SUPPORTING INFORMATION

11-Step Total Synthesis of Pallambins C and D

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Experimental Procedures and Characterization Data

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General Experimental. All reactions were carried out under an inert argon atmosphere with dry solvents under anhydrous conditions unless otherwise stated. Dry acetonitrile (MeCN), dichloromethane (DCM), diethyl ether (Et₂O), tetrahydrofuran (THF), toluene (PhMe) and triethylamine (Et₃N) were obtained by passing the previously degassed solvents through activated alumina columns. Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Yields refer to chromatographically and spectroscopically (¹H NMR) homogeneous material, unless otherwise stated. Reactions were monitored by thin layer chromatography (TLC) carried out on 0.25 mm E. Merck silica plates (60F-254), using UV light as the visualizing agent and an acidic solution of p-anisaldehyde and heat, or KMnO₄ and heat as developing agents. Flash silica gel chromatography was performed using E. Merck silica gel (60, particle size 0.043–0.063 mm), flash alumina chromatography was performed using Brockmann Grade 1 aluminum oxide (activated, basic, 58 Å, 60 mesh powder. NMR spectra were recorded on Bruker DRX-600 and AMX-400 instruments and were calibrated using residual undeuterated solvent as an internal reference (CDCl₃ ¹H NMR = 7.26 ppm, ¹³C NMR = 77.16 ppm; C₆D₆ ¹H NMR = 7.16 ppm, ¹³C NMR = 128.06 ppm). The following abbreviations were used to explain NMR peak multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. High-resolution mass spectra (HRMS) were recorded on an Agilent LC/MSD TOF mass spectrometer by electrospray ionization time-of-flight (ESI-TOF) reflectron experiments. The UCSD small molecule X-ray facility collected and analyzed all X-ray diffraction data.
General procedure for addition of dimethyl malonate to vinyl ethers by using I₂

SnCl₄ solution (1.0 M in heptane, 0.4 mL) was slowly added to a mixture of dimethyl malonate (0.4 mmol) and 1,8-diazabicyclo-[5.4.0]undec-7-ene (DBU) (0.4 mmol) in DCM (0.9 mL) at room temperature. The mixture was stirred for 10 min. Then vinyl ether (0.2 mmol in 0.1 mL DCM) and I₂ (0.2 mmol) were added successively. After the indicated time, the reaction was quenched by the addition of sat. Na₂S₂O₃ (2 mL) and 1M HCl (2 mL). The aqueous phase was extracted with EtOAc (2 mL × 3), and the combined organic phase was dried over Na₂SO₄, and concentrated in vacuo. The crude was purified via PTLC to yield the desired product.

General procedure for addition of dimethyl ethylmalonate to vinyl ethers using I₂

SnCl₄ solution (1.0 M in heptane, 0.4 mL) was slowly added to a mixture of dimethyl ethylmalonate (0.4 mmol) and DBU (0.4 mmol) in DCE (0.9 mL) at room temperature. The mixture was stirred for 10 min at 45 °C. Then vinyl ether (0.2 mmol in 0.1 mL DCE) and I₂ (0.2 mmol) were added successively at this temperature. After the indicated time, the reaction was quenched by the addition of sat. Na₂S₂O₃ (2 mL) and 1M HCl (2 mL) at room temperature. The aqueous phase was extracted with EtOAc (2 mL × 3), and the combined organic phase was dried over Na₂SO₄, and concentrated in vacuo. The crude was purified via PTLC to yield the desired product.
Figure S1. General operation process for the addition of malonate to vinyl ether in the presence of iodine

1. **Step 1**: Place DBU in a test tube
2. **Step 2**: Add solvent, malonate, and SnCl₄ solution
3. **Step 3**: Stirring for 10 minutes
4. **Step 4**: Add vinyl ether and I₂
5. **Step 5**: Stirring for indicated time
dimethyl 2-((2S,3R)-3-iodotetrahydro-2H-pyran-2-yl)malonate (16)

Yield: 92%
Physical state: colorless oil;
TLC: Rf = 0.28 (20% EtOAc in hexanes);

$^1$H NMR (600 MHz, CDCl$_3$) δ 4.38 (ddd, J = 12.0, 10.3, 4.4 Hz, 1H), 4.17 – 4.10 (m, 3H), 3.78 (s, 3H), 3.77 (s, 3H), 3.57 (td, J = 12.0, 2.3 Hz, 1H), 2.58 (d, J = 13.6 Hz, 1H), 2.28 – 2.15 (m, 1H), 1.87 – 1.76 (m, 1H), 1.51 – 1.47 (m, 1H);

$^{13}$C NMR (151 MHz, CDCl$_3$) δ 168.4, 167.0, 81.0, 69.3, 56.0, 52.9, 52.7, 38.3, 29.4, 28.6;

HRMS (m/z): calcd for C$_{10}$H$_{15}$I0$_5$ [M+H]$^+$ 343.0042, found 343.0050.

dimethyl 2-ethyl-2-((2S,3R)-3-iodotetrahydro-2H-pyran-2-yl) malonate (17)

Yield: 76%
Physical state: colorless oil;
TLC: Rf = 0.41 (20% EtOAc in hexanes);

$^1$H NMR (600 MHz, CDCl$_3$) δ 4.36 (ddd, J = 10.9, 9.2, 4.0 Hz, 1H), 4.19 (d, J = 9.2 Hz, 1H), 4.14 – 4.07 (m, 1H), 3.77 (s, 3H), 3.76 (s, 3H), 3.53 (td, J = 11.5, 3.0 Hz, 1H), 2.56 – 2.48 (m, 1H), 2.28 – 2.17 (m, 2H), 2.03 – 1.94 (m, 1H), 1.83 – 1.72 (m, 1H), 1.54 – 1.47 (m, 1H), 0.98 (t, J = 7.4 Hz, 3H);

$^{13}$C NMR (151 MHz, CDCl$_3$) δ 169.9, 169.8, 84.6, 69.0, 63.2, 52.5 (2C), 38.8, 28.8, 27.3, 26.0, 10.1;

HRMS (m/z): calcd for C$_{12}$H$_{19}$I0$_5$ [M+H]$^+$ 371.0355, found 371.0352.

methyl (S)-2-((2S,3R)-3-iodotetrahydro-2H-pyran-2-yl)-3-oxo-butanoate (18)
Yield: 52% (dr=1:1)

Physical state: colorless oil;

TLC: Rf= 0.41 (20% EtOAc in hexanes);

$^1$H NMR (600 MHz, CDCl$_3$) δ 4.40 (ddd, J = 12.0, 10.3, 4.3 Hz, 0.5H), 4.21 (dd, J = 10.3, 3.7 Hz, 0.5H), 4.17 – 4.06 (m, 4H), 4.00 (d, J = 3.7 Hz, 1H), 3.78 (s, 1.5H), 3.77 (s, 1.5H), 3.59 – 3.50 (m, 1H), 2.58 (t, J = 16.0 Hz, 1H), 2.27 (s, 1.5H), 2.26 (s, 1.5H), 2.26 – 2.15 (m, 1H), 1.86 – 1.71 (m, 1H), 1.53-1.45 (m, 1H);

$^{13}$C NMR (151 MHz, CDCl$_3$) δ 201.9, 201.4, 169.2, 167.2, 81.4, 80.6, 69.3, 69.1, 63.0 (2C), 52.8, 52.5, 38.3, 38.2, 30.6, 29.4, 29.3 (2C), 29.2, 28.5;

HRMS (m/z): calcd for C$_{10}$H$_{15}$IO$_4$ [M+H]$^+$ 327.0093, found 327.0099.

**dimethyl 2-((2S,3S,4S,5R,6R)-4,5-bis(benzyloxy)-6-((benzyloxy)methyl)-3-iodotetrahydro-2H-pyran-2-yl)malonate (19)**

Yield: 73%

Physical state: colorless oil;

TLC: Rf= 0.19 (20% EtOAc in hexanes);

$^1$H NMR (600 MHz, CDCl$_3$) δ 7.38 – 7.27 (m, 13H), 7.23 – 7.15 (m, 2H), 4.85 – 4.78 (m, 2H), 4.74 (d, J = 11.1 Hz, 1H), 4.65 (d, J = 11.4 Hz, 1H), 4.60 (d, J = 12.0 Hz, 1H), 4.51 (d, J = 11.3 Hz, 1H), 4.50 (d, J = 11.3 Hz, 1H), 4.46 (d, J = 12.0 Hz, 1H), 3.99 (d, J = 8.7 Hz, 1H), 3.92 (dt, J = 8.4, 4.3 Hz, 1H), 3.87 (t, J = 7.3 Hz, 1H), 3.76-3.67 (m, 2H), 3.73 (s, 4H), 3.69 (s, 4H), 3.13 (dd, J = 7.2, 3.5 Hz, 1H);
\[^{13}\text{C NMR}\] (151 MHz, CDCl\textsubscript{3}) ; \(\delta\) 167.4, 166.4, 138.4, 138.1, 137.3, 128.6 (2C), 128.5 (2C), 128.4 (4C), 128.2, 128.1 (2C), 127.9, 127.8 (2C), 127.7, 77.4, 76.1, 75.2, 74.9, 74.3, 73.5, 71.8, 68.8, 53.5, 53.1, 53.0, 31.8;

HRMS (m/z): calcd for C\textsubscript{32}H\textsubscript{35}IO\textsubscript{8} [M+H]\textsuperscript{+} 675.1455, found 675.1465.

dimethyl 2-((2S,3\textit{R})-3-iodotetrahydrofuran-2-yl)malonate (20)

\begin{center}
\begin{tikzpicture}
\path[->,>={Latex[round]},thick] (0,0) .. controls (0.5,1) and (0.5,2) .. (0,3);
\path[->,>={Latex[round]},thick] (0,3) .. controls (0.5,4) and (0.5,5) .. (0,6);
\path[->,>={Latex[round]},thick] (0,6) .. controls (0.5,7) and (0.5,8) .. (0,9);
\path[->,>={Latex[round]},thick] (0,9) .. controls (0.5,10) and (0.5,11) .. (0,12);
\path[->,>={Latex[round]},thick] (0,12) .. controls (0.5,13) and (0.5,14) .. (0,15);
\path[->,>={Latex[round]},thick] (0,15) .. controls (0.5,16) and (0.5,17) .. (0,18);
\end{tikzpicture}
\end{center}

Yield: 89%

Physical state: colorless oil;

TLC: \(R_f= 0.25\) (20\% EtOAc in hexanes);

\[^1\text{H NMR}\] (600 MHz, CDCl\textsubscript{3}) \(\delta\) 4.81 (dd, \(J = 7.1, 5.1\) Hz, 1H), 4.38 (dt, \(J = 7.2, 5.0\) Hz, 1H), 4.04 – 3.93 (m, 2H), 3.78 (s, 6H), 3.54 (d, \(J = 7.1\) Hz, 1H), 2.48 (dq, \(J = 14.5, 7.3\) Hz, 1H), 2.32 (ddt, \(J = 13.7, 6.7, 5.0\) Hz, 1H);

\[^{13}\text{C NMR}\] (151 MHz, CDCl\textsubscript{3}) ; \(\delta\) 167.2, 166.9, 86.5, 67.9, 55.3, 53.0 (2C), 38.7, 20.5;

HRMS (m/z): calcd for C\textsubscript{9}H\textsubscript{13}IO\textsubscript{5} [M+H]\textsuperscript{+} 328.9886, found 328.9878.

dimethyl 2-ethyl-2-((2S,3\textit{R})-3-iodotetrahydrofuran-2-yl)malonate (21)

\begin{center}
\begin{tikzpicture}
\path[->,>={Latex[round]},thick] (0,0) .. controls (0.5,1) and (0.5,2) .. (0,3);
\path[->,>={Latex[round]},thick] (0,3) .. controls (0.5,4) and (0.5,5) .. (0,6);
\path[->,>={Latex[round]},thick] (0,6) .. controls (0.5,7) and (0.5,8) .. (0,9);
\path[->,>={Latex[round]},thick] (0,9) .. controls (0.5,10) and (0.5,11) .. (0,12);
\path[->,>={Latex[round]},thick] (0,12) .. controls (0.5,13) and (0.5,14) .. (0,15);
\path[->,>={Latex[round]},thick] (0,15) .. controls (0.5,16) and (0.5,17) .. (0,18);
\end{tikzpicture}
\end{center}

Yield: 80%

Physical state: colorless oil;

TLC: \(R_f= 0.43\) (20\% EtOAc in hexanes);

\[^1\text{H NMR}\] (600 MHz, CDCl\textsubscript{3}) \(\delta\) 4.91 (d, \(J = 3.1\) Hz, 1H), 4.70 – 4.64 (m, 1H), 4.02 (ddd, \(J = 8.9, 7.2, 2.0\) Hz, 1H), 3.96 (ddd, \(J = 10.3, 8.5, 5.1\) Hz, 1H), 3.76 (s, 3H), 3.74 (s, 3H), 2.26 (ddt, \(J = 14.0, 5.1, 2.0\) Hz, 1H), 2.18 – 2.10 (m, 1H), 2.10 – 1.94 (m, 2H), 0.93 (t, \(J = 7.5\) Hz, 3H);

\[^{13}\text{C NMR}\] (151 MHz, CDCl\textsubscript{3}) ; \(\delta\) 170.3, 169.9, 90.6, 67.9, 63.4, 52.7, 52.6, 39.8, 26.1, 23.5, 9.5;
dimethyl 2-(1-ethoxy-2-iodoethyl)malonate (22)

Yield: 77%
Physical state: colorless oil;
TLC: Rf= 0.38 (20% EtOAc in hexanes);

$^1$H NMR (600 MHz, CDCl$_3$) δ 3.76 (s, 3H), 3.75 (s, 3H), 3.79-3.73 (m, 2H), 3.69 (dd, $J = 9.0$, 7.0 Hz, 1H), 3.54 (ddd, $J = 11.1$, 2.6, 1.1 Hz, 1H), 3.52 – 3.47 (m, 1H), 3.44 (ddd, $J = 11.1$, 2.9, 1.3 Hz, 1H), 1.18 (t, $J = 7.0$ Hz, 3H);

$^{13}$C NMR (151 MHz, CDCl$_3$) ; δ 167.6, 167.4, 76.1, 66.3, 57.1, 52.9 (2C), 15.4, 8.4;

HRMS (m/z): calcd for C$_{11}$H$_{17}$I0$_5$ [M+H]$^+$ 357.0199, found 357.0204.

HRMS (m/z): calcd for C$_{9}$H$_{15}$I0$_5$ [M+H]$^+$ 331.0042, found 331.0035.
In this section the final synthetic route is depicted along with an in-depth look at some of the failed routes and thoughts that went into the evolution of our final strategy. For the purposes of contextualizing the current studies, we define a reaction step as one in which a substrate is converted to a product in a single reaction flask (irrespective of the number of transformations) without intermediate workup in a separate flask or purification. If the substrate leaves the flask, this must constitute the end of a step.

1. $\text{NMMe}_2 \xrightarrow{\text{MeO, Et, OMe}} \xrightarrow{\text{Ti(OPr)}_4, \text{TMDS}} \xrightarrow{\text{Bu}_4\text{NB}_{\text{r}, \text{aq KOH}}} \xrightarrow{\text{cat. CuBr•DMS, HMPA}} \xrightarrow{\text{HMPA (75%)}} \xrightarrow{\text{O}_2, \text{hv, MB}} \xrightarrow{\text{L.A., dr (C-8)}} \xrightarrow{\text{BF}_{3}\cdot\text{OEt}_{2}, \text{CH(OMe)}_3} \xrightarrow{\text{AcBr (57%)}} \xrightarrow{\text{AIBN, Bu}_3\text{SnH}} \xrightarrow{\text{LiHMDS, PhSeCl, H}_2\text{O}_2} \xrightarrow{\text{LiHMDS, MeCHO, Et}_3\text{N, MsCl}} (94\%, \text{one-pot})

pallidin C (3) and D (4)
Evolution of synthetic strategy to enone 6

1) Initial γ-arylation strategy

2) Alternative Robinson annulation strategy

3) Aldehyde construction via Claisen rearrangement and subsequent aromatization

4) Attempts to catalyze Claisen rearrangement

5) Attempts to capture aldehyde

6) Variation of Claisen reaction type

After many failed attempts at catalysis of the Claisen-rearrangement, and failure to capture the resulting aldehyde we examined variations of the traditional Claisen-rearrangement.

Use of Crabtree’s cat. to generate the (E)-olefin improved the yield of 5, but was abandoned due to the projected cost of the catalyst needed to supply a total synthesis of paliambins. Attempts to isomerize the (Z)-olefin to the (E)-olefin were unsuccessful.

Corey, E. J.; Watt, D. S. J. Am. Chem. Soc. 1973, 95, 2303.
Hyde, A. M.; Buchwald, S. L. Angew. Chem. Int. Ed. 2008, 47, 1771.

Castro, A. M. M. Chem. Rev. 2004, 104, 2939.
Rehbein, J.; Hiersemann, M. Synthesis 2013, 45, 1121.

Generation of this particular silyl ketene acetal proceeded in poor yield and was unrealistic in our hands. This instability hampered our efforts to explore the use of an Ireland–Claisen rearrangement.

Use of an orthoester in a Johnson-Claisen rearrangement consistently gave 20% isolated yield of the desired product despite optimization efforts. Although these particular conditions were unsuitable to supply material for our synthetic campaign it was ultimately this excersise that led us to the use of Eschenmoser–Claisen conditions.
Evolution of [3.2.1] bicycle construction and C8 diastereoselectivity

1) Initial exploration of [3.2.1] bicycle formation via β-keto ester

2) Treatment of furan with singlet oxygen

The use of singlet oxygen directly generated the reactive enal/one species thru oxidative scission of the furan heterocycle. This effectively reduced the step count of the synthesis by 1, but left much to be desired as removal of the unsightly ester would be non-trivial.

3) Mukaiyama aldol approach to [3.2.1] bicycle core

Although the net desired cyclization took place under Mukaiyama aldol conditions, we observed no selectivity at C8. An examination of various Lewis-acids, solvents and temperature combinations led to the discovery that TiCl₄ and BF₃•0Et₂ could promote selectivity at C8.

4) Order of addition and effect on diastereoselectivity
Evolution of C9–C11 reduction

1) Failed attempts at C9–C11 reduction

2) Application of Shenvi's conditions to model substrate

3) Application of Shenvi's conditions to complete system

Extensive attempts at optimization failed to yield the desired product in good yield. Our efforts were further hampered by an inability to track reaction progress by TLC or LC/MS. Purification of the crude reaction mixture was non-trivial, often leading to contaminated fractions. Alternative metal-centers (Co, Fe) were examined as candidates to carry out the desired transformation with no success.
Evolution of C9–C11 reduction continued

4) Utilization of SmI₂ to achieve reduction

Although SmI₂ was able to accomplish the desired reduction, the operationally challenging nature of the reaction along with competitive formation of various byproducts led to the abandonment of this approach.

ca. 30% yield desired product undesired diastereomer elimination product allylic alcohol

Dahlen, A.; Hilmersson, G. Tetrahedron Letters 2003, 44, 2661.

5) Derivatization of enal to further explore C9–C11 reduction leads to unexpected discovery

The enal was converted to an acetal in an effort to examine selectivity with an electronically different olefin. To our surprise this resulted in spontaneous cyclization forming ring C.

expected product observed product

6) Attempts to reduce tertiary ether

Although the desired reduction of the C-9 ether took place, we were unable to achieve selectivity leaving no functional handle for D-ring construction.

7) Halogen installation and subsequent reduction

During this reduction process the ketone is reduced to an alcohol first in presence of SmI₂ followed by reduction of the chloride.

Our initial studies utilized a tertiary chloride as these conditions were less susceptible to generation of undesired side products.
Evolution of \( \gamma \)-lactone construction

1) Envisioned epoxide opening and Mitsunobu strategy

2) Epoxide stability

3) Utilization of diol

4) Prevost conditions and radical cyclization (model substrate)

5) Prevost conditions and radical cyclization (pallamin system)

Mueller, A.; Jennings, M. P. Org. Lett. 2008, 10, 1649.

Wei, H.-X.; Willis, S.; Li, G. Syn. Comm. 1999, 29, 2959.

Clive, D. L. J.; Beaulieu, P. L. J. Chem. Soc., Chem. Commun. 1983, 307.
Evolution of γ-lactone construction continued:
6) Mukaiyama type ring closure

7) Sakurai type ring closure

8) Iodomalonation screening table

| Entry | Solvent | Condition       | Yield /% | Comment                                                  |
|-------|---------|-----------------|----------|----------------------------------------------------------|
| 1     | THF     | NaH             | 0        | byproduct A was obtained.                                |
| 2     | THF     | NaH, 15-crown-5 | 0        | byproduct A was obtained.                                |
| 3     | THF     | DBU             | 0        | byproduct A was obtained.                                |
| 4     | THF     | Et$_3$N         | 0        | byproduct A was obtained.                                |
| 5     | DCM     | Ti(PrO)$_4$     | 0        | byproduct B was obtained.                                |
| 6     | DCM     | TiCl$_4$, Et$_3$N | complex |                                                          |
| 7     | DCM     | TiCl$_4$, DBU   | complex  |                                                          |
| 8     | DCM     | Zn(OTf)$_2$, DBU | complex |                                                          |
| 9     | DCM     | SnCl$_4$, DBU   | 60       | vinyl ether (3 eq.), malonate (1 eq.)                    |
| 10    | DCM     | SnCl$_4$, DBU   | 78       |                                                          |
| 11    | THF     | SnCl$_4$, DBU   | complex  |                                                          |
| 12    | MeCN    | SnCl$_4$, DBU   | complex  |                                                          |
| 13    | PhMe    | SnCl$_4$, DBU   | 33       |                                                          |
| 14    | DCM     | SnCl$_4$, DBU   | 92       | vinyl ether (1 eq.), malonate (2 eq.)                    |
| 15    | DCM     | CeCl$_3$, DBU   | complex  |                                                          |
| 16    | DCM     | InCl$_3$, DBU   | complex  |                                                          |
| 17    | DCM     | AgOAc           | complex  |                                                          |
Experimental: A flame dried 1L flask equipped with stir bar under Ar atmosphere was charged with PhMe (255 mL), furfuryl alcohol (4.44 mL, 51.2 mmol) and 1,1-dimethoxy-\(N,N\)-dimethylpropan-1-amine (11.3 g, 76.8 mmol). The flask was fitted with a reflux condenser and the mixture was heated to 110 °C and stirred for 5 h. The reaction was cooled to room temperature and residual methanol was removed by rotatory evaporation (300 mbar at 40 °C). The PhMe solution was next degassed with Ar for 10 minutes at room temperature, then 1,1,3,3-tetramethyldisiloxane (TMDS) (18.1 mL, 102.4 mmol) was added followed by slow, careful addition of Ti(O\(i\)Pr)\(_4\) (22.7 mL, 76.8 mmol). The mixture was then heated to 50 °C and allowed to stir for 12 h. The reaction was cooled to room temperature and treated with 2.5 L of a 2:1 mixture of THF:1M HCl and allowed to stir (medium stirring intensity to avoid emulsion) for 1 hour. The aqueous layer was extracted with Et\(_2\)O (2 x 500 mL) then EtOAc (2 x 500 mL). The combined organic extracts were washed with sat. aq. NaHCO\(_3\) (300 mL), dried over Na\(_2\)SO\(_4\) and concentrated in vacuo. The crude product was purified via silica gel chromatography (3% EtOAc/97% hexanes) to yield 5.29 g (75% yield) of aldehyde 5.

Physical state: pale yellow oil;

TLC: \(R_f = 0.53\) (20% EtOAc in hexanes);

\(^1\)H and \(^{13}\)C NMR are known and in agreement with reported literature values.\(^1\)
Compound 6:

Experimental: A round bottom flask with stir bar was charged with PhMe (500 mL) aldehyde 5 (5.29 g, 38.3 mmol), tetrabutylammonium bromide (1.23 g, 3.83 mmol). The mixture was cooled to 0 °C with an ice water bath, 60% aqueous KOH solution (117 mL) was added followed by dropwise addition of ethyl vinyl ketone (5.75 mL, 57.5 mmol) in 55 mL of PhMe over 30 minutes. The mixture was then warmed to 25 °C and stirred until TLC analysis indicated complete formation of enone 6 (ca. 12 h). The organic phase was separated, extracted with Et₂O (100 mL x 3). The combined organic extracts were washed with 1M HCl (100 mL), dried over MgSO₄ and concentrated in vacuo. The crude was purified via silica gel chromatography (10% EtOAc/ 90% hexanes) to yield 5.32 g (68% yield) of enone 6.

Physical state: colorless oil;

TLC: Rf= 0.55 (20% EtOAc in hexanes);

¹H NMR (600 MHz, CDCl₃) δ 7.22 (d, J = 1.9 Hz, 1H), 6.70 – 6.64 (m, 1H), 6.23 (d, J = 1.9 Hz, 1H), 2.44 (ddd, J = 17.0, 7.2, 4.7 Hz, 1H), 2.37 (ddd, J = 17.0, 9.9, 4.7 Hz, 1H), 2.26 (s, 3H), 2.23 – 2.16 (m, 1H), 2.05 – 1.98 (m, 1H), 1.83 (d, J = 1.4 Hz, 3H), 1.44 (s, 3H);

¹³C NMR (151 MHz, CDCl₃) δ 199.8, 152.8, 147.2, 139.8, 133.8, 123.6, 110.5, 37.4, 35.9, 35.0, 28.1, 16.1, 14.1;

HRMS (m/z): calcd for C₁₃H₁₆O₂ [M+H]⁺ 205.1229, found 205.1233.
Compound 7:

![Chemical Structure]

**Experimental:** A flame dried flask under Ar with stir bar was charged with CuBr·DMS (380 mg, 1.84 mmol). The CuBr·DMS was gently dried under high vacuum with a heat gun, taking care to avoid decomposition. The flask was backfilled with Ar, THF (34 mL) was added and the mixture was cooled to −78 °C. Vinylmagnesium bromide (25.8 mL of a 1.0 M solution in THF) was added dropwise to give a cloudy yellow solution. HMPA (5.1 mL, 29.4 mmol) was added immediately and the solution was allowed to stir at −78 °C for 10 minutes. A premixed solution of enone 6 (1.5 g, 7.3 mmol) and TMSCl (3.7 mL, 29.4 mmol) in THF (14 mL) under Ar was added dropwise to the mixture at −78 °C giving an orange-yellow solution. The mixture was stirred at −78 °C for 1 h. The reaction vessel was removed from the cooling bath and the mixture was poured into 20 mL of a 9:1 mixture of sat. aq. NH₄Cl:conc. NH₄OH and 30 mL of Et₂O. The mixture was warmed to room temperature and allowed to stir for 30 minutes. The aqueous layer was extracted with EtOAc (20 mL × 3). The organic extracts were washed with 9:1 NH₄Cl/ NH₄OH solution until the aqueous phase was no longer blue. The organic layer was then washed with brine, dried over K₂CO₃ and concentrated *in vacuo*. The crude was purified via chromatography on silica gel (0% to 15% EtOAc in hexanes) to give silyl enol ether 7 (1.7 g) as a yellow oil in 75% yield.

**Physical State:** yellow oil;

**TLC:** Rf = 0.7 (20% EtOAc in hexanes):

**¹H NMR** (600 MHz, CDCl₃) δ 7.13 (d, J = 1.9 Hz, 1H), 6.11 (d, J = 1.9 Hz, 1H), 5.71 (ddd, J = 16.9, 10.0, 8.7 Hz, 1H), 5.09 (dd, J = 10.0, 2.1 Hz, 1H), 5.02 (dd, J = 17.0, 1.5 Hz, 1H), 2.78 (d, J = 8.7 Hz, 1H), 2.33 (s, 3H), 1.94 – 1.88 (m, 1H), 1.88 – 1.81 (m, 2H), 1.79 – 1.72 (m, 1H), 1.56 (s, 3H), 1.11 (s, 3H), 0.05 (s, 9H);

**¹³C NMR** (151 MHz, CDCl₃) δ 145.32, 143.60, 137.60, 137.47, 124.46, 115.61, 111.39, 110.44, 76.37, 76.16, 75.95, 53.03, 34.40, 29.56, 27.34, 26.09, 14.22, 13.45, -0.19;
HRMS (m/z): calcd for C\textsubscript{18}H\textsubscript{28}O\textsubscript{2}Si [M+H]\textsuperscript{+} 305.1937, found 305.1933.

**Compound 8:**

\[\text{O}_2, \text{h}, \text{methylene blue}\]
\[\text{DCM, } -10^\circ\text{C, 1 h then thiourea 25 }^\circ\text{C, 4 h}\]

**Experimental:** A large tube under Ar equipped with stir bar was charged with DCM (100 mL) and a trace amount of methylene blue so that the solution took on a light blue color. The mixture was cooled to –10 °C (methanol/ice bath) in a 1 L beaker and silyl enol ether 7 (1.5 g, 4.9 mmol) as a solution in DCM (1 mL) was added in one portion. The Ar balloon was replaced with an O\textsubscript{2} balloon and O\textsubscript{2} was continuously bubbled through the solution. The mixture was irradiated at –10 °C with a 150 watt halogen lamp for 1.5 h (lamp was placed ca. 20 cm away taking care to wipe away any condensation from the beaker exterior with acetone and lab tissue during irradiation). Once the reaction was judged to be complete by TLC (ca. 1 h) irradiation was ceased and the O\textsubscript{2} balloon was replaced with an Ar balloon. Ar was bubbled through the solution continuously for 5 minutes. The tube was removed from the –10 °C bath and thiourea (570 mg, 7.5 mmol) was added immediately. The tube was wrapped in aluminum foil and the solution was allowed to warm to 25 °C under Ar atmosphere and stirred for 4 h. The reaction was diluted with DCM (75 mL) and washed with H\textsubscript{2}O (3 x 25 mL). The aqueous layer was extracted with DCM (75 mL x 3) and the combined organic extracts were treated with activated charcoal (added until the solution becomes black) to remove any residual methylene blue. The black organic extract was dried over Na\textsubscript{2}SO\textsubscript{4} and the resulting black slurry was filtered through Celite® and concentrated \textit{in vacuo} to give 1.4 g of 8 as a yellow oil. The crude was taken forward through the next step without further purification.

**Compound 9:**
Experimental: A flame dried round bottom flask under Ar equipped with stir bar was charged with Et₂O (78 mL), and a solution of TiCl₄ (6.5 mL, 1.0 M in toluene). The solution was cooled to -78 °C, and crude 8 (1.4 g, 4.37 mmol) dissolved in Et₂O (10 mL) was added dropwise to the mixture at –78 °C. The reaction was allowed to stir at –78 °C for 1 h. The reaction was removed from the cooling bath, diluted with EtOAc (40 mL), treated with 1M HCl (10 mL) and allowed to warm to room temperature. The aqueous phase was extracted with EtOAc (50 mL × 3), the combined organic extracts were dried over Na₂SO₄, and concentrated in vacuo. The crude was purified via silica gel chromatography (20%-40% EtOAc in hexanes) to yield the desired [3.2.1] bicycle 9 (716 mg, 58%) over 2 steps. The orientation of the C8 alcohol was confirmed by X-ray crystallographic analysis (for coordinates, see attached CIF file “baran402”)

Physical state: white solid;

TLC: Rᵥ = 0.34 (40% EtOAc in hexanes);

¹H NMR (600 MHz, CDCl₃) δ 10.12 (d, J = 5.0 Hz, 1H), 6.18 (d, J = 5.0 Hz, 1H), 6.18 (d, J = 5.0 Hz, 1H), 5.28 (dd, J = 10.2, 1.9 Hz, 1H), 5.24 – 5.16 (m, 1H), 3.41 (bs, 1H), 2.68 (dd, J = 10.0, 2.0 Hz, 1H), 2.42 (dd, J = 18.3, 8.0 Hz, 1H), 2.25 (ddd, J = 18.3, 11.1, 9.7 Hz, 1H), 1.98 (ddd, J = 13.3, 11.1, 8.0 Hz, 1H), 1.65 – 1.56 (m, 1H), 1.42 (s, 3H), 1.17 (s, 3H), 1.07 (s, 3H);

¹³C NMR (151 MHz, CDCl₃) ; δ 211.4, 192.5, 177.3, 131.9, 124.5, 122.2, 79.1, 64.0, 58.8, 48.3, 36.3, 23.6, 22.0, 12.0;

HRMS (m/z): calcd for C₁₅H₂₀O₃ [M+H]⁺ 249.1485 found 249.1486.
X-ray crystal structure of 9 (for coordinates, see attached CIF file “baran402”)
Compound S1:

Experimental: A flame dried round bottom flask under Ar equipped with stir bar was charged with Et₂O (5.6 mL), and a solution of BF₃•OEt₂ (0.062 mL, 0.50 mmol). The solution was cooled to −78 °C, and crude 8 (106 mg, 0.33 mmol) dissolved in Et₂O (1 mL) was added dropwise to the mixture at −78 °C. The reaction was allowed to stir at −78 °C for 1 h. The reaction was removed from the cooling bath, diluted with EtOAc (5 mL), treated with 1M HCl (1 mL) and allowed to warm to room temperature. The aqueous phase was extracted with EtOAc (5 mL × 3), the combined organic extracts were dried over Na₂SO₄, and concentrated in vacuo. The crude was purified via silica gel chromatography (20%-40% EtOAc in hexanes) to yield S1 (37 mg, 45%) over 2 steps. The orientation of the C8 alcohol was confirmed by X-ray crystallographic analysis (for coordinates, see attached CIF file “baran384”)

Physical state: white solid;

TLC: Rf = 0.34 (40% EtOAc in hexanes);

¹H NMR (600 MHz, CDCl₃) δ 9.88 (d, J = 3.2 Hz, 1H), 6.30 (d, J = 3.2 Hz, 1H), 5.46 (dt, J = 16.6, 9.9 Hz, 1H), 5.27 (dd, J = 10.2, 1.8 Hz, 1H), 5.20 (d, J = 1.8 Hz, 1H), 4.66 (s, 1H), 2.60 (dd, J = 17.2, 12.3, 9.2 Hz, 1H), 2.36 (dd, J = 17.2, 7.2 Hz, 1H), 2.34 – 2.29 (m, 1H), 2.09 – 1.95 (m, 1H), 2.09 – 1.95 (m, 1H), 1.55 (ddd, J = 12.3, 9.2, 2.1 Hz, 1H), 1.40 (s, 3H), 1.17 (s, 3H), 1.01 (s, 3H);

¹³C NMR (151 MHz, CDCl₃) ; δ 210.7, 192.5, 181.7, 131.8, 121.8, 120.3, 81.6, 61.7, 58.7, 47.7, 36.4, 36.2, 23.9, 22.5, 13.4;

HRMS (m/z): calcd for C₁₅H₂₀O₃ [M+H]⁺ 249.1485 found 249.1488.

Compound 11:
**Experimental:** A flame dried culture tube equipped with stir bar under Ar was charged with anhydrous MgSO₄ (483 mg, 4.02 mmol), enal 9 (40 mg, 0.16 mmol) as a solution in DCM (3.2 mL) and trimethyl orthoformate (0.025 mL, 0.24 mmol). The mixture was cooled to 0 °C and BF₃·OEt₂ (0.025 mL, 0.18 mmol) was added dropwise. The reaction was stirred at 0 °C until TLC analysis indicated complete consumption of enal 9 (ca. 1 h). Freshly distilled acetyl bromide (0.012 mL, 0.16 mmol) was then added at 0 °C and the reaction was allowed to stir at 0 °C for 1 h. The reaction was then warmed to room temperature and stirred until judged complete by TLC analysis (ca. 3 h). The mixture was diluted with DCM (3 mL), filtered through Celite® and washed with sat. aq. NaHCO₃. The aqueous layer was extracted with Et₂O (4 x 5 mL), dried over Na₂SO₄ and concentrated in vacuo. The crude was purified via silica gel chromatography (10% EtOAc/90% hexanes) to yield 11 (32 mg, 57% yield). The structure of 11 was confirmed by X-ray crystallographic analysis (for coordinates, see attached CIF file “baran570_a”)

**Physical state:** colorless oil;

**TLC:** Rf = 0.34 (10% EtOAc in hexanes);

**¹H NMR (600 MHz, CDCl₃) δ:** 5.38 (dt, J = 16.6, 9.9 Hz, 1H), 5.21 (dd, J = 10.1, 1.8 Hz, 1H), 5.14 (dd, J = 16.6, 1.9 Hz, 1H), 5.04 (d, J = 4.7 Hz, 1H), 3.37 (s, 3H), 2.80 (dd, J = 14.9, 4.8 Hz, 1H), 2.76 (d, J = 14.8 Hz, 1H), 2.60 (ddd, J = 18.5, 11.5, 9.7 Hz, 1H), 2.33 (dd, J = 18.4, 8.1 Hz, 1H), 2.29 (dd, J = 9.7, 2.5 Hz, 1H), 2.16 (ddd, J = 14.4, 9.5, 2.5 Hz, 1H) 1.80 (ddd, J = 14.3, 11.5, 8.1 Hz, 1H), 1.48 (s, 3H), 1.01 (s, 3H), 0.98 (s, 3H);

**¹³C NMR (151 MHz, CDCl₃) δ:** 211.9, 132.6, 121.4, 104.0, 93.7, 80.9, 63.2, 55.8, 55.1, 51.6, 49.9, 35.8, 33.3, 23.8, 20.3, 13.7;

**HRMS (m/z):** calcd for C₁₆H₂₃BrO₃ [M+H]⁺ 343.0809 found 343.0806.
X-ray crystal structure of 11 (for coordinates, see attached CIF file “baran570_a”)
Compound 12:

Experimental: A culture tube equipped with stir bar under Ar was charged with 11 (32 mg, 0.09 mmol) in 0.450 mL PhMe (thoroughly degassed with Ar), Bu$_3$SnH (0.036 mL, 0.135 mmol) and AIBN (2 mg, 0.009 mmol). The mixture was heated to 110 °C and allowed to stir for 1 h. The mixture was cooled to room temperature and the solvent was removed in vacuo. The residue was purified via silica gel chromatography (residue loaded in PhMe, initially eluted with 0%EtOAc/100% hexanes, then 3%EtOAc-10% EtOAc in hexanes) to yield the desired dehalogenated tricycle 12 (21 mg, 90% yield).

Physical state: yellow oil;

TLC: R$_f$ = 0.35 (20% EtOAc in hexanes);

$^1$H NMR (600 MHz, C$_6$D$_6$) δ: 5.32 (dt, $J = 16.6, 10.1$ Hz, 1H), 5.00 (dd, $J = 10.2, 2.1$ Hz, 1H), 4.96 (dd, $J = 16.7, 2.2$ Hz, 1H), 4.82 (dd, $J = 5.9, 1.7$ Hz, 1H), 3.16 (s, 3H), 2.26 (dd, $J = 10.0, 2.0$ Hz, 1H), 2.20 (dd, $J = 17.9, 8.2$ Hz, 1H), 2.10 (ddd, $J = 18.0, 11.0, 9.6$ Hz, 1H), 2.05 – 1.99 (m, 2H), 1.98 – 1.90 (m, 1H), 1.47 (ddd, $J = 13.5, 11.0, 8.2$ Hz, 1H), 1.35 (s, 3H), 1.30 (s, 3H), 1.06 (ddd, $J = 13.4, 8.7, 1.8$ Hz, 1H), 0.65 (s, 3H);

$^{13}$C NMR (151 MHz, C$_6$D$_6$) δ: 210.5, 134.0, 119.9, 106.4, 92.7, 64.6, 59.5, 55.1, 54.6, 42.9, 36.8, 35.6, 34.5, 21.9, 21.8, 13.3

HRMS (m/z): calcd for C$_{16}$H$_{28}$O$_3$ [M+H]$^+$ 265.1725, found 265.1722.
Compound 13:

Experimental: A flame dried culture tube equipped with stir bar under Ar was charged with LiHMDS (0.1 mL, 1.0 M in THF, 0.1 mmol) followed by a solution of acetal 12 (13.2 mg, 0.05 mmol) in THF (0.1 mL). The solution was cooled to – 78 °C and stirred for 30 min. PhSeCl (19.2 mg, 0.1 mmol) in THF (0.1 mL) was added at this temperature. After 1 hour, the reaction was quenched by the addition of sat. NH₄Cl (50 μL). The mixture was concentrated in vacuo. DCM (0.5 mL) was added to the crude and the solution was cooled to 0 °C. H₂O₂ (0.25 mmol) was added at this temperature and the reaction was allowed to stir for 2 h at 0 °C. The reaction was quenched by the addition of sat. Na₂S₂O₃ and the aqueous phase was extracted with EtOAc (2 mL × 3). The combined organic phase was dried over Na₂SO₄, and concentrated in vacuo. The crude was purified via PTLC (10% EtOAc in hexanes, developed three times) to yield enone 13 (7.9 mg, 60%) in one-pot.

Physical state: white foam;

TLC: Rf = 0.44 (20% EtOAc/hexanes);

¹H NMR (600 MHz, CDCl₃); δ 6.72 (dd, J = 9.6, 2.1 Hz, 1H), 5.90 (d, J = 9.6 Hz, 1H), 5.62 – 5.54 (m, 1H), 5.19 – 5.12 (m, 2H), 5.09 (d, J = 5.4 Hz, 1H), 3.31 (s, 3H), 2.58 (dd, J = 9.3, 8.1 Hz, 1H), 2.43 (dd, J = 9.5, 2.0 Hz, 1H), 2.08 (dd, J = 13.5, 9.4 Hz, 1H), 1.91 (ddd, J = 13.4, 8.0, 5.3 Hz, 1H), 1.23 (s, 3H), 1.05 (s, 3H), 1.03 (s, 3H);

¹³C NMR (151 MHz, CDCl₃); δ 202.0, 157.3, 133.1, 127.1, 120.8, 107.0, 92.8, 63.8, 62.3, 54.8, 54.5, 46.4, 35.7, 25.5, 19.3, 13.1;

HRMS (m/z): calcd for C₁₆H₂₂O [M+H]⁺ 263.1647, found 263.1652.
**Compound 14:**

![Chemical Structure](image)

**Experimental:** A flame dried culture tube equipped with stir bar under Ar was charged with 13 (7.9 mg, 0.03 mmol) in PhCl (0.3 mL). Pyridine (9.7 μL, 0.12 mmol) and PPTS (30 mg, 0.12 mmol) were added to the solution of enone. The reaction mixture was stirred at 130 °C for 6 h. Once the reaction was determined to be complete by TLC analysis the solution was cooled to room temperature and the reaction was quenched by the addition of sat. NaHCO₃ (1 mL). The aqueous phase was extracted with EtOAc (2 mL × 3), the combined organic phase was dried over Na₂SO₄, and concentrated in vacuo. The crude was taken forward and used in next reaction sequence without further purification.
Compound 15:

**Experimental:** A flame dried culture tube equipped with stir bar under Ar was charged with dimethyl malonate (20 mg, 0.15 mmol) and DBU (23 μL, 0.15 mmol) in DCM (0.3 mL) at room temperature. A SnCl$_4$ solution (0.15 mL, 1.0 M in heptane, 0.15 mmol) was added dropwise and the mixture was stirred for 10 min at room temperature. Crude vinyl ether 14 in 0.5 mL DCM was added followed immediately by addition of I$_2$ (7.5 mg, 0.03 mmol). The reaction was stirred at room temperature for 1 hour. The reaction was quenched by the addition of sat. aq. Na$_2$S$_2$O$_3$ (2 mL) and 1M HCl (2 mL). The aqueous phase was extracted with EtOAc (2 mL × 3), the combined organic phase was dried over Na$_2$SO$_4$, and concentrated in vacuo. The crude was purified via PTLC (20 % EtOAc in hexanes) to yield 15 (9.9 mg, 87%) over 2 steps.

**Physical state:** colorless oil;

**TLC:** R$_f$ = 0.31 (20% EtOAc/hexanes);

$^1$H NMR: (600 MHz, CDCl$_3$); δ 6.73 (dd, $J = 9.6, 2.1$ Hz, 1H), 5.89 (d, $J = 9.6$ Hz, 1H), 5.54 (ddd, $J = 16.8, 10.3, 9.6$ Hz, 1H), 5.27 – 5.18 (m, 1H), 5.17 – 5.10 (m, 1H), 4.69 (dd, $J = 10.1, 3.2$ Hz, 1H), 4.25 (dd, $J = 10.1, 7.4$ Hz, 1H), 3.84 (d, $J = 3.3$ Hz, 1H), 3.80 (s, 3H), 3.78 (s, 3H), 2.82 (d, $J = 7.4$ Hz, 1H), 2.55 (dd, $J = 9.6, 2.1$ Hz, 1H), 1.28 (s, 3H), 1.18 (s, 3H), 0.96 (s, 3H);

$^{13}$C NMR: (151 MHz, CDCl$_3$); δ 200.8, 167.5, 166.7, 156.6, 132.3, 127.3, 121.6, 91.4, 83.2, 67.5, 62.4, 62.3, 52.9 (2C), 51.6, 46.7, 21.9, 20.3, 19.1, 12.4;

**HRMS (m/z):** calcd for C$_{20}$H$_{25}$IO$_6$ [M+H]$^+$ 489.0774, found 489.0768.
Pallambin C (3) and D (4):

**Experimental:** A culture tube was charged with a solution of **15** (2.0 mg, 0.004 mmol) in MeOH (0.12 mL). A 2.0 M NaOH aq. sol. (0.1 mL, 0.2 mmol) was added to the mixture and the reaction was stirred for 6 h. After the completion of hydrolysis, TMSCl (25 μL, 0.2 mmol) was added and the resulting mixture was concentrated *in vacuo*. The mixture was then subjected to azeotropic removal of H₂O with benzene (2 mL × 2). Next, MeCN (0.2 mL) and Et₃N (5.6 μL, 0.04 mmol) were added to the reaction flask and the mixture was heated to 60 °C and stirred for 12 h. Upon completion of decarboxylation and lactonization, the solvent was removed *in vacuo*. THF (0.2 mL) was added to the reaction vessel and the mixture was cooled to –78 °C. LiHMDS (100 μL, 0.1 M in THF) was added and the reaction mixture was allowed to stir for 30 min at this temperature. MeCHO (1.1 μL in 0.1 mL THF) was added and the reaction mixture was allowed to stir for 2 h. The aldol reaction was quenched by the addition of 0.1 M TMSCl solution in MeOH (100 μL). The organic residue was concentrated in vacuo. DCM (0.3 mL), Et₃N (17 μL, 0.12 mmol), DMAP (one crystal), and MsCl (1.5 μL, 0.02 mmol) were added to the reaction vessel successively. The reaction was stirred for 8 h and quenched by the addition of sat. aq. NH₄Cl (2 mL); the aq. phase was extracted with EtOAc (2 mL × 3), washed with sat. aq. NaHCO₃ and brine. The combined organic phase was dried over Na₂SO₄, and concentrated *in vacuo*. The crude was purified via PTLC (50% EtOAc in hexanes, developed twice) to afford pallambin C and D (1.2 mg, C:D=1:2, 94%) in one-pot.

**Pallambin C (3)**
pallamin C (3)

**Physical state:** colorless oil;

**TLC:** \( R_f = 0.35 \) (50% EtOAc/hexanes);

\(^1\)H NMR (600 MHz, CDCl\(_3\)); \( \delta \) 6.72 – 6.64 (m, 2H), 5.89 (d, \( J = 9.6 \) Hz, 1H), 5.54 (dt, \( J = 16.9, 9.8 \) Hz, 1H), 5.23 – 5.15 (m, 2H), 4.88 (dd, \( J = 6.8, 3.3 \) Hz, 1H), 4.84 (d, \( J = 3.2 \) Hz, 1H), 2.83 (dd, \( J = 9.5, 2.1 \) Hz, 1H), 2.53 (d, \( J = 6.8 \) Hz, 1H), 2.26 (d, \( J = 7.3 \) Hz, 3H), 1.42 (s, 2H), 1.14 (s, 2H), 1.04 (s, 2H);

\(^1\)H NMR (600 MHz, CDCl\(_3\)); \( \delta \) 201.6, 168.4, 157.1, 144.9, 132.6, 127.0, 126.0, 121.8, 94.2, 83.1, 82.3, 64.0, 62.8, 60.8, 47.0, 22.4, 19.7, 14.6, 12.9;

**HRMS (m/z):** calcd for C\(_{19}\)H\(_{22}\)O\(_4\) [M+H]\(^+\) 315.1596, found 315.1599.
Pallambin D (4)

Physical state: white solid;
mp 183.8-185.0 °C (lit.² mp 191 °C);
TLC: \( R_f = 0.35 \) (50% EtOAc/hexanes);

\(^1\)H NMR (600 MHz, CDCl₃)\( \delta \) 7.01 (qd, \( J = 7.2, 1.1 \) Hz, 1H), 6.69 (dd, \( J = 9.5, 2.2 \) Hz, 1H), 5.89 (d, \( J = 9.5 \) Hz, 1H), 5.53 (ddd, \( J = 16.9, 10.2, 9.5 \) Hz, 1H), 5.21 – 5.14 (m, 2H), 5.09 (dd, \( J = 3.6, 1.1 \) Hz, 1H), 4.90 (dd, \( J = 7.0, 3.5 \) Hz, 1H), 2.76 (dd, \( J = 9.6, 2.2 \) Hz, 1H), 2.56 (d, \( J = 7.0 \) Hz, 1H), 2.04 (d, \( J = 7.2 \) Hz, 3H), 1.42 (s, 3H), 1.16 (s, 3H), 1.01 (s, 3H);

\(^{13}\)C NMR (151 MHz, CDCl₃) ; \( \delta \) 201.6, 169.6, 157.1, 141.9, 132.4, 127.6, 126.9, 121.8, 94.5, 83.8, 77.8, 64.0, 62.8, 60.6, 47.0, 22.5, 19.8, 16.2, 12.9;

HRMS (m/z): calcd for C\(_{19}\)H\(_{22}\)O\(_4\) [M+H]\(^+\) 315.1596, found 315.1599.

Pallambin C \(^1\)H spectra comparison (3):
| H  | Natural\(^3\) (600M, CDCl\(_3\), solvent signal 7.28, δ ppm) | Literature\(^4\) (400M, CDCl\(_3\), solvent signal 7.26, δ ppm) | Synthetic (600M, CDCl\(_3\), solvent signal 7.26, δ ppm) |
|----|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|
| 1  | 6.69 (m)                                        | 6.68 (m)                                        | 6.68 (m)                                        |
| 2  | 5.89 (d, 9.6)                                   | 5.89 (d, 9.6)                                   | 5.89 (d, 9.6)                                   |
| 5  | 2.84 (dd, 9.9, 2.0)                             | 2.83 (dd, 9.5, 1.6)                             | 2.83 (dd, 9.5, 2.1)                             |
| 6  | 5.54 (dt, 17.0, 9.9)                            | 5.54 (dt, 16.9, 9.8)                            | 5.54 (dt, 16.9, 9.8)                            |
| 7  | 5.19 (2H, m)                                    | 5.18 (2H, m)                                    | 5.17 (2H, m)                                    |
| 9  | 2.54 (d, 6.7)                                   | 2.53 (d, 6.7)                                   | 2.53 (d, 6.8)                                   |
| 11 | 4.89 (dd, 6.8, 3.3)                             | 4.88 (dd, 6.7, 3.2)                             | 4.88 (dd, 6.8, 3.3)                             |
| 12 | 4.85 (d, 3.3)                                   | 4.84 (d, 3.2)                                   | 4.84 (d, 3.2)                                   |
| 14 | 6.69 (m)                                        | 6.67 (m)                                        | 6.68 (m)                                        |
| 15 | 2.26 (3H, d, 7.3)                               | 2.25 (3H, d, 7.3)                               | 2.26 (3H, d, 7.3)                               |
| 17 | 1.15 (3H, s)                                    | 1.14 (3H, s)                                    | 1.14 (3H, s)                                    |
| 18 | 1.04 (3H, s)                                    | 1.04 (3H, s)                                    | 1.04 (3H, s)                                    |
| 19 | 1.42 (3H, s)                                    | 1.42 (3H, s)                                    | 1.42 (3H, s)                                    |
Pallamin C $^{13}$C spectra comparison (3):

![Chemical Structure](image)

| C  | Natural$^3$ (150M, CDCl$_3$, solvent signal 77.00, δ ppm) | Literature$^4$ (100M, CDCl$_3$, solvent signal 77.16, δ ppm) | Synthetic (151M, CDCl$_3$, solvent signal 77.16, δ ppm) |
|----|----------------------------------------------------------|-----------------------------------------------------------|----------------------------------------------------------|
| 1  | 156.9                                                   | 157.1                                                     | 157.1                                                     |
| 2  | 126.8                                                   | 127.0                                                     | 127.0                                                     |
| 3  | 201.3                                                   | 201.6                                                     | 201.6                                                     |
| 4  | 62.6                                                    | 62.8                                                      | 62.8                                                      |
| 5  | 63.8                                                    | 64.0                                                      | 64.0                                                      |
| 6  | 132.2                                                   | 132.4                                                     | 132.3                                                     |
| 7  | 121.5                                                   | 121.8                                                     | 121.8                                                     |
| 8  | 94.0                                                    | 94.2                                                      | 94.2                                                      |
| 9  | 60.6                                                    | 60.8                                                      | 60.8                                                      |
| 10 | 46.8                                                    | 47.0                                                      | 47.0                                                      |
| 11 | 82.9                                                    | 83.1                                                      | 83.1                                                      |
| 12 | 82.1                                                    | 82.3                                                      | 82.3                                                      |
| 13 | 125.9                                                   | 126.1                                                     | 126.0                                                     |
| 14 | 144.6                                                   | 144.8                                                     | 144.9                                                     |
| 15 | 14.4                                                    | 14.6                                                      | 14.6                                                      |
| 16 | 168.1                                                   | 168.4                                                     | 168.4                                                     |
| 17 | 22.2                                                    | 22.4                                                      | 22.4                                                      |
| 18 | 12.7                                                    | 12.9                                                      | 12.9                                                      |
| 19 | 19.5                                                    | 19.7                                                      | 19.7                                                      |
Pallamin C (3)

Synthetic

Natural
Pallamin D $^1$H spectra comparison (4):

| H  | Natural\(^3\) (600M, CDCl\(_3\), solvent signal 7.28, $\delta$ ppm) | Literature\(^4\) (400M, CDCl\(_3\), solvent signal 7.26, $\delta$ ppm) | Synthetic (600M, CDCl\(_3\), solvent signal 7.26, $\delta$ ppm) |
|----|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|
| 1  | 6.70 (dd, 9.6, 2.1)                              | 6.69 (dd, 9.5, 1.9)                              | 6.69 (dd, 9.5, 2.2)                              |
| 2  | 5.91 (d, 9.6)                                    | 5.89 (d, 9.6)                                    | 5.89 (d, 9.6)                                    |
| 5  | 2.78 (dd, 9.9, 2.0)                              | 2.76 (dd, 9.4, 1.8)                              | 2.76 (dd, 9.3, 2.1)                              |
| 6  | 5.55 (dt, 16.9, 9.9)                             | 5.53 (dt, 16.9, 9.8)                             | 5.53 (dt, 16.9, 9.8)                             |
| 7  | 5.19 (2H, m)                                    | 5.17 (2H, m)                                    | 5.16 (m)                                        |
| 9  | 2.58 (d, 7.0)                                    | 2.56 (d, 7.0)                                    | 2.56 (d, 7.0)                                    |
| 11 | 4.92 (dd, 7.0, 3.6)                              | 4.90 (dd, 7.0, 3.6)                              | 4.90 (dd, 7.0, 3.5)                              |
| 12 | 5.11 (dd, 3.5, 0.8)                              | 5.09 (d, 3.2)                                    | 5.09 (d, 3.6)                                    |
| 14 | 7.07 (qd, 7.2, 0.8)                              | 7.00 (q, 7.3)                                    | 7.01 (q, 7.2)                                    |
| 15 | 2.06 (3H, d, 7.2)                                | 2.03 (3H, d, 7.2)                                | 2.04 (3H, d, 7.2)                                |
| 17 | 1.18 (3H, s)                                    | 1.16 (3H, s)                                    | 1.16 (3H, s)                                    |
| 18 | 1.03 (3H, s)                                    | 1.01 (3H, s)                                    | 1.01 (3H, s)                                    |
| 19 | 1.44 (3H, s)                                    | 1.42 (3H, s)                                    | 1.42 (3H, s)                                    |
Pallambin D $^{13}$C spectra comparison (4):

![Chemical Structure](image)

| C  | Natural$^3$ (150M, CDCl$_3$, solvent signal 77.00, δ ppm) | Literature$^4$ (100M, CDCl$_3$, solvent signal 77.16, δ ppm) | Synthetic (151M, CDCl$_3$, solvent signal 77.16, δ ppm) |
|----|---------------------------------------------------------|--------------------------------------------------------|----------------------------------------------------|
| 1  | 157.0                                                   | 157.1                                                  | 157.1                                              |
| 2  | 126.8                                                   | 127.0                                                  | 126.9                                              |
| 3  | 201.3                                                   | 201.6                                                  | 201.6                                              |
| 4  | 62.7                                                    | 62.8                                                   | 62.8                                               |
| 5  | 63.9                                                    | 64.0                                                   | 64.0                                               |
| 6  | 132.2                                                   | 132.4                                                  | 132.4                                              |
| 7  | 121.5                                                   | 121.7                                                  | 121.8                                              |
| 8  | 94.4                                                    | 94.5                                                   | 94.5                                               |
| 9  | 60.3                                                    | 60.6                                                   | 60.6                                               |
| 10 | 46.7                                                    | 47.0                                                   | 47.0                                               |
| 11 | 83.6                                                    | 83.8                                                   | 83.8                                               |
| 12 | 77.6                                                    | 77.8                                                   | 77.8                                               |
| 13 | 127.5                                                   | 127.7                                                  | 127.6                                              |
| 14 | 141.7                                                   | 141.9                                                  | 141.9                                              |
| 15 | 16.0                                                    | 16.2                                                   | 16.2                                               |
| 16 | 169.3                                                   | 169.5                                                  | 169.6                                              |
| 17 | 22.3                                                    | 22.5                                                   | 22.5                                               |
| 18 | 12.7                                                    | 12.8                                                   | 12.9                                               |
| 19 | 19.6                                                    | 19.8                                                   | 19.8                                               |
Pallamin D (4)

Synthetic

Natural
(in CDCl₃, 151 MHz)
20
(in CDCl$_3$, 151 MHz)
(in CDCl₃, 151 MHz)
22
(in CDCl₃, 151 MHz)
(in CDCl₃, 600 MHz)
(in CDCl₃, 600 MHz)
(in CDCl₃, 600 MHz)
(in CDCl₃, 151 MHz)
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