by TLC analysis. The mixture was concentrated through a short plug of silica gel with CH2Cl2 elution to give a 6:1 E/Z crude mixture of (2Z)-tert-butyldimethylsilyl 4-oxo-2-(prop-1-en-1-yl)pent-2-enoate (6b) as a pale yellow liquid (2.55 g, 123% mass recovery). Because of the propensity of this silyl ester to undergo desilylation during attempts at more careful chromatographic treatments, this crude mixture was directly used for dimerization studies without further purification.
Paracaseolide A Biosynthesis, Wang and Hoye

Supplementary Information

Page S9 of S85

(2E)-tert-butyldimethylsilyl 4-oxo-2-((1E)-prop-1-en-1-yl)pent-2-enoate (Z-6b):

1H NMR (500 MHz, CDCl3) δ 6.12 (ddq, J = 0.6, 15.7, 6.2 Hz, 1H, CH3), 6.08 (br d, J = 15.7 Hz, 1H, CH=CH2CH3), 5.97 (br s, 1H, CHC(=O)CH3), 2.23 (s, 3H, C(=O)CH3), 1.88 (br d, J = 5.2 Hz, 3H, CHCH3), 0.94, (s, 9H, SiMe2C(CH3)3), and 0.42 (s, 6H, Si(CH3)2C(CH3)3).

13C NMR (125 MHz, CDCl3) δ 196.3, 168.2, 147.0, 138.2, 128.6, 122.6, 30.5, 25.7, 19.3, 17.9, and -4.7.

GC-LRMS (ES, 70 eV): tR = 7.54 min. m/z: 268 (M+), 253 (M+-CH3) and 211 (M+-C(CH3)3).

IR (neat, of the E/Z mixture of alkenes): 2956, 2932, 2859, 1716, 1689, 1582, 1384, 1375, 1253, 1191, and 961 cm⁻¹.

Hydrolysis of TBS-esters 6b to butenolides 3b.

A sample of the crude mixture of 3E- and 3Z-(2Z)-tert-butyldimethylsilyl 4-oxo-2-(prop-1-en-1-yl)pent-2-enoates (6b, 156 mg, 0.58 mmol) and wet CH2Cl2 (12 mL, 1 drop of water was added) were combined in 20 mL glass vial. Silica gel (500 mg) and a stir bar were added, and the slurry was stirred at room temperature for 48 h. This mixture was filtered. The residue was washed with CH2Cl2 three times, and combined with the filtrate. This combined solution was then concentrated and purified using column chromatography on silica gel (hexanes:ethyl acetate = 5:1 to 3:1 to 1:1) to give a 7:1 E:Z mixture of 5-hydroxy-5-methyl-3-(prop-1-en-1-yl)furan-2(5H)-one (3b, 52 mg, 58% yield) as a pale yellow oil. The following NMR data were extracted from this mixture.

(E)-5-Hydroxy-5-methyl-3-(prop-1-en-1-yl)furan-2(5H)-one (E-3b):

1H NMR (500 MHz, CDCl3) δ 6.83 (d, J = 0.6 Hz, 1H, H4), 6.81 (dq, J = 15.5, 6.9 Hz, 1H, H2'), 6.08 (ddq, J = 0.6, 15.9, 1.8 Hz, 1H, H1'), 1.86 (ddd, J = 0.6, 1.7, 6.8 Hz, 3H, H3'), and 1.69 (s, 3H, C5-C(CH3)).

13C NMR (125 MHz, CDCl3) δ 170.2, 144.1, 136.0, 130.9, 119.4, 104.2, 25.0, and 19.3.

HRMS (ESI-TOF): Calcd for (C8H10NaO3)+ 177.0522. Found: 177.0524.

IR (neat, of the E/Z mixture of alkenes): 3370, 2994, 2939, 1742, 1665, 1445, 1414, 1167, 1114, 1055, 967, and 925 cm⁻¹.

(Z)-5-Hydroxy-5-methyl-3-(prop-1-en-1-yl)furan-2(5H)-one (Z-3b):

1H NMR (500 MHz, CDCl3) δ 7.01 (br s, 1H, H4), 6.14 (ddq, J = 0.5, 11.5, 7.0 Hz, 1H, H2'), 6.07 (ddq, J = 0.9, 12.0, 1.7 Hz, 1H, H1'), 1.86 (ddd, J = 0.6, 1.5, 6.9 Hz, 3H, H3'), and 1.74 (s, 3H, C5-C(CH3)).

13C NMR (125 MHz, CDCl3) δ 171.5, 146.4, 135.9, 129.8, 117.3, 104.9, 25.1, and 16.0.

HRMS (ESI-TOF): Calcd for (C9H10NaO3)+ 179.0520. Found: 179.0520.

IR (neat, of the E/Z mixture of alkenes): 3370, 2994, 2939, 1742, 1665, 1445, 1414, 1167, 1114, 1055, 967, and 925 cm⁻¹.
Preparation of bis(tert-butyldimethylsilyl)
(3R,4S,5R,6R)-5,6-diacetyl-3-methyl-4-(((E)-prop-1-en-1-yl)cyclohex-1-ene-1,4-dicarboxylate (10b).

To a small glass vial was added the crude mixture of E/Z isomers of (2Z)-tert-butyldimethylsilyl
4-oxo-2-(prop-1-en-1-yl)pent-2-enoates (6b, 158 mg, 0.59 mmol). The headspace was flushed with N₂ and
the vial was sealed with a Teflon-lined cap. The reaction mixture was placed in a 135 °C oil bath for 17 h to
produce a mixture of 151 mg of bis(tert-butyldimethylsilyl)
(3R,4S,5R,6R)-5,6-diacetyl-3-methyl-4-(((E)-prop-1-en-1-yl)cyclohex-1-ene-1,4-dicarboxylate (10b) and
tert-butyldimethylsilyl (Z)-4-oxo-2-((Z)-prop-1-en-1-yl)pent-2-enoate (Z-6b). The small mass loss was due
to the fact that some of the Z-6b vaporized and re-condensed on the cap and was not collected). This crude
mixture was used directly without purification.

¹H NMR (500 MHz, CDCl₃) δ 6.92 [dd, J = 3.1, 1.1 Hz, 1H, =CHCH(CH₃)], 5.56 (dq, J = 15.9, 6.5 Hz, 1H,
CH=CHCH₃), 5.23 (dq, J = 15.8, 1.7 Hz, 1H, CH=CHCH₃), 3.75 (dd, J = 2.0, 2.0, 1.3 Hz, 1H, H₇c), 3.70
(d, J = 2.2 Hz, 1H, H₇b), 3.38 [ddq, J = 3.0, 1.9, 7.4 Hz, 1H, H₅], 2.27 (s, 3H, C₆(=O)CH₃), 2.26 (s, 3H,
C₆(=O)CH₃), 1.60 (dd, J = 6.5, 1.6 Hz, 3H, CH=CHCH₃), 1.28 [d, J = 7.4, 3H, C₅(CH₃)], 0.95 [s, 9H,
-Si₆Me₂C(CH₃)₃], 0.94 [s, 9H, -Si₆Me₂C(CH₃)₃], 0.29, 0.274, 0.272, and 0.26 (four singlets, 4 × 3H,
Si(CH₃)₂C(CH₃)₃).

¹³C NMR (125 MHz, CDCl₃) δ 207.2, 206.3, 174.2, 166.5, 147.9, 129.2, 127.8, 125.8, 58.3, 52.3, 48.7, 34.7,
29.1, 28.1, 25.9, 25.8, 18.2, 18.0, 17.9, 16.7, -4.6, -4.7, -4.79, and -4.80.

IR (neat) 2922, 2354, 2320, 1767, 1712, 1454, 1387, 1250, 1196, 1164, 1056, 1021, 973, 919, and 836 cm⁻¹.

HRMS (ESI-TOF): Calcd for (C₂₈H₆₈NaO₆Si₂)⁺ 559.2882. Found: 559.2895.
Dimerization experiment of \((2Z)\)-tert-butyldimethylsilyl 4-oxo-2-(prop-1-en-1-yl)pent-2-enoate (6b) at ambient temperature (35 °C)

To a small glass vial was added a DCM solution of the crude mixture of E/Z isomers (ca. 5.5:1) of (2Z)-tert-butyldimethylsilyl 4-oxo-2-(prop-1-en-1-yl)pent-2-enoates (6b) and bis(2-ethylhexyl) phthalate (DEHP) as an internal standard. The DCM was evaporated. The relative initial quantity of the three components in the resulting neat mixture was measured by \(\text{H}^1\) NMR spectroscopic analysis of an aliquot. The headspace of the vial was flushed with N\(_2\) and the vial was sealed with a Teflon-lined cap. The reaction mixture was placed in a 35 °C oil bath for 10 days. The crude reaction mixture was directly subjected to \(\text{H}^1\) NMR analysis. The relative amount of the four components was calculated relative to the DEHP proton resonances. The crude \(\text{H}^1\) NMR spectra at \(t = 0\) and \(t = 10\) days as well as expansions are provided on pages S66-S69.

Preparation of \((3S,4R,7R,7aS)\)-4-acetyl-3-hydroxy-3,7-dimethyl-1-oxo-7a-((E)-prop-1-en-1-yl)-1,3,3a,4,7,7a-hexahydroisobenzofuran-5-carboxylic acid (7b-h).

To a 20 mL glass vial was added the bis(tert-butyldimethylsilyl) ester 10b (75 mg, 0.14 mmol), CDCl\(_3\) (5 mL), and HOAc (1 mL). The reaction mixture was stirred at room temperature for 24 h. The solution was concentrated and the residue purified by flash column chromatography (hexanes:ethyl acetate:acetic acid = 50:50:1) to give (3S,4R,7R,7aS)-4-acetyl-3-hydroxy-3,7-dimethyl-1-oxo-7a-((E)-prop-1-en-1-yl)-1,3,3a,4,7,7a-hexahydroisobenzofuran-5-carboxylic acid (7b-h, 31 mg, 72% yield) as an off-white solid. This material showed marginal solubility in CDCl\(_3\), but the NMR spectra in that solvent were relatively sharp. They also indicated the presence of at least three distinct species, the major of which comprised >90% of the spectral intensity.
Presumably this reflects the presence of epimeric acylals and/or open and closed species among the various ketoacids. The sample was much more soluble in CD3OD, but the spectra were quite broad, suggestive of dynamic processes.

\[ \text{\textbf{1H NMR}} \ (500 \text{ MHz, CDCl}_3) \ \delta \ 7.07 \ [\text{dd}, \ J = 2.1, 2.1 \text{ Hz}, 1\text{H}, \text{C}=\text{CHCH(CH}_3)]_\text{3}], 5.76 \ (\text{dq}, \ J = 16.0, 6.3 \text{ Hz}, 1\text{H}, \text{CH}=\text{CHCH}_3), 5.30 \ (\text{dq}, \ J = 15.7, 1.8 \text{ Hz}, 1\text{H}, \text{CH}=\text{CHCH}_3), 3.70 \ (\text{br s}, 1\text{H}, H7c), 2.99-2.90 \ (\text{m}, 2\text{H}, H7b \text{ and } OH), 2.57 \ (\text{br s}, 1\text{H}, H5), 2.29 \ (s, 3\text{H}, C(=O)CH_3), 1.81 \ (s, 3\text{H}, C(OH)CH_3), 1.67 \ (\text{dd}, \ J = 6.4, 1.6 \text{ Hz}, 3\text{H}, \text{CH}=\text{CHCH}_3), \text{ and } 1.21 \ [\text{d}, \ J = 7.5, 3\text{H}, C5(CH_3)]. \]

\[ \text{\textbf{1H NMR}} \ (500 \text{ MHz, CD}_3\text{OD}) \ \delta \ 6.89 \ [\text{br s}, 1\text{H}, \text{C}=\text{CHCH(CH}_3)]_\text{3}], 5.68 \ (\text{dq}, \ J = 15.7, 6.3 \text{ Hz}, 1\text{H}, \text{CH}=\text{CHCH}_3), 5.31 \ (\text{br dq}, \ J = 15.9, 1.7 \text{ Hz}, 1\text{H}, \text{CH}=\text{CHCH}_3), 3.68 \ (\text{br s}, 1\text{H}, H7c), 2.94 \ (\text{br s}, 1\text{H}, H7b), 2.56 \ (\text{br s}, 1\text{H}, H5), 2.28 \ (\text{br s}, 3\text{H}, C(=O)CH_3), 1.75 \ (\text{br s}, 3\text{H}, C(OH)CH_3), 1.63 \ (\text{dd}, \ J = 6.5, 1.2 \text{ Hz}, 3\text{H}, \text{CH}=\text{CHCH}_3), \text{ and } 1.17 \ [\text{br d}, \ J = 7.3, 3\text{H}, C5(CH_3)]. \]

\[ \text{\textbf{13C NMR}} \ (125 \text{ MHz, CDCl}_3, \text{ chemical shifts taken from the HSQC data}) \ \delta \ 147 \ (C4), 128 \ (=\text{CHCH}_3), 127 \ (HC=\text{CHCH}_3), 51 \ (C5), 44 \ (C7c), 34 \ (C7b), 28 \ (C(=O)CH_3), 27 \ C(OH)CH_3), 18 \ (=\text{CHCH}_3), \text{ and } 15 \ (\text{and } C5CH). \]

\[ \text{\textbf{13C NMR}} \ (125 \text{ MHz, CD}_3\text{OD}) \ \delta \ 209.9 \ (\text{br s}), 178.9, 169.6, 145.2 \ (\text{br s}), 129.8 \ (\text{br s}), 129.1 \ (\text{br s}), 128.9, 106.5, 53.3 \ (\text{br s}), 50.9 \ (\text{br s}), 46.2, 35.7, 28.9 \ (\text{br s}), 26.7 \ (\text{br s}), 18.5, \text{ and } 15.6 \ (\text{br s}). \]

\[ \text{\textbf{IR}} \ (\text{neat}): 2956, 2923, 2854, 2358, 1751, 1699, 1457, 1355, 1246, 1191, 1163, 1057, 1017, 971, \text{ and } 914 \ \text{cm}^{-1}. \]

\[ \text{\textbf{HRMS}} \ (\text{ESI-TOF}): \text{ Calcd for } (\text{C}_{16}\text{H}_{20}\text{NaO}_6)^+ 331.1152 \text{ Found: } 331.1153. \]

\[ \text{\textbf{mp}} \ 170-174 ^\circ \text{C} \text{ (accompanied by sweating; NMR spectrum of material upon cooling was that of dimer } 1b. \]

**Deuterium exchange of H7c in CD3OD**

The solution of 7b-h in CD3OD was observed to lose signal intensity in the \textbf{1H NMR} spectrum for proton H7c at ambient temperature. The half-life for this exchange was ca. 3.2 days at ambient temperature (ca. 21 °C).

**X-ray structure determination of 7b**

A single crystal used for X-ray analysis was prepared by dissolving a portion of this purified product in CH2Cl2 (containing ~5% residual EtOAc). This solution was transferred to a small vial, which was then placed inside a larger capped vial containing pentane. Upon standing at room temperature for 3 days white crystals of suitable quality were formed.

The crystallographic data (excluding structure factors) for this structure have been deposited into the Cambridge Crystallographic Data Centre (CCDC). The deposition number is CCDC 1042989. Copies of the data can be obtained ( , free of charge) by contacting the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, or by linking to http://www.ccdc.cam.ac.uk/pages/Home.aspx.
Preparation of truncated paracaseolide A

\((1aR,5R,5aS,7aS,7bR,7cS)\)-rel-(±)-1a,5,5a,7a,7b,7c-hexahydro-1a,5,7a-trimethyl-5a-(1\(E\))-1-propen-1-yl difuro[2,3,4-cd:4',3',2'-hi]isobenzofuran-3,6-dione [(±)-1b]

The acid (7b-h, 1.0 mg, 3.2 \(\mu\)mol) was added to a glass vial. The headspace was flushed with \(N_2\). The vial was sealed with a Teflon-lined cap and placed in a 110 °C oil bath. After 22 h the \(^1\)H NMR spectrum of the sample showed that clean conversion had occurred to give the truncated (±)-paracaseolide A (1b, 0.7 mg, after re-evaporation of the NMR solvent). The overall cleanliness of this reaction can be seen from inspection of the \(^1\)H NMR spectrum, a copy of which is included later in this Supplementary Information.

Preparation of truncated paracaseolide A

\((1aR,5R,5aS,7aS,7bR,7cS)\)-rel-(±)-1a,5,5a,7a,7b,7c-hexahydro-1a,5,7a-trimethyl-5a-(1\(E\))-1-propen-1-yl difuro[2,3,4-cd:4',3',2'-hi]isobenzofuran-3,6-dione [(±)-1b]

5-Hydroxy-5-methyl-3-(prop-1-en-1-yl)furan-2(5H)-one (3b, 35 mg, 0.23 mmol) was placed in a 2 mL vial with a Teflon cap. The headspace was flushed with \(N_2\). The reaction vial was capped and heated to 110 °C for 48 h. The crude mixture was directly subjected to MPLC (hexanes:ethyl acetate = 1:1) to give unreacted 5-hydroxy-5-methyl-3-(prop-1-en-1-yl)furan-2(5H)-ones (3b, 8 mg, \(E\):\(Z\) = 3:4) followed by the truncated paracaseolide A analog (±)-1b (13.9 mg, 42%) as a white powder.

\[^1\]H NMR (CDCl\(_3\), 500 MHz): \(\delta\) 7.26 (dd, \(J = 7.6, 3.3\) Hz, 1H, \(\text{H}_4\)), 5.87 (dq, \(J = 15.7, 6.5\) Hz, 1H, \(=\text{CHCH}_3\)), 5.53 (dq, \(J = 15.7, 1.6\) Hz, 1H, \(\text{HC}=\text{CHCH}_3\)), 3.38 (dd, \(J = 9.5, 3.3\) Hz, 1H, \(\text{H}7c\)), 3.30 (d, \(J = 9.5\) Hz, 1H, \(\text{H}7b\)), 3.11 (dq, \(J = 7.4, 7.4\) Hz, 1H, \(\text{H}_5\)), 1.80 (dd, \(J = 6.5, 1.7\) Hz, 3H, \(=\text{CHCH}_3\)), 1.76 (s, 3H, (\(\text{C}1a\)CH\(_3\))), 1.63, (s, 3H, (\(\text{C}7a\)CH\(_3\))), and 1.05 (d, \(J = 7.3\) Hz, 3H, \(\text{H}(\text{C}5)\text{CH}_3\)).

\[^{13}\]C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 175.3, 166.4, 144.7, 133.0, 129.5, 127.5, 115.6, 114.1, 58.7, 50.4, 46.5, 39.3, 26.9, 25.9, 18.4, and 12.1.

IR (neat): 2923, 2854, 1771, 1390, 1312, and 911 cm\(^{-1}\).

HRMS (ESI-TOF): Calcd for (\(\text{C}_{16}\text{H}_{18}\text{NaO}_5\))\(^+\) 313.1046. Found: 313.1062.

mp 200-201 °C.

X-ray structure determination of (±)-1b

A single crystal used for X-ray analysis was prepared by dissolving a portion of this purified product in \(\text{CH}_2\text{Cl}_2\). This solution was transferred to a small vial, which was then placed inside a larger capped vial containing pentane. Upon standing at room temperature for several days white crystals of suitable quality were formed.

The crystallographic data (excluding structure factors) for this structure have been deposited into the
Cambridge Crystallographic Data Centre (CCDC). The deposition number is CCDC 1042994. Copies of the data can be obtained (free of charge) by contacting the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, or by linking to http://www.ccdc.cam.ac.uk/pages/Home.aspx.

Preparation of methyl (2Z,3E)-2-(2-oxopropylidene)hexadec-3-enoate (11)

(±)-(E)-5-Hydroxy-5-methyl-3-(tetradec-1-enyl)furan-2(5H)-one (3a, 18.3 mg, 0.059 mmol) was placed in a 14x45 mm (1 dram) vial. Acetone (2 mL), MeI (25 µL, 0.08 mmol), and K2CO3 (15 mg, 0.10 mmol) were added. The vial was sealed with a Teflon cap and stirred at room temperature for 18 h. The reaction mixture was partitioned between ethyl acetate and brine. The organic layer was washed again with brine, filtered through a plug of Na2SO4, concentrated, and purified using MPLC on silica gel (hexanes:ethyl acetate = 4:1) to give methyl (2Z,3E)-2-(2-oxopropylidene)hexadec-3-enoate (11) as a colorless oil (10.4 mg, 55%).

1H NMR (CDCl3, 500 MHz): δ 6.12-6.04 (m, 3H, =C=Hs), 3.90 (s, 3H, CO2CH3), 2.24 (s, 3H, COC(CH3)3), 2.21-2.16 (nfom, 2H, =CHCH2CH2), 1.42 (br pentet, J = 7.3 Hz, 2H, =CHCH2CH2), 1.32-1.22 (m, 18H, -(C=H2)9), and 0.88, (t, J = 6.9 Hz, 3H, CH2CH3).

13C NMR (125 MHz, CDCl3) δ 196.5, 168.9, 145.7, 144.5, 126.7, 124.0, 52.8, 33.6, 32.1, 30.7, 29.87, 29.84 (br), 29.7, 29.60, 29.56, 29.4, 28.6, 22.9, and 14.3.

IR (neat): 2924, 2853, 1740, 1690, 1585, 1378, 1250, 1198, 1175, and 963 cm⁻¹.

HRMS (ESI-TOF): Calcd for (C20H34NaO3)+ 345.2400 Found: 345.2397.

Preparation of (±)-dimethyl (3R,4S,5R,6R)-5,6-diacetyl-3-dodecyl-4-((E)-tetradec-1-en-1-yl)cyclohex-1-ene-1,4-dicarboxylate [(±)-10a]

(±)-Methyl (2Z,3E)-2-(2-oxopropylidene)hexadec-3-enoate (11, 5 mg, 16 µmol) was placed in a 2 mL vial with a Teflon cap. The headspace was flushed with N2. The reaction vial was heated to 80 °C for 60 h. The crude material was directly purified by flash column chromatography (hexanes: ethyl acetate = 5:1 – 3:1) to
give of (±)-dimethyl (3R,4S,5R,6R)-5,6-diacetyl-3-dodecyl-4-((E)-tetradec-1-en-1-yl)cyclohex-1-ene-1,4-dicarboxylate ((±)-10a, 5 mg, 100 %) as a colorless oil.

1H NMR (500 MHz, CDCl3) δ 7.13 [dd, J = 3.1, 1.1 Hz, 1H, =CCH(CH2CH2)], 5.43 (dt, J = 15.9, 6.8 Hz, 1H, CH=CHCH3), 5.18 (dt, J = 15.9, 1.2 Hz, 1H, CH=CHCH3), 3.77 (br dt, J = 15.9, 1.2 Hz, 1H, CH=CHCH3), 3.75 (s, 3H, C7aO2C6H3), 3.73 (d, J = 2.2 Hz, 1H, H7b), 3.70 (s, 3H, C6O2C6H3), 3.08 (br ddt, J = 11.1, 2.7, 2.1 Hz, 1H, H5), 2.28 [s, 3H, C7a(=O)C6H3], 2.27 [s, 3H, C7b(=O)C6H3], 1.96-1.83 (m, 3H), 1.62-1.52 (m, 1H), 1.49-1.40 (m, 1H), 1.40-1.09 (m, 39H), 0.88 (t, J = 7.0 Hz, 3H, CH2C6H3), and 0.88 (t, J = 7.0 Hz, CH2C6H3).

13C NMR (125 MHz, CDCl3) δ 207.3, 206.3, 174.3, 167.0, 145.1, 133.2, 127.9, 124.2, 57.6, 52.3, 51.9, 48.4, 40.0, 32.8, 32.2, 31.0, 29.95, 29.94, 29.90 (br), 29.87, 29.65, 29.61, 29.4, 29.1, 28.8, 28.40, 28.36, 22.9, and 14.4.

IR (neat): 2923, 2853, 1770, 1748, 1715, 1436, 1356, 1268, 1241, 1170, and 1048 cm⁻¹.

HRMS (ESI-TOF): Calcd for (C₄₀H₆₈NaO₆)⁺ 667.4908 Found: 667.4941

NMR-based assignment of the relative configuration (i.e., as an exo adduct) of (±)-10a

Difference NOE experiments (carried out in C₆D₆ for better chemical shift dispersion) gave several key enhancements that were consistent with the assignment of the relative configuration shown above for (±)-10a. Namely: irradiation of Hx enhanced H7b, Hy, one of the diastereotopic protons Hz, and one of the two methyl ketone resonance, although we did not make a definitive assignment of which resonance was associated with which methyl group (and it did not enhance H7c or H5) and irradiation of either H7c or H7b enhanced both sets of methyl ketone protons.

Chemical shift arguments are also consistent with the assignment. There are close similarities of the shifts and multiplicity of key protons in (±)-10a vis-a-vis the bis-TBS ester of the truncated analog 10b. The relative configuration of that latter compound is secure because it was desilylated to produce 1b, for which a single crystal X-ray structure had been obtained. Namely, resonances for the following protons had nearly identical chemical shifts and multiplicities in the 1H NMR spectra (CDCl3) of (±)-10a and 10b: H7c, H7b, and both methyl ketone Me's.

Preparation of
(±)-(3S,3aR,4R,7R,7aS)-4-acetyl-7-dodecyl-3-hydroxy-3-methyl-1-oxo-7a-((E)-tetradec-1-en-1-yl)-1,3,3a,4,7,7a-hexahydroisobenzofuran-5-carboxylic acid [(±)-7a]

(±)-(E)-5-Hydroxy-5-methyl-3-(tetradec-1-etyl)furan-2(5H)-one (3a, 64 mg, 0.21 mmol) was placed in a 2 mL vial with a Teflon cap. The headspace was flushed with N₂. The reaction vial was heated to 60 °C for 72 h. The crude material was directly purified by flash column chromatography (hexanes:ethyl acetate:acetic acid = 50:50:1) to give recovered starting material (3a, 23 mg) and (±)-(3S,3aR,4R,7R,7aS)-4-acetyl-7-dodecyl-3-hydroxy-3-methyl-1-oxo-7a-((E)-tetradec-1-en-1-yl)-1,3,3a,4,7,7a-hexahydroisobenzofuran-5-carboxylic acid [(±)-7a, 29 mg, 45 %] as a colorless sticky oil. 

Preparation of
(±)-(3S,3aR,4R,7R,7aS)-4-acetyl-7-dodecyl-3-hydroxy-3-methyl-1-oxo-7a-((E)-tetradec-1-en-1-yl)-1,3,3a,4,7,7a-hexahydroisobenzofuran-5-carboxylic acid [(±)-7a]

(±)-(E)-5-Hydroxy-5-methyl-3-(tetradec-1-enyl)furan-2(5H)-one (3a, 64 mg, 0.21 mmol) was placed in a 2 mL vial with a Teflon cap. The headspace was flushed with N₂. The reaction vial was heated to 60 °C for 72 h. The crude material was directly purified by flash column chromatography (hexanes:ethyl acetate:acetic acid = 50:50:1) to give recovered starting material (3a, 23 mg) and (±)-(3S,3aR,4R,7R,7aS)-4-acetyl-7-dodecyl-3-hydroxy-3-methyl-1-oxo-7a-((E)-tetradec-1-en-1-yl)-1,3,3a,4,7,7a-hexahydroisobenzofuran-5-carboxylic acid [(±)-7a, 29 mg, 45 %] as a colorless sticky oil.
$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.28 [br s, 1H, C=CHCH(CH$_2$)], 5.69 (br dt, $J = 15.7$, 6.4 Hz, 1H, CH=CHCH$_2$), 5.26 (br d, $J = 15.9$ Hz, 1H, CH=CHCH$_2$), 3.72 (br s, 1H, H7c), 2.71 (br s, 1H, H7b), 2.61 (br s, 1H, H5), 2.25 (very br s, 3H, C(=O)CH$_3$), 1.97 (br dt, $J = 7$, 7 Hz, 1H, =CHCH$_2$), 1.79 (very br s, 3H, C(OH)CH$_3$), 1.51 (br s, 1H), 1.35-1.16 (m, ~41H), and 0.88 [t, $J = 7.0$ Hz, 6H, CH$_2$CH$_3$ (2x)].

$^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 133.8, 126.6, 52 (br), 50 (br), 44.8 (br), 40.6 (br), 32.9, 32.1, 29.91 (br), 29.89, 29.87, 29.84, 29.80 (br), 29.7, 29.6, 29.4, 22.9, and 14.4. [Because this compound appears to exist as an equilibrating mixture of pseudo-acids and/or hemiketals ($^1$H NMR), many resonances in the core of this structure were either broad or not observed in this $^{13}$C NMR spectrum.]

IR (neat): 2923, 2853, 1770, 1758, 1696, 1464, 1246, 1056, and 911 cm$^{-1}$.

HRMS (ESI-TOF): Calcd for (C$_{38}$H$_{64}$NaO$_6$)$^+$ 639.4595 Found: 639.4595.

Preparation of (±)-paracaseolide A

(1aR,5R,5aS,7aS,7bR,7cS)-rel-(±)-5-dodecyl-1a,5,5a,7a,7b,7c-hexahydro-1a,7a-dimethyl-5a-(1E)-1-tetradecean-1-yldifuro[2,3,4-c'd:4',3',2'hi]isobenzofuran-3,6-dione [(±)-1a]

In a glass vial was added the acid 7a-h (4.7 mg, 7.6 µmol). The headspace was flushed with N$_2$. The vial was sealed with a Teflon-lined cap and placed in a 110 °C oil bath. After 22 h the $^1$H NMR spectrum of the sample showed that clean conversion had occurred to give (±)-paracaseolide A (1a, 4.3 mg, after re-evaporation of the NMR solvent). The overall cleanliness of this reaction can be seen from inspection of the $^1$H NMR spectrum, a copy of which is included later in this Supplementary Information.
III. Computational Methods

DFT calculations were carried out using Gaussian 09. Geometries were optimized using the M06-2X functional developed by Truhlar et al or the B3LYP functional. The double-$\zeta$ 6-31G(d), cc-pVDZ, or triple-$\zeta$ 6-311+G(d,p) basis sets were used. The SMD continuum solvation model was used with 2-butanol as the solvent, chosen to mimic the medium for the neat reaction conditions, during the frequency calculation and the geometry optimization (unless otherwise indicated). The "grid=ultrafine" option was applied during the numerical integrations. The harmonic vibrational frequency calculations were carried out using 298 K as the thermal correction for the free energies. Every optimized transition state structure geometry showed only one imaginary frequency.

First, we used DFT calculations to evaluate the relative energies of transition state (TS) structures corresponding to the exo vs. the endo modes of dimerization of $3b$ [SMD/M06-2X/6-31G(d) in 2-butanol]. The TS structures for both of these modes of addition are shown on following pages. Both homochiral and heterochiral possibilities (i.e., dimerization of two copies of the same enantiomer or one copy of each enantiomer of $3b$) as well as approaches of the two molecules with inward vs. outward orientations of the hydroxyl groups were examined. The two heterochiral-TS structures for the exo mode of addition converged to the same (bis-pericyclic) structure (TSexo-2) during the optimization.

| $G_{rel}$ (kcal•mol⁻¹) | Homochiral: hydroxyls in on diene and out on dienophile | Heterochiral: hydroxyls in on both diene and dienophile (lowest $G$, endo TS) | Heterochiral: hydroxyls out on both the diene and dienophile | Homochiral: hydroxyls out on diene and in on dienophile | Homochiral: hydroxyls out on both diene and dienophile | Heterochiral: hydroxyls in on diene and out on dienophile | Homochiral: hydroxyls in on both diene and dienophile (lowest $G$, exo TS) |
|------------------------|----------------------------------------------------------|-----------------------------------------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|-----------------------------------------------------------------|-------------------------------------------------|
| TSendo-1               | 4.7                                                      | Homochiral: hydroxyls in on diene and out on dienophile         | Heterochiral: hydroxyls in on both diene and dienophile (lowest $G$, endo TS) | Heterochiral: hydroxyls out on both the diene and dienophile | Homochiral: hydroxyls out on diene and in on dienophile | Heterochiral: hydroxyls in on diene and out on dienophile | Homochiral: hydroxyls in on both diene and dienophile (lowest $G$, exo TS) |
| TSendo-2               | 2.9                                                      | Heterochiral: hydroxyls in on both diene and dienophile (lowest $G$, endo TS) | Heterochiral: hydroxyls out on both the diene and dienophile | Homochiral: hydroxyls out on diene and in on dienophile | Homochiral: hydroxyls out on both diene and dienophile | Heterochiral: hydroxyls in on diene and out on dienophile | Homochiral: hydroxyls in on both diene and dienophile (lowest $G$, exo TS) |
| TSendo-3               | 8.1                                                      | Heterochiral: hydroxyls out on both the diene and dienophile | Homochiral: hydroxyls out on diene and in on dienophile | Homochiral: hydroxyls out on both diene and dienophile | Heterochiral: hydroxyls in on diene and out on dienophile | Homochiral: hydroxyls in on both diene and dienophile (lowest $G$, exo TS) |
| TSendo-4               | 3.7                                                      | Homochiral: hydroxyls out on diene and in on dienophile         | Homochiral: hydroxyls out on both diene and dienophile | Heterochiral: hydroxyls in on diene and out on dienophile | Homochiral: hydroxyls in on both diene and dienophile (lowest $G$, exo TS) |
| TSEXO-1               | 4.6                                                      | Homochiral: hydroxyls out on both diene and dienophile         | Homochiral: hydroxyls out on both diene and dienophile | Heterochiral: hydroxyls in on diene and out on dienophile | Homochiral: hydroxyls in on both diene and dienophile (lowest $G$, exo TS) |
| TSEXO-2               | 2.3                                                      | Heterochiral: hydroxyls in on diene and out on dienophile       | Homochiral: hydroxyls out on both diene and dienophile | Heterochiral: hydroxyls in on diene and out on dienophile | Homochiral: hydroxyls in on both diene and dienophile (lowest $G$, exo TS) |
| TSEXO-3               | 0                                                        | Homochiral: hydroxyls in on both diene and dienophile (lowest $G$, exo TS) | Homochiral: hydroxyls out on both diene and dienophile | Heterochiral: hydroxyls in on diene and out on dienophile | Homochiral: hydroxyls in on both diene and dienophile (lowest $G$, exo TS) |

Second, we optimized the lowest energy endo and exo TS structures (i.e., TSendo-2 and TSEXO-3) with several other combinations of functional and basis set. A gas-phase calculation (i.e., no SMD) was also performed. Specifically, the following combinations were used: SMD/M06-2X/6-311+G(d,p), SMD/M06-2X/cc-pVDZ, SMD/B3LYP/6-311+G(d,p) in 2-butanol, and M06-2X/6-311+G(d,p) without SMD solvation. All of the resulting TS geometries were very similar; the TS energies are given in Table S1 (below). The optimized structure of TSendo-2 and TSEXO-3 at the SMD/M06-2X/6-311+G(d,p) level are those given in the manuscript (as "TSendo" and "TSEXO").

Third, we examined a conformational analog of TSendo-2 in which the dienophile has an s-trans geometry at the SMD/M06-2X/6-311+G(d,p) level. The resulting TSendo-2s-trans had a $G_{rel}$ 0.8 kcal•mol⁻¹ higher than the energy of the s-cis-containing TSendo-2.

Last, we optimized monomer $3b$ and the product structure PD (co-ordinates for both below) from an exo DA dimerization at the SMD/M06-2X/6-311+G(d,p) level to determine the computed free energy of reaction (-14.0 kcal•mol⁻¹), which is also now given in the manuscript.
Table S1. Energies of $\text{TS}_{\text{exo}}$ and $\text{TS}_{\text{endo}}$ with different functional/basis set/solvation combinations

| Method                  | Structure | $H$ (Hartree/Particle) | $G$ (Hartree/Particle) | $H_{\text{rel}}$ (kcal•mol$^{-1}$) | $G_{\text{rel}}$ (kcal•mol$^{-1}$) |
|------------------------|-----------|------------------------|------------------------|-----------------------------------|-----------------------------------|
| SMD/M06-2X/6-31G(d)    | $\text{TS}_{\text{exo}}$ | -1072.262291           | -1072.333059           | 0.0                               | 0.0                               |
| in 2-butanol            | $\text{TS}_{\text{endo}}$ | -1072.258385           | -1072.328436           | 2.5                               | 2.9                               |
| SMD/M06-2X/6-311+G(d,p)| $\text{TS}_{\text{exo}}$ | -1072.595731           | -1072.666831           | 0.0                               | 0.0                               |
| in 2-butanol            | $\text{TS}_{\text{endo}}$ | -1072.590218           | -1072.660629           | 3.5                               | 3.9                               |
| SMD/M06-2X/6-311+G(d,p)| $\text{TS}_{\text{exo}}$ | -1072.558434           | -1072.629637           | 0.0                               | 0.0                               |
| in gas phase            | $\text{TS}_{\text{endo}}$ | -1072.548248           | -1072.619829           | 6.4                               | 6.2                               |
| SMD/M06-2X/cc-pVDZ      | $\text{TS}_{\text{exo}}$ | -1072.384888           | -1072.455101           | 0.0                               | 0.0                               |
| in 2-butanol            | $\text{TS}_{\text{endo}}$ | -1072.379505           | -1072.450097           | 3.4                               | 3.1                               |
| SMD/B3LYP/6-311+G(d,p)  | $\text{TS}_{\text{exo}}$ | -1073.029730           | -1073.103066           | 0.0                               | 0.0                               |
| in 2-butanol            | $\text{TS}_{\text{endo}}$ | -1073.023419           | -1073.096053           | 4.0                               | 4.4                               |

† These are the TS structures (and energies) presented in the manuscript.
**TS structure for TS\textsubscript{endo-1}**

![TS structure for TS\textsubscript{endo-1}](image)

**Imaginary frequency: -411.3425 cm\(^{-1}\)**

| Center Number | Atomic Number | Atomic Type | Coordinates (Angstroms) |
|---------------|---------------|-------------|------------------------|
|               |               |             | X          | Y          | Z          |
| 1             | 6             | 0           | -1.588845  | 0.048150  | -0.541480  |
| 2             | 6             | 0           | -2.529889  | 1.083225  | -0.188519  |
| 3             | 6             | 0           | -2.293487  | 2.401553  | -0.316568  |
| 4             | 6             | 0           | -1.147341  | -0.538479 | 2.148195   |
| 5             | 6             | 0           | 0.143990   | -0.953094 | 1.993001   |
| 6             | 6             | 0           | -0.295266  | 0.178270  | -1.056084  |
| 7             | 1             | 0           | -3.478186  | 0.743661  | 0.228515   |
| 8             | 1             | 0           | -1.392579  | 0.495934  | 1.923016   |
| 9             | 1             | 0           | 0.460493   | -1.920718 | 2.380553   |
| 10            | 1             | 0           | -0.022201  | 1.026521  | -1.678114  |
| 11            | 1             | 0           | -1.355849  | 2.737189  | -0.762081  |
| 12            | 6             | 0           | -1.956040  | -1.372415 | -0.558222  |
| 13            | 8             | 0           | -2.998762  | -1.903819 | -0.238641  |
| 14            | 6             | 0           | 0.047589   | -1.191751 | -1.661607  |
| 15            | 8             | 0           | -0.916731  | -2.089388 | -1.067252  |
| 16            | 6             | 0           | 1.082586   | -0.201397 | 1.260247   |
| 17            | 6             | 0           | 0.829857   | 0.855803  | 0.386021   |
| 18            | 6             | 0           | 2.189289   | 1.339714  | -0.120805  |
| 19            | 1             | 0           | 0.098608   | 1.635463  | 0.609687   |
| 20            | 6             | 0           | 2.504547   | -0.571508 | 1.133589   |
|   |   |   |   |   |   |
|---|---|---|---|---|---|
| 21| 8 | 0 | 3.101844 | -1.480727 | 1.663170 |
| 22| 8 | 0 | 3.115518 | 0.303596  | 0.302665 |
| 23| 6 | 0 | -2.212860| -1.359285 | 2.786517 |
| 24| 1 | 0 | -1.845620| -2.350671 | 3.065388 |
| 25| 1 | 0 | -2.601076| -0.857085 | 3.680732 |
| 26| 1 | 0 | -3.058326| -1.484637 | 2.097928 |
| 27| 6 | 0 | -3.261721| 3.468133  | 0.080660 |
| 28| 1 | 0 | -2.815391| 4.147519  | 0.816676 |
| 29| 1 | 0 | -3.538222| 4.083188  | -0.784238|
| 30| 1 | 0 | -4.172630| 3.041883  | 0.510050 |
| 31| 6 | 0 | 1.414722 | -1.815211 | -1.482833|
| 32| 1 | 0 | 1.486055 | -2.684648 | -2.145536|
| 33| 1 | 0 | 2.193179 | -1.100335 | -1.756731|
| 34| 1 | 0 | 1.566519 | -2.169791 | -0.463336|
| 35| 8 | 0 | -0.259502| -1.034519 | -3.018515|
| 36| 1 | 0 | -0.041166| -1.864789 | -3.476463|
| 37| 8 | 0 | 2.209254 | 1.417124  | -1.504260|
| 38| 1 | 0 | 3.017284 | 1.886905  | -1.775126|
| 39| 6 | 0 | 2.621987 | 2.639097  | 0.532466 |
| 40| 1 | 0 | 3.641292 | 2.883813  | 0.215941 |
| 41| 1 | 0 | 1.947730 | 3.443645  | 0.227383 |
| 42| 1 | 0 | 2.602408 | 2.543989  | 1.620953 |
**TS structure for TS\textsubscript{endo}-2**

Imaginary frequency: \(-429.9500\ \text{cm}^{-1}\)

---

| Center Number | Atomic Number | Atomic Type | Coordinates (Angstroms) |
|---------------|---------------|-------------|-------------------------|
| 1             | 6             | 0           | 1.570973 0.038078 0.559134 |
| 2             | 6             | 0           | 2.690384 0.870674 0.170578 |
| 3             | 6             | 0           | 2.638739 2.208067 0.061772 |
| 4             | 6             | 0           | 1.251333 -0.764880 -2.005612 |
| 5             | 6             | 0           | -0.042965 -1.173654 -1.857347 |
| 6             | 6             | 0           | 0.296531 0.420849 0.983080 |
| 7             | 1             | 0           | 3.616027 0.343864 -0.061957 |
| 8             | 1             | 0           | 1.473603 0.296807 -1.938029 |
| 9             | 1             | 0           | -0.328829 -2.197970 -2.091930 |
| 10            | 1             | 0           | 0.125469 1.406655 1.406859 |
| 11            | 1             | 0           | 1.710910 2.726119 0.309033 |
| 12            | 6             | 0           | 1.711434 -1.403216 0.793344 |
| 13            | 8             | 0           | 2.666644 -2.130230 0.620369 |
| 14            | 6             | 0           | -0.275391 -0.781374 1.749186 |
| 15            | 8             | 0           | 0.552964 -1.875593 1.336995 |
| 16            | 6             | 0           | -1.016269 -0.335306 -1.285986 |
| 17            | 6             | 0           | -0.817856 0.857030 -0.595866 |
| 18            | 6             | 0           | -2.199480 1.352867 -0.163676 |
| 19            | 1             | 0           | -0.095626 1.611585 -0.907642 |
| 20            | 6             | 0           | -2.427796 -0.734525 -1.120064 |
|   |    |   |          |          |          |
|---|----|----|----------|----------|----------|
|21 | 8  | 0  | -2.986387| -1.734188| -1.502470|
|22 | 8  | 0  | -3.094228|  0.263633| -0.488301|
|23 | 6  | 0  | -0.120783| -0.581829|  3.250722|
|24 | 1  | 0  | -0.756179|  0.247209|  3.577863|
|25 | 1  | 0  | -0.430987| -1.495895|  3.764022|
|26 | 1  | 0  |  0.917510| -0.352816|  3.506129|
|27 | 8  | 0  | -1.574954| -1.176534|  1.435448|
|28 | 1  | 0  | -2.163831| -0.444323|  1.699246|
|29 | 6  | 0  |  2.358542| -1.654812| -2.453629|
|30 | 1  | 0  |  2.045849| -2.701861| -2.485497|
|31 | 1  | 0  |  2.706811| -1.356841| -3.450565|
|32 | 1  | 0  |  3.215805| -1.568906| -1.776253|
|33 | 6  | 0  |  3.789747|  3.063997| -0.359690|
|34 | 1  | 0  |  3.539884|  3.645284| -1.255503|
|35 | 1  | 0  |  4.043307|  3.789395|  0.422756|
|36 | 1  | 0  |  4.677090|  2.461896| -0.575014|
|37 | 6  | 0  | -2.654888|  2.579991| -0.927557|
|38 | 1  | 0  | -3.684977|  2.824874| -0.649002|
|39 | 1  | 0  | -2.005489|  3.425439| -0.686304|
|40 | 1  | 0  | -2.615418|  2.390741| -2.003078|
|41 | 8  | 0  | -2.242485|  1.550008|  1.218475|
|42 | 1  | 0  | -3.076912|  2.000224|  1.440408|
TS structure for TS_{endo-3}

Imaginary frequency: \(-407.7633\) cm\(^{-1}\)

| Center Number | Atomic Number | Atomic Type | Coordinates (Angstroms) |
|---------------|---------------|-------------|-------------------------|
| 1             | 6             | 0           | -1.598563 \(0.085071\) \(-0.535560\) |
| 2             | 6             | 0           | -2.503460 \(1.143660\) \(-0.157200\) |
| 3             | 6             | 0           | -2.228920 \(2.456701\) \(-0.258707\) |
| 4             | 6             | 0           | -1.133849 \(-0.598582\) \(2.131792\) |
| 5             | 6             | 0           | 0.157553 \(-1.007112\) \(1.961511\) |
| 6             | 6             | 0           | -0.301551 \(0.178052\) \(-1.045874\) |
| 7             | 1             | 0           | -3.459621 \(0.823864\) \(0.257306\) |
| 8             | 1             | 0           | -1.380255 \(0.441856\) \(1.937232\) |
| 9             | 1             | 0           | 0.474683 \(-1.985838\) \(2.319945\) |
| 10            | 1             | 0           | -0.024709 \(1.024150\) \(-1.669215\) |
| 11            | 1             | 0           | -1.284802 \(2.775488\) \(-0.703051\) |
| 12            | 6             | 0           | -2.028864 \(-1.315018\) \(-0.600136\) |
| 13            | 8             | 0           | -3.094408 \(-1.807307\) \(-0.293543\) |
| 14            | 6             | 0           | 0.009292 \(-1.198660\) \(-1.660654\) |
| 15            | 8             | 0           | -1.030176 \(-2.060112\) \(-1.143633\) |
| 16            | 6             | 0           | 1.094636 \(-0.233335\) \(1.249135\) |
| 17            | 6             | 0           | 0.843212 \(0.846436\) \(0.406186\) |
| 18            | 6             | 0           | 2.208576 \(1.359815\) \(-0.058301\) |
| 19            | 1             | 0           | 0.114787 \(1.623705\) \(0.641735\) |
| 20            | 6             | 0           | 2.515779 \(-0.604557\) \(1.100212\) |
|   |   |   |            |            |            |
|---|---|---|------------|------------|------------|
| 21| 8 | 0 | 3.114065   | -1.530541  | 1.595659   |
| 22| 8 | 0 | 3.118493   | 0.281171   | 0.269556   |
| 23| 6 | 0 | -2.196602  | -1.440870  | 2.746289   |
| 24| 1 | 0 | -1.819506  | -2.430723  | 3.017453   |
| 25| 1 | 0 | -2.604510  | -0.955266  | 3.640679   |
| 26| 1 | 0 | -3.031062  | -1.569403  | 2.044303   |
| 27| 6 | 0 | -3.162398  | 3.542017   | 0.169780   |
| 28| 1 | 0 | -2.692331  | 4.184581   | 0.923849   |
| 29| 1 | 0 | -3.420160  | 4.190016   | -0.676505  |
| 30| 1 | 0 | -4.085504  | 3.132741   | 0.589484   |
| 31| 8 | 0 | 2.491149   | 2.450592   | 0.764439   |
| 32| 1 | 0 | 3.329756   | 2.846440   | 0.469126   |
| 33| 6 | 0 | 2.399133   | 1.700236   | -1.520625  |
| 34| 1 | 0 | 1.741392   | 2.532339   | -1.787823  |
| 35| 1 | 0 | 3.437478   | 2.008393   | -1.679774  |
| 36| 1 | 0 | 2.185559   | 0.849412   | -2.171044  |
| 37| 6 | 0 | 1.319580   | -1.915020  | -1.407529  |
| 38| 1 | 0 | 1.352755   | -2.796725  | -2.057095  |
| 39| 1 | 0 | 2.171008   | -1.275407  | -1.649271  |
| 40| 1 | 0 | 1.394828   | -2.266618  | -0.378884  |
| 41| 8 | 0 | -0.197582  | -0.999156  | -3.029325  |
| 42| 1 | 0 | 0.026559   | -1.823195  | -3.495587  |
TS structure for TS$_{endo}$-4

Imaginary frequency: $-426.9161$ cm$^{-1}$

| Center Number | Atomic Number | Atomic Type | Coordinates (Angstroms) |
|---------------|---------------|-------------|-------------------------|
| 1             | 6             | 0           | 1.580038 0.033963 0.565672 |
| 2             | 6             | 0           | 2.614079 0.980567 0.211805 |
| 3             | 6             | 0           | 2.463838 2.315956 0.230073 |
| 4             | 6             | 0           | 1.214578 -0.637520 -2.061478 |
| 5             | 6             | 0           | -0.075428 -1.059673 -1.907216 |
| 6             | 6             | 0           | 0.286723 0.285716 1.036596 |
| 7             | 1             | 0           | 3.560940 0.549192 -0.113416 |
| 8             | 1             | 0           | 1.437153 0.417465 -1.924463 |
| 9             | 1             | 0           | -0.367005 -2.064191 -2.210806 |
| 10            | 1             | 0           | 0.076614 1.200099 1.587160 |
| 11            | 1             | 0           | 1.520140 2.743367 0.572618 |
| 12            | 6             | 0           | 1.832694 -1.407023 0.658687 |
| 13            | 8             | 0           | 2.842865 -2.033322 0.410192 |
| 14            | 6             | 0           | -0.196916 -1.021193 1.670556 |
| 15            | 8             | 0           | 0.724910 -2.016673 1.161784 |
| 16            | 6             | 0           | -1.03509 0.260738 -1.263797 |
| 17            | 6             | 0           | -0.818279 0.873675 -0.486382 |
| 18            | 6             | 0           | -2.200898 1.394861 -0.086012 |
| 19            | 1             | 0           | -0.088038 1.640889 -0.744780 |
| 20            | 6             | 0           | -2.454044 -0.648010 -1.115844 |
|   |   |   | x-coordinate | y-coordinate | z-coordinate |
|---|---|---|---------------|--------------|--------------|
| 21 | 8 | 0 | -3.022365 | -1.622099 | -1.549558 |
| 22 | 8 | 0 | -3.100072 | 0.309202 | -0.411130 |
| 23 | 6 | 0 | -0.054571 | -0.991024 | 3.184137 |
| 24 | 1 | 0 | -0.732274 | -0.243529 | 3.605929 |
| 25 | 1 | 0 | -0.306719 | -1.975217 | 3.592118 |
| 26 | 1 | 0 | 0.972328 | -0.744664 | 3.466239 |
| 27 | 8 | 0 | -1.482461 | -1.355957 | 1.285105 |
| 28 | 1 | 0 | -1.804916 | -2.074350 | 1.856348 |
| 29 | 6 | 0 | 2.307697 | -1.488982 | -2.607133 |
| 30 | 1 | 0 | 1.996452 | -2.532739 | -2.702283 |
| 31 | 1 | 0 | 2.620291 | -1.120097 | -3.592277 |
| 32 | 1 | 0 | 3.188275 | -1.446481 | -1.955845 |
| 33 | 6 | 0 | 3.528553 | 3.286436 | -0.168739 |
| 34 | 1 | 0 | 3.187891 | 3.926044 | -0.991792 |
| 35 | 1 | 0 | 3.779436 | 3.955240 | 0.663420 |
| 36 | 1 | 0 | 4.439505 | 2.771162 | -0.486334 |
| 37 | 8 | 0 | -2.457444 | 2.465123 | -0.945951 |
| 38 | 1 | 0 | -3.306855 | 2.864415 | -0.688952 |
| 39 | 6 | 0 | -2.440329 | 1.768959 | 1.360503 |
| 40 | 1 | 0 | -1.775201 | 2.589350 | 1.644321 |
| 41 | 1 | 0 | -3.476762 | 2.104175 | 1.472185 |
| 42 | 1 | 0 | -2.277484 | 0.913860 | 2.018498 |
TS structure for TS$_{\text{exo-1}}$

Imaginary frequency: -382.0468 cm$^{-1}$

| Center Number | Atomic Number | Atomic Type | Coordinates (Å)          |
|---------------|---------------|-------------|--------------------------|
| 1             | 6             | 0           | 1.196264, -0.515698, -0.888305 |
| 2             | 6             | 0           | 0.475684, -1.610503, -1.434422 |
| 3             | 6             | 0           | -0.808807, -1.491957, -1.848309 |
| 4             | 6             | 0           | 0.808808, -1.491951, 1.848310  |
| 5             | 6             | 0           | -0.475683, -1.610501, 1.434424  |
| 6             | 6             | 0           | 0.737420, 0.784610, -0.689977   |
| 7             | 1             | 0           | 0.957528, -2.587143, -1.416437  |
| 8             | 1             | 0           | 1.255087, -0.499359, 1.917244   |
| 9             | 1             | 0           | -0.957525, -2.587142, 1.416438  |
| 10            | 1             | 0           | 0.092961, 1.256933, -1.421455   |
| 11            | 1             | 0           | -1.255089, -0.499366, -1.917241 |
| 12            | 6             | 0           | 2.582652, -0.604096, -0.407316  |
| 13            | 8             | 0           | 3.332221, -1.555350, -0.392820  |
| 14            | 6             | 0           | 1.960908, 1.611363, -0.273670   |
| 15            | 8             | 0           | 2.971919, 0.620735, 0.034667    |
| 16            | 6             | 0           | -1.196265, -0.515698, 0.888307  |
| 17            | 6             | 0           | -0.737421, 0.784611, 0.689977   |
| 18            | 6             | 0           | -1.960910, 1.611363, 0.273668   |
| 19            | 1             | 0           | -0.092963, 1.256935, 1.421454   |
| 20            | 6             | 0           | -2.582652, -0.604096, 0.407316  |
|    |    |    |          |          |          |
|----|----|----|----------|----------|----------|
| 21 |  8 |  0 | -3.332221 | -1.555352 |  0.392822 |
| 22 |  8 |  0 | -2.971919 |  0.620733 | -0.034669 |
| 23 |  6 |  0 |  1.657973 | -2.634913 |  2.287153 |
| 24 |  1 |  0 |  2.544901 | -2.711137 |  1.642944 |
| 25 |  1 |  0 |  2.025753 | -2.482259 |  3.308770 |
| 26 |  1 |  0 |  1.112125 | -3.581332 |  2.244505 |
| 27 |  6 |  0 | -1.657969 | -2.634921 | -2.287150 |
| 28 |  1 |  0 | -2.544890 | -2.711156 | -1.642933 |
| 29 |  1 |  0 | -2.025760 | -2.482264 | -3.308763 |
| 30 |  1 |  0 | -1.112114 | -3.581336 | -2.244514 |
| 31 |  6 |  0 | -1.872667 |  2.541628 | -0.918495 |
| 32 |  1 |  0 | -2.807960 |  3.106019 | -0.993985 |
| 33 |  1 |  0 | -1.045803 |  3.245396 | -0.787501 |
| 34 |  1 |  0 | -1.739997 |  1.990694 | -1.851911 |
| 35 |  8 |  0 | -2.334396 |  2.298275 |  1.430482 |
| 36 |  1 |  0 | -3.092013 |  2.870326 |  1.216213 |
| 37 |  8 |  0 |  2.334393 |  2.298276 | -1.430484 |
| 38 |  1 |  0 |  3.092008 |  2.870329 | -1.216216 |
| 39 |  6 |  0 |  1.872666 |  2.541629 |  0.918493 |
| 40 |  1 |  0 |  2.807959 |  3.106019 |  0.993983 |
| 41 |  1 |  0 |  1.045801 |  3.245396 |  0.787499 |
| 42 |  1 |  0 |  1.739997 |  1.990695 |  1.851909 |
TS structure for TS\textsubscript{exo-2}

![TS structure for TS\textsubscript{exo-2}](image)

Imaginary frequency: -385.5927 cm\(^{-1}\)

| Center Number | Atomic Number | Atomic Type | Coordinates (Angstroms) |
|---------------|---------------|-------------|-------------------------|
|               |               |             | X                  | Y                  | Z                  |
| 1             | 6             | 0           | 1.199783           | -0.533092          | -0.858853          |
| 2             | 6             | 0           | 0.495490           | -1.642720          | -1.393504          |
| 3             | 6             | 0           | -0.782015          | -1.534880          | -1.833272          |
| 4             | 6             | 0           | 0.766763           | -1.498703          | 1.878439           |
| 5             | 6             | 0           | -0.515118          | -1.603143          | 1.451787           |
| 6             | 6             | 0           | 0.722263           | 0.767316           | -0.693374          |
| 7             | 1             | 0           | 0.978921           | -2.617623          | -1.345788          |
| 8             | 1             | 0           | 1.229153           | -0.512987          | 1.938803           |
| 9             | 1             | 0           | -1.010095          | -2.573242          | 1.438254           |
| 10            | 1             | 0           | 0.063610           | 1.223998           | -1.424564          |
| 11            | 1             | 0           | -1.227725          | -0.544582          | -1.931280          |
| 12            | 6             | 0           | 2.574883           | -0.598563          | -0.342469          |
| 13            | 8             | 0           | 3.334384           | -1.540583          | -0.288199          |
| 14            | 6             | 0           | 1.941226           | 1.612432           | -0.303840          |
| 15            | 8             | 0           | 2.938145           | 0.639356           | 0.090199           |
| 16            | 6             | 0           | -1.210369          | -0.505185          | 0.880806           |
| 17            | 6             | 0           | -0.720211          | 0.787265           | 0.681052           |
| 18            | 6             | 0           | -1.912955          | 1.627589           | 0.211926           |
| 19            | 1             | 0           | -0.076870          | 1.238918           | 1.427954           |
| 20            | 6             | 0           | -2.576686          | -0.579209          | 0.347959           |
|   |   |   |       |       |       |
|---|---|---|-------|-------|-------|
|21 | 8 | 0 | -3.343274 | -1.518176 |  0.320393 |
|22 | 8 | 0 | -2.931912 |  0.646859 | -0.115884 |
|23 | 6 | 0 |  1.595611 | -2.649873 |  2.334515 |
|24 | 1 | 0 |  2.480944 | -2.748938 |  1.691012 |
|25 | 1 | 0 |  1.966478 | -2.490754 |  3.353978 |
|26 | 1 | 0 |  1.034238 | -3.587662 |  2.303463 |
|27 | 6 | 0 | -1.622429 | -2.688827 | -2.259141 |
|28 | 1 | 0 | -2.515844 | -2.754442 | -1.622418 |
|29 | 1 | 0 | -1.980568 | -2.557042 | -3.287064 |
|30 | 1 | 0 | -1.074823 | -3.632879 | -2.192299 |
|31 | 8 | 0 |  2.348591 |  2.212951 | -1.498316 |
|32 | 1 | 0 |  3.114549 |  2.782353 | -1.308028 |
|33 | 6 | 0 |  1.823269 |  2.629476 |  0.811492 |
|34 | 1 | 0 |  2.749887 |  3.210649 |  0.861883 |
|35 | 1 | 0 |  0.992391 |  3.308426 |  0.598883 |
|36 | 1 | 0 |  1.673953 |  2.155829 |  1.783879 |
|37 | 6 | 0 | -2.460681 |  2.507261 |  1.322692 |
|38 | 1 | 0 | -1.714863 |  3.257555 |  1.598561 |
|39 | 1 | 0 | -3.367170 |  3.012825 |  0.974491 |
|40 | 1 | 0 | -2.707137 |  1.905019 |  2.200723 |
|41 | 8 | 0 | -1.616649 |  2.356970 | -0.929073 |
|42 | 1 | 0 | -2.356248 |  2.962703 | -1.110682 |
TS structure for TSexo-3

Imaginary frequency: -394.7486 cm\(^{-1}\)

| Center Number | Atomic Number | Atomic Type | Coordinates (Angstroms) |
|---------------|---------------|-------------|-------------------------|
|               |               |             | X           | Y           | Z               |
| 1             | 6             | 0           | 1.184355   | -0.512468  | -0.894271       |
| 2             | 6             | 0           | 0.461789   | -1.600844  | -1.446535       |
| 3             | 6             | 0           | -0.826603  | -1.476693  | -1.850053       |
| 4             | 6             | 0           | 0.826584   | -1.476690  | 1.850061        |
| 5             | 6             | 0           | -0.461803  | -1.600841  | 1.446530        |
| 6             | 6             | 0           | 0.714612   | 0.786740   | -0.676606       |
| 7             | 1             | 0           | 0.942169   | -2.578355  | -1.440275       |
| 8             | 1             | 0           | 1.270485   | -0.482856  | 1.911701        |
| 9             | 1             | 0           | -0.942186  | -2.578350  | 1.440276        |
| 10            | 1             | 0           | 0.064338   | 1.266644   | -1.401473       |
| 11            | 1             | 0           | -1.270499  | -0.482858  | -1.911706       |
| 12            | 6             | 0           | 2.565777   | -0.607517  | -0.407642       |
| 13            | 8             | 0           | 3.319925   | -1.557458  | -0.410942       |
| 14            | 6             | 0           | 1.927740   | 1.603581   | -0.212657       |
| 15            | 8             | 0           | 2.954716   | 0.610904   | 0.047044        |
| 16            | 6             | 0           | -1.184360  | -0.512464  | 0.894251        |
| 17            | 6             | 0           | -0.714605  | 0.786740   | 0.676593        |
| 18            | 6             | 0           | -1.927724  | 1.603598   | 0.212651        |
| 19            | 1             | 0           | -0.064325  | 1.266630   | 1.401465        |
| 20            | 6             | 0           | -2.565779  | -0.607498  | 0.407614        |
| 21            | 8             | 0           | -3.319940  | -1.557429  | 0.410916        |
|    |   |   |         |         |         |
|----|---|---|---------|---------|---------|
| 22 | 8 | 0 | -2.954699 | 0.610924 | -0.047083 |
| 23 | 6 | 0 | -2.438651 | 2.525969 | 1.304431  |
| 24 | 1 | 0 | -1.681372 | 3.284309 | 1.521047  |
| 25 | 1 | 0 | -3.357533 | 3.018225 | 0.969628  |
| 26 | 1 | 0 | -2.651834 | 1.959749 | 2.214553  |
| 27 | 6 | 0 | 2.438657  | 2.525990 | -1.304409 |
| 28 | 1 | 0 | 1.681366  | 3.284324 | -1.521003 |
| 29 | 1 | 0 | 3.357528  | 3.018253 | -0.969588 |
| 30 | 1 | 0 | 2.651851  | 1.959801 | -2.214548 |
| 31 | 8 | 0 | 1.675205  | 2.288661 | 0.967359  |
| 32 | 1 | 0 | 2.425182  | 2.882657 | 1.144644  |
| 33 | 8 | 0 | -1.675185 | 2.288715 | -0.967342 |
| 34 | 1 | 0 | -2.425042 | 2.882909 | -1.144463 |
| 35 | 6 | 0 | 1.681575  | -2.614928| 2.289660  |
| 36 | 1 | 0 | 2.561211  | -2.694958| 1.635646  |
| 37 | 1 | 0 | 2.061335  | -2.453393| 3.305527  |
| 38 | 1 | 0 | 1.137008  | -3.562661| 2.261027  |
| 39 | 6 | 0 | -1.681601 | -2.614936| -2.289622 |
| 40 | 1 | 0 | -2.561223 | -2.694961| -1.635588 |
| 41 | 1 | 0 | -2.061384 | -2.453415| -3.305482 |
| 42 | 1 | 0 | -1.137032 | -3.562669| -2.260990 |
Structure for TS\textsubscript{endo-2\textsubscript{a}-trans}

![Image of molecule structure]

Imaginary frequency: -457.5097 cm\textsuperscript{-1}

| Center Number | Atomic Number | Atomic Type | X Coordinates (Angstroms) | Y Coordinates (Angstroms) | Z Coordinates (Angstroms) |
|---------------|---------------|-------------|---------------------------|---------------------------|---------------------------|
| 1             | 6             | 0           | -1.439597                 | 0.515449                  | 0.265325                  |
| 2             | 6             | 0           | -2.456018                 | 0.218633                  | 1.259751                  |
| 3             | 6             | 0           | -3.771392                 | 0.083558                  | 1.036697                  |
| 4             | 6             | 0           | -1.154699                 | -2.018970                 | -0.378062                 |
| 5             | 6             | 0           | 0.080143                  | -1.897034                 | -0.950805                 |
| 6             | 6             | 0           | -0.143181                 | 0.964106                  | 0.541788                  |
| 7             | 1             | 0           | -2.080863                 | 0.110891                  | 2.276988                  |
| 8             | 1             | 0           | -1.233673                 | -1.937676                 | 0.701333                  |
| 9             | 1             | 0           | 0.235180                  | -2.157873                 | -1.994595                 |
| 10            | 1             | 0           | 0.080093                  | 1.408695                  | 1.505594                  |
| 11            | 1             | 0           | -4.156332                 | 0.207179                  | 0.028840                  |
| 12            | 6             | 0           | -1.692044                 | 0.732960                  | -1.165669                 |
| 13            | 8             | 0           | -2.684152                 | 0.539795                  | -1.827999                 |
| 14            | 6             | 0           | 0.324033                  | 1.725145                  | -0.706936                 |
| 15            | 8             | 0           | -0.582890                 | 1.286723                  | -1.727617                 |
| 16            | 6             | 0           | 1.136452                  | -1.299946                 | -0.248878                 |
| 17            | 6             | 0           | 1.054632                  | -0.583286                 | 0.940619                  |
| 18            | 6             | 0           | 2.469993                  | -0.129229                 | 1.289577                  |
| 19            | 1             | 0           | 0.421390                  | -0.879015                 | 1.769976                  |
| 20            | 6             | 0           | 2.495822                  | -1.123292                 | -0.795574                 |
| 21            | 8             | 0           | 2.953006                  | -1.518676                 | -1.837289                 |
| 22 | 8  | 0  | 3.250224 | -0.462129 | 0.110640 |
| 23 | 6  | 0  | 0.166743 | 3.223899  | -0.504285 |
| 24 | 1  | 0  | 0.861957 | 3.560951  | 0.268362  |
| 25 | 1  | 0  | 0.391742 | 3.735857  | -1.441488 |
| 26 | 1  | 0  | -0.851809| 3.462891  | -0.192349 |
| 27 | 8  | 0  | 1.586331 | 1.418650  | -1.213987 |
| 28 | 1  | 0  | 2.245554 | 1.773399  | -0.599876 |
| 29 | 6  | 0  | -2.369934| -2.484737 | -1.092235 |
| 30 | 1  | 0  | -2.236407| -2.474209 | -2.174807 |
| 31 | 1  | 0  | -2.624849| -3.501759 | -0.773436 |
| 32 | 1  | 0  | -3.225751| -1.853112 | -0.829045 |
| 33 | 6  | 0  | -4.766665| -0.217891 | 2.109956  |
| 34 | 1  | 0  | -5.516447| 0.576823  | 2.176386  |
| 35 | 1  | 0  | -5.310892| -1.140277 | 1.882685  |
| 36 | 1  | 0  | -4.287197| -0.328137 | 3.084589  |
| 37 | 6  | 0  | 3.057485 | -0.878737 | 2.467095  |
| 38 | 1  | 0  | 4.099893 | -0.580352 | 2.604782  |
| 39 | 1  | 0  | 2.490984 | -0.642627 | 3.369389  |
| 40 | 1  | 0  | 3.017180 | -1.953853 | 2.286629  |
| 41 | 8  | 0  | 2.522969 | 1.253311  | 1.466376  |
| 42 | 1  | 0  | 3.365715 | 1.487037  | 1.878846  |
Structure for 3b

| Center Number | Atomic Number | Atomic Type | Coordinates (Angstroms) |
|---------------|---------------|-------------|-------------------------|
|               |               |             | X           | Y           | Z           |
| 1             | 6             | 0           | 0.391688    | -0.369921   | -0.012026   |
| 2             | 6             | 0           | -0.708362   | -1.131312   | -0.031929   |
| 3             | 6             | 0           | -1.952141   | -0.282238   | -0.037791   |
| 4             | 1             | 0           | -0.762440   | -2.214706   | -0.043272   |
| 5             | 6             | 0           | 1.784803    | -0.799366   | 0.004154    |
| 6             | 1             | 0           | 1.931830    | -1.879032   | 0.006914    |
| 7             | 6             | 0           | 2.849695    | 0.012000    | 0.017400    |
| 8             | 1             | 0           | 2.700884    | 1.088868    | 0.014197    |
| 9             | 6             | 0           | 4.262214    | -0.476648   | 0.036685    |
| 10            | 1             | 0           | 4.812047    | -0.104053   | -0.835711   |
| 11            | 1             | 0           | 4.788854    | -0.101442   | 0.922182    |
| 12            | 1             | 0           | 4.311312    | -1.569348   | 0.039112    |
| 13            | 8             | 0           | -1.426581   | 1.069329    | -0.033945   |
| 14            | 6             | 0           | -0.075367   | 1.051043    | -0.007615   |
| 15            | 8             | 0           | 0.569246    | 2.071514    | 0.017564    |
| 16            | 8             | 0           | -2.742024   | -0.461255   | -1.167824   |
| 17            | 1             | 0           | -2.167805   | -0.429284   | -1.952890   |
| 18            | 6             | 0           | -2.831789   | -0.457979   | 1.181283    |
| 19            | 1             | 0           | -3.669326   | 0.242534    | 1.123671    |
| 20            | 1             | 0           | -3.218460   | -1.479636   | 1.209287    |
| 21            | 1             | 0           | -2.256478   | -0.264075   | 2.089182    |
Structure for TS_{exo}

![Structure diagram]

Imaginary frequency: -394.9802 cm\(^{-1}\)

| Center Number | Atomic Number | Atomic Type | X         | Y         | Z         |
|---------------|---------------|-------------|-----------|-----------|-----------|
| 1             | 6             | 0           | 1.201026  | 0.523337  | 0.863555  |
| 2             | 6             | 0           | 0.504192  | 1.623952  | 1.423021  |
| 3             | 6             | 0           | -0.770231 | 1.515426  | 1.867905  |
| 4             | 6             | 0           | 0.770867  | 1.514391  | -1.868040 |
| 5             | 6             | 0           | -0.503608 | 1.623553  | -1.423417 |
| 6             | 6             | 0           | 0.708891  | -0.771095 | 0.674824  |
| 7             | 1             | 0           | 0.989944  | 2.596349  | 1.393200  |
| 8             | 1             | 0           | 1.220415  | 0.526828  | -1.953415 |
| 9             | 1             | 0           | -0.988941 | 2.596166  | -1.393816 |
| 10            | 1             | 0           | 0.059254  | -1.221752 | 1.415662  |
| 11            | 1             | 0           | -1.220175 | 0.528073  | 1.953598  |
| 12            | 6             | 0           | 2.572609  | 0.586932  | 0.347926  |
| 13            | 8             | 0           | 3.342720  | 1.518537  | 0.319088  |
| 14            | 6             | 0           | 1.903649  | -1.620452 | 0.228570  |
| 15            | 8             | 0           | 2.931532  | -0.642978 | -0.093889 |
| 16            | 6             | 0           | -1.200931 | 0.523339  | -0.863815 |
| 17            | 6             | 0           | -0.709227 | -0.771202 | -0.674723 |
| 18            | 6             | 0           | -1.904247 | -1.620055 | -0.228261 |
| 19            | 1             | 0           | -0.059772 | -1.222316 | -1.415436 |
| 20            | 6             | 0           | -2.572457 | 0.587549  | -0.348095 |
| 21            | 8             | 0           | -3.342249 | 1.519422  | -0.319404 |
|   |   |   |          |          |          |
|---|---|---|----------|----------|----------|
|22 | 8 | 0 | -2.931760 | -0.642134 | 0.094067 |
|23 | 6 | 0 | -2.427210 | -2.493059 | -1.353048 |
|24 | 1 | 0 | -1.665722 | -3.226777 | -1.623402 |
|25 | 1 | 0 | -3.330190 | -3.012320 | -1.022017 |
|26 | 1 | 0 | -2.667224 | -1.883794 | -2.225816 |
|27 | 6 | 0 | 2.426224  | -2.493458 | 1.353528  |
|28 | 1 | 0 | 1.664317  | -3.226611 | 1.624230  |
|29 | 1 | 0 | 3.328816  | -3.013415 | 1.022520  |
|30 | 1 | 0 | 2.666791  | -1.884090 | 2.226072  |
|31 | 8 | 0 | 1.630571  | -2.356368 | -0.915764 |
|32 | 1 | 0 | 2.350205  | -2.983615 | -1.067527 |
|33 | 8 | 0 | -1.631400 | -2.355920 | 0.916175  |
|34 | 1 | 0 | -2.351336 | -2.982757 | 1.068190  |
|35 | 6 | 0 | 1.596244  | 2.664405  | -2.328472 |
|36 | 1 | 0 | 2.504063  | 2.741258  | -1.717671 |
|37 | 1 | 0 | 1.929415  | 2.515176  | -3.360417 |
|38 | 1 | 0 | 1.047589  | 3.605337  | -2.263004 |
|39 | 6 | 0 | -1.595063 | 2.665938  | 2.328080  |
|40 | 1 | 0 | -2.502647 | 2.743287  | 1.716988  |
|41 | 1 | 0 | -1.928639 | 2.516950  | 3.359927  |
|42 | 1 | 0 | -1.045837 | 3.606543  | 2.262711  |
Structure for TS$_{endo}$

![Diagram of a molecular structure]

Imaginary frequency: -437.6419 cm$^{-1}$

| Center Number | Atomic Number | Atomic Type | Coordinates (Angstroms) |
|---------------|---------------|-------------|-------------------------|
|               | 1             | 6           | 0        | 1.570975 | 0.020680 | 0.537543 |
|               | 2             | 6           | 0        | 2.681436 | 0.871720 | 0.162343 |
|               | 3             | 6           | 0        | 2.623684 | 2.210175 | 0.108915 |
|               | 4             | 6           | 0        | 1.231568 | -0.716476 | -2.028356 |
|               | 5             | 6           | 0        | -0.057436 | -1.137579 | -1.878688 |
|               | 6             | 6           | 0        | 0.300251  | 0.387335  | 0.984627  |
|               | 7             | 1           | 0        | 3.603220  | 0.360321  | -0.108012 |
|               | 8             | 1           | 0        | 1.442673  | 0.344667  | -1.949445 |
|               | 9             | 1           | 0        | -0.336300 | -2.158529 | -2.127563 |
|               | 10            | 1           | 0        | 0.131608  | 1.359956  | 1.433660  |
|               | 11            | 1           | 0        | 1.699226  | 2.713103  | 0.389775  |
|               | 12            | 6           | 0        | 1.726434  | -1.419752 | 0.753715  |
|               | 13            | 8           | 0        | 2.684720  | -2.133984 | 0.569564  |
|               | 14            | 6           | 0        | -0.254683 | -0.829344 | 1.738739  |
|               | 15            | 8           | 0        | 0.579851  | -1.910738 | 1.300240  |
|               | 16            | 6           | 0        | -1.027559 | -0.315128 | -1.283568 |
|               | 17            | 6           | 0        | -0.823081 | 0.863609  | -0.574251 |
|               | 18            | 6           | 0        | -2.198348 | 1.361485  | -0.129593 |
|               | 19            | 1           | 0        | -0.101415 | 1.619618  | -0.875616 |
|               | 20            | 6           | 0        | -2.439390 | -0.711711 | -1.118009 |
|               | 21            | 8           | 0        | -3.001786 | -1.701274 | -1.511614 |
| 22 | 8 | 0 | -3.097440 | 0.272611 | -0.467008 |
| 23 | 6 | 0 | -0.088901 | -0.648479 | 3.239147 |
| 24 | 1 | 0 | -0.724227 | 0.172838 | 3.579281 |
| 25 | 1 | 0 | -0.388061 | -1.569212 | 3.743007 |
| 26 | 1 | 0 | 0.949566 | -0.417403 | 3.483955 |
| 27 | 8 | 0 | -1.551805 | -1.234157 | 1.423819 |
| 28 | 1 | 0 | -2.160750 | -0.563051 | 1.766752 |
| 29 | 6 | 0 | 2.339398 | -1.585093 | -2.509554 |
| 30 | 1 | 0 | 2.058752 | -2.639332 | -2.501816 |
| 31 | 1 | 0 | 2.619754 | -1.300676 | -3.530116 |
| 32 | 1 | 0 | 3.229323 | -1.451176 | -1.888157 |
| 33 | 6 | 0 | 3.763793 | 3.085730 | -0.297751 |
| 34 | 1 | 0 | 3.494069 | 3.698960 | -1.163524 |
| 35 | 1 | 0 | 4.023661 | 3.779811 | 0.507755 |
| 36 | 1 | 0 | 4.647898 | 2.497486 | -0.550315 |
| 37 | 6 | 0 | -2.651964 | 2.595212 | -0.880632 |
| 38 | 1 | 0 | -3.675944 | 2.843635 | -0.590270 |
| 39 | 1 | 0 | -1.994176 | 3.431768 | -0.639178 |
| 40 | 1 | 0 | -2.622655 | 2.412079 | -1.955725 |
| 41 | 8 | 0 | -2.242104 | 1.538189 | 1.252970 |
| 42 | 1 | 0 | -3.044763 | 2.025657 | 1.484012 |
Structure for PD

![Structure of PD](image)

| Center Number | Atomic Number | Atomic Type | Coordinates (Angstroms) |
|---------------|---------------|-------------|-------------------------|
| Center Number | Atomic Number | Atomic Type | X           | Y           | Z           |
| 1             | 6             | 0           | 1.350032    | -0.375947   | 0.020502    |
| 2             | 6             | 0           | 1.426013    | -1.550859   | -0.928124   |
| 3             | 6             | 0           | 0.483500    | -1.946668   | -1.778414   |
| 4             | 6             | 0           | 1.156111    | -0.892710   | 1.496801    |
| 5             | 6             | 0           | -0.274401   | -1.343027   | 1.636899    |
| 6             | 6             | 0           | 0.335165    | 0.743781    | -0.342415   |
| 7             | 1             | 0           | 2.352941    | -2.116951   | -0.862227   |
| 8             | 1             | 0           | 1.303777    | -0.030265   | 2.157091    |
| 9             | 1             | 0           | -0.495734   | -2.269007   | 2.161905    |
| 10            | 1             | 0           | 0.209932    | 0.739925    | -1.426889   |
| 11            | 1             | 0           | -0.448035   | -1.392350   | -1.850929   |
| 12            | 6             | 0           | 2.678528    | 0.369291    | -0.081822   |
| 13            | 8             | 0           | 3.784067    | -0.102339   | -0.098726   |
| 14            | 6             | 0           | 1.098073    | 2.038654    | 0.013071    |
| 15            | 8             | 0           | 2.486619    | 1.692427    | -0.199439   |
| 16            | 6             | 0           | -1.244555   | -0.621569   | 1.089226    |
| 17            | 6             | 0           | -1.039610   | 0.655384    | 0.340303    |
| 18            | 6             | 0           | -2.315341   | 0.728305    | -0.531108   |
| 19            | 1             | 0           | -1.124248   | 1.473389    | 1.061976    |
| 20            | 6             | 0           | -2.684793   | -0.934242   | 1.057215    |
| 21            | 8             | 0           | -3.303749   | -1.784453   | 1.644163    |
| 22 | 8 | 0 | -3.289104 | -0.056269 | 0.227519 |
| 23 | 6 | 0 | -2.908475 | 2.102025 | -0.726360 |
| 24 | 1 | 0 | -2.230374 | 2.703970 | -1.33125 |
| 25 | 1 | 0 | -3.864391 | 2.017015 | -1.249604 |
| 26 | 1 | 0 | -3.069522 | 2.592059 | 0.234386 |
| 27 | 6 | 0 | 0.786220 | 3.238065 | -0.847823 |
| 28 | 1 | 0 | -0.250731 | 3.535649 | -0.683985 |
| 29 | 1 | 0 | 1.437457 | 4.070736 | -0.569367 |
| 30 | 1 | 0 | 0.936026 | 3.003803 | -1.902176 |
| 31 | 8 | 0 | 0.935314 | 2.311967 | 1.373731 |
| 32 | 1 | 0 | 1.352431 | 3.159685 | 1.577754 |
| 33 | 8 | 0 | -2.091643 | 0.075826 | -1.738802 |
| 34 | 1 | 0 | -2.867847 | 0.179343 | -2.305920 |
| 35 | 6 | 0 | 2.124874 | -1.997025 | 1.912332 |
| 36 | 1 | 0 | 3.164258 | -1.694428 | 1.778992 |
| 37 | 1 | 0 | 1.971271 | -2.225318 | 2.969612 |
| 38 | 1 | 0 | 1.951877 | -2.912724 | 1.342741 |
| 39 | 6 | 0 | 0.621910 | -3.142492 | -2.670760 |
| 40 | 1 | 0 | -0.176642 | -3.864261 | -2.474479 |
| 41 | 1 | 0 | 0.533032 | -2.852544 | -3.722193 |
| 42 | 1 | 0 | 1.582998 | -3.640797 | -2.528257 |
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Paracaseolide A Biosynthesis, Wang and Hoye

Supplementary Information

Page S47 of S85
Paracaseolide A Biosynthesis, Wang and Hoye

Supplementary Information

Page S48 of S85
(±)-1a paracaseolide A
(±)-1a paracaseolide A
\((\pm)-S3\) 5-epi-paracaseolide A
TBSO

S5

ppm 200 180 160 140 120 100 80 60 40 20 0
Paracaseolide A Biosynthesis, Wang and Hoye

Supplementary Information

Page S56 of S85
5b

TBS

ppm 200 180 160 140 120 100 80 60 40 20 0
$E$-$6b : Z$-$6b$

$= 6 : 1$
$E-6b : Z-6b$

$= 6 : 1$
Paracaseolide A Biosynthesis, Wang and Hoye

3b

Supplementary Information

Page S62 of S85
Paracaseolide A Biosynthesis, Wang and Hoye

Supplementary Information

Page S65 of S85
Paracaseolide A Biosynthesis, Wang and Hoye

Supplementary Information

Page S66 of S85

bis(2-ethylhexyl) phthalate (DEHP) + CO₂TBS + CO₂TBS

1 : 3.6 : 0.66

t = 0
bis(2-ethylhexyl) phthalate (DEHP) + \[
\text{\begin{align*}
&\text{\ce{\text{Me} =C= C= C= C=O}} \quad \text{CO}_2\text{TBS} \\
&\text{\ce{\text{Me} =C= C= C= C=O}} \quad \text{CO}_2\text{TBS}
\end{align*}}
\]

\[
1 : 0.35 : 0.43 : 1.6
\]

\(t = 10\) days

(at 35 °C, neat, O\(_2\)-free)
Paracaseolide A Biosynthesis, Wang and Hoye

Supplementary Information

bis(2-ethylhexyl) phthalate (DEHP) + \( \text{CO}_2\text{TBS} \) + \( \text{CO}_2\text{TBS} \) + \( \text{CO}_2\text{TBS} \)

\( A \) + \( B \) + \( C \) + \( D \)

A, B, C, D

B + C (B:C = 5.5:1)

B + C (B:C = 1:1.2)

A, A, D

A, A, D, D

A, A, D, D

A, A, D

t = 0

t = 10 days
(at 35 °C, neat, O\(_2\)-free)
Paracaseolide A Biosynthesis, Wang and Hoye

Supplementary Information

Page S69 of S85

bis(2-ethylhexyl) phthalate (DEHP) + \( \text{A} \) + \( \text{B} \) + \( \text{C} \) + \( \text{D} \)

\( t = 0 \)

\( t = 10 \) days

(at 35 °C, neat, O\(_2\)-free)
$7b-h$
Paracaseolide A Biosynthesis, Wang and Hoye

Supplementary Information

Page S72 of S85

\[
\begin{align*}
\text{7b-h} \\
\text{CO}_2\text{H} & \quad \text{H} \\
\text{HO} & \quad \text{O} \\
\text{O} & \quad \text{O} \\
\text{H} & \quad \text{7b-h}
\end{align*}
\]
Paracaseolide A Biosynthesis, Wang and Hoye

Supplementary Information

Page S73 of S85
NMR spectrum of crude product mixture

Paracaseolide A Biosynthesis, Wang and Hoye
Supplementary Information
Page S75 of S85
(±)-1b
Paracaseolide A Biosynthesis, Wang and Hoye

Supplementary Information

Page S82 of S85

7a-h
(±)-1a

Paracaseolide A Biosynthesis, Wang and Hoye

Supplementary Information